

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

**Form 20-F**

(Mark One)

- ☐ **REGISTRATION STATEMENT PURSUANT TO SECTION 12(b) OR (g) OF THE SECURITIES EXCHANGE ACT OF 1934**  
**OR**
- ☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**  
For the fiscal year ended December 31, 2017  
**OR**
- ☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**  
For the transition period from \_\_\_\_\_ to \_\_\_\_\_  
**OR**
- ☐ **SHELL COMPANY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**  
Date of event requiring this shell company report \_\_\_\_\_  
Commission file number 001-38067

**VERONA PHARMA PLC**

(EXACT NAME OF REGISTRANT AS SPECIFIED IN ITS CHARTER)

**Not Applicable**

(Translation of Registrant's Name into English)

**United Kingdom**

(Jurisdiction of incorporation or organization)

**3 More London Riverside  
London SE1 2RE  
United Kingdom**

(Address of principal executive offices)

**Jan-Anders Karlsson  
Chief Executive Officer  
Verona Pharma plc**

**3 More London Riverside  
London SE1 2RE  
United Kingdom**

**Tel: +44 303 283 4200**

(Name, Telephone, E-mail and/or Facsimile number and Address of Company Contact Person)

**Securities registered or to be registered pursuant to Section 12(b) of the Act.**

Title of each class

Name of each exchange on which registered

**American Depositary Shares,  
each representing 8 ordinary shares,  
nominal value £0.05 per share**

**The Nasdaq Stock Market LLC**

**Securities registered or to be registered pursuant to Section 12(g) of the Act. None**

**Securities for which there is a reporting obligation pursuant to Section 15(d) of the Act. None**

Indicate the number of outstanding shares of each of the issuer's classes of capital or common stock as of the close of the period covered by the annual report.

**Ordinary shares, nominal value £0.05 per share: 105,017,400 as of December 31, 2017**

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

If this report is an annual or transition report, indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934. ☐ Yes ☒ No

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

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

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

Large accelerated filer ☐ Accelerated filer ☐ Non-accelerated filer ☒ Emerging growth company ☒

If an emerging growth company that prepares its financial statements in accordance with U.S. GAAP, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards<sup>†</sup> provided pursuant to Section 13(a) of the Exchange Act. ☐

<sup>†</sup> The term “new or revised financial accounting standard” refers to any update issued by the Financial Accounting Standards Board to its Accounting Standards Codification after April 5, 2012.

Indicate by check mark which basis of accounting the registrant has used to prepare the financial statements included in this filing:

U.S. GAAP ☐ International Financial Reporting Standards as issued by the International Accounting Standards Board ☒ Other ☐

If “Other” has been checked in response to the previous question, indicate by check mark which financial statement item the registrant has elected to follow. ☐ Item 17 ☐ Item 18

If this is an Annual Report, indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). ☐ Yes ☒ No

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## GENERAL INFORMATION

All references in this Annual Report on Form 20-F, or the Annual Report, to “Verona,” the “company,” the “group”, “we,” “us” and “our” refer to Verona Pharma plc and its consolidated subsidiaries.

## PRESENTATION OF FINANCIAL AND OTHER DATA

We report under International Financial Reporting Standards as issued by the International Accounting Standards Board, or IFRS. None of the financial statements in this Annual Report were prepared in accordance with generally accepted accounting principles in the United States. We present our financial statements in pounds sterling and in accordance with IFRS. We have made rounding adjustments to some of the figures included in this Annual Report. Accordingly, numerical figures shown as totals in some tables may not be an arithmetic aggregation of the figures that preceded them. All references in this Annual Report to “\$,” “US\$,” and “U.S. dollars” mean U.S. dollars and all references to “£” and “GBP” mean pounds sterling, unless otherwise noted.

## CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report contains statements that constitute forward-looking statements. All statements other than statements of historical facts contained in this Annual Report, including statements regarding our future results of operations and financial position, business strategy, on-going clinical trials, product candidate development plans, product approvals, research and development costs, timing and likelihood of success, plans and objectives of management for future operations and future results of anticipated products, are forward-looking statements. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. These statements involve known and unknown risks, uncertainties and other important factors, including those identified under “Risk Factors” in this Annual Report, that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

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 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 Annual Report and the documents that we reference in this Annual Report 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.

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

## PART I



**ITEM 1: IDENTITY OF DIRECTORS, SENIOR MANAGEMENT AND ADVISORS**

Not applicable.

**ITEM 2: OFFER STATISTICS AND EXPECTED TIMETABLE**

Not applicable.

**ITEM 3: KEY INFORMATION****A. Selected Financial Data.**

The following selected consolidated financial data should be read in conjunction with “Operating and Financial Review and Prospects,” our consolidated financial statements and related notes, and other financial information included in this Annual Report. We have derived the consolidated statement of comprehensive income data and the consolidated statement of financial position data as of December 31, 2017 and 2016 from our audited financial statements included elsewhere in this Annual Report. Our historical results are not necessarily indicative of the results that should be expected in the future.

	Year Ended December 31,		
	2015	2016	2017
	(£'000s, except per ordinary share data)		
Consolidated statement of comprehensive income data:			
Research and development costs	(7,270)	(4,522)	(23,717)
General and administrative costs	(1,706)	(2,498)	(6,039)
Operating loss	(8,976)	(7,020)	(29,756)
Finance income	45	1,841	7,018
Finance expense	(73)	(794)	(2,465)
Loss before taxation	(9,004)	(5,973)	(25,203)
Taxation — credit	1,509	954	4,706
Loss for the year	(7,495)	(5,019)	(20,497)
Other comprehensive income / (loss) :			
Exchange differences on translating foreign operations	4	43	(29)
Total comprehensive loss attributable to owners of the company	(7,491)	(4,976)	(20,526)
Loss per ordinary share — basic and diluted (pence)	(37.1)	(15.0)	(23.4)

	Year Ended December 31,		
	2015	2016	2017
	(£'000s)		
Consolidated statement of financial position data:			
Cash and cash equivalents	3,524	39,785	31,443
Short term investments	—	—	48,819
Total assets	7,840	46,143	89,504
Share premium	26,650	58,526	118,862
Total liabilities	2,407	11,674	9,623
Accumulated loss	23,752	28,728	49,254
Total equity	5,434	34,469	79,881

Our business is primarily conducted in the United Kingdom, and we maintain our books and records in pounds sterling.

## **B. Capitalization and Indebtedness.**

Not applicable.

## **C. Reasons for the Offer and Use of Proceeds.**

Not applicable.

## **D. Risk Factors.**

*You should carefully consider the risks and uncertainties described below and the other information in this Annual Report. Our business, financial condition or results of operations could be materially and adversely affected if any of these risks occur.*

### **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 £5.0 million and £20.5 million for the years ended December 31, 2016 and 2017, respectively. As of December 31, 2017, we had an accumulated loss of £49.3 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 2 clinical trials and initiate and conduct our planned Phase 1 and 2 and PK clinical trials and any other future clinical trials of RPL554 for the treatment of COPD;
- develop RPL554 as DPI and pMDI 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;
- conduct pre-clinical studies to support RPL554 and potentially other future products;
- develop the manufacturing process and produce clinical and commercial supplies of RPL554;
- 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, the United Kingdom and possibly elsewhere.

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

We have devoted substantially all of our financial resources and efforts to the research and development and pre-clinical studies and clinical trials of 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 our ADS holders and shareholders to lose all or a part of their 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, 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 short-term investments will enable us to fund our operating expenses and capital expenditure requirements through the end of our Phase 2 development of nebulized RPL554 and our proof-of-concept development with DPI and pMDI formulations of RPL554 for the treatment of COPD, as well as our Phase 2 development of nebulized 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 2 clinical trials and our planned Phase 1 and 2 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;
- 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 pMDI 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, 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;
- unexpected operational or clinical issues may prevent completion or interpretation of clinical study results;
- 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 investors to evaluate the success of our business to date and to assess our future viability.**

Since our inception in 2005, we have devoted substantially all of our resources to developing 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 investors 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, restrict our operations or require us to relinquish rights to our technologies or product candidates.**

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of securities offerings, debt financings, license and collaboration agreements and research grants. If we raise capital through securities offerings, the ownership interest of our ADS holders and shareholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect these holders' rights as holders of our ADSs 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 ADS holders and 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 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 UK 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;
- inability to achieve or maintain double blinding of RPL554;
- unexpected technical issues during manufacture of RPL554 and the corresponding drug product;
- inability to manufacture sufficient quantities of RPL554 for use in clinical trials;
- 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 patient enrollment in twelve Phase 1 and 2 clinical trials of RPL554; ten of these have been reported, one is expected to report late in the first quarter of 2018 and the other is expected to report early in the second quarter of 2018. In the trials which have reported to date, which were all Phase 1 or Phase 2a studies, 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. Higher than expected numbers of patients could also discontinue participation in the clinical trials. 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:

- 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, with the required level of statistical significance, for its proposed indication;
- 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, for other reasons, not be sufficient to support the submission of an NDA in the United States, an MMA in the EU, or other comparable submission to obtain regulatory approval in other countries;
- the FDA, the EMA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies;
- the approval policies or regulations of the FDA, the EMA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval; and
- the FDA, the EMA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials.

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 record-keeping for RPL554 will be subject to extensive and ongoing regulatory requirements. These requirements include payment of annual user fees, submissions of safety and other post-marketing information and reports, facility registration and drug listing, as well as continued compliance with cGMP requirements for the manufacture of 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 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 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.

The policies of the FDA and of other regulatory authorities may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, certain policies of the Trump administration may impact our business and industry. Namely, the Trump administration has taken several executive actions, including the issuance of a number of Executive Orders, that could impose significant burdens on, or otherwise materially delay, FDA's ability to engage in routine oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. It is difficult to predict how these orders will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose restrictions on FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted. In addition, if we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

**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 empanelled, 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 current 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. For example, the Budget Control Act of 2011 has, among other things, led to aggregate reductions of Medicare payments to providers of 2% per fiscal year, which, due to subsequent legislative amendments to the statute, will remain in effect through 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 laws and any laws enacted in the future may result in additional reductions in Medicare and other health care funding, which could have a material adverse effect on our customers and accordingly, our financial operations.

Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, CMS may develop new payment and delivery models, such as bundled payment models. 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 active in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, results of operations, financial condition and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for 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 or EU 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 toward clinical trial costs, tax credits for qualified clinical testing and application fee waivers. In addition, if a product receives the first FDA approval of that drug for the indication for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as

a showing of clinical superiority over the product with orphan exclusivity or where the manufacturer is unable to assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the rare disease or condition. Under the FDA's regulations, the FDA will deny orphan drug exclusivity to a designated drug upon approval if the FDA has already approved another drug with the same active ingredient for the same indication, unless the drug is demonstrated to be clinically superior to the previously approved drug. In the EU, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity following approval. This period may be reduced to six years if the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity.

We plan to seek orphan drug designation from the FDA and the EMA for 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 clinically superior on the basis of greater safety, greater effectiveness, or a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process. In addition, while we intend to seek orphan drug designation for RPL554 for the treatment of CF, we may never receive such designation.

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 response to lawsuits against the FDA in 2014 and 2016, Congress included a provision in the Food and Drug Administration Reauthorization Act, or FDARA, enacted in August 2017, that amended the FDCA to require that, as a condition to awarding exclusivity to a designated orphan drug that is the same as a previously approved drug, such drug must demonstrate clinical superiority over the previously approved drug upon approval. In the future, there is the potential for additional legal challenges to the FDA's orphan drug framework, and it is uncertain how new challenges, regulations, or Congressional actions in the orphan drug space 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, frequency, and ease of administration;
- cost-effectiveness;

- marketing and distribution support;
- availability of adequate coverage, reimbursement and adequate payment from health maintenance organizations and other insurers, both public and private; and
- other potential advantages over alternative treatment methods.

If 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 provide assurance that upon a regulatory inspection of us or our CROs or other third parties performing services in connection with our clinical trials, such regulatory authority will determine that any of our clinical trials complies with GCP regulations. In addition, our clinical trials must be conducted with product produced under applicable cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

Further, these investigators and CROs are not our employees and we will not be able to control, other than by contract, the amount of resources, including time, which they devote to 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 pMDI 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 production 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 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 one CMO. 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.

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, pMDI, 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 provide assurance that all of the potentially relevant prior art relating to our patents and patent applications has been found. If such prior art exists, it can invalidate a patent or prevent a patent from issuing from a pending patent application. Even if patents do successfully issue and even if such patents cover 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 manufacturers, suppliers and other parties that we use to conduct our pre-clinical and clinical trials and any future collaborators, may be lost or we may suffer security breaches.**



In the ordinary course of our business, we and our manufacturers, suppliers and third parties that we use to conduct our pre-clinical and clinical trials, collect and store sensitive data, including intellectual property, clinical trial data, proprietary business information and personally identifiable information of our clinical trial subjects and employees, in our and third party data centers and on our and third party networks. The secure processing, maintenance and transmission of this information is critical to our operations. 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, and that of our manufacturers, suppliers and other third parties that we use to conduct our pre-clinical and clinical trials, could experience serious disruptions that could distract our operations and cause delays in our research and development work.**

Our information technology and other internal infrastructure systems, including corporate firewalls, servers, leased lines and connection to the Internet, and that of our manufacturers, suppliers and other third parties that we use to conduct our pre-clinical and clinical trials, face the risk of systemic failure that could disrupt our operations. A significant disruption in the availability of these information technology and other internal infrastructure systems could cause interruptions in our collaborations and delays in our research and development work.

#### **Risks Related to Employee Matters and Managing Growth**

**Our future growth and ability to compete depends on 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, our senior vice president, chemistry manufacturing and controls, Peter Spargo, our vice president, regulatory affairs, Desiree Luthman and our commercial director, Richard Hennings.

The loss of key managers and senior scientists could delay our research and development activities. In addition, the competition for qualified personnel in the biopharmaceutical and pharmaceutical field is intense, and our future success depends upon our ability to attract, retain and motivate highly skilled scientific, technical and managerial employees. We face competition for personnel from other companies, universities, public and private research institutions and other organizations. If our recruitment and retention efforts are unsuccessful in the future, it may be difficult for us to achieve our product candidate development objectives, raise additional capital and implement our business strategy.

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

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, regulatory affairs and sales and marketing. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such

anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

## **Risks Related to Our ADSs 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 continue to incur increased costs as a result of operating as a public company in the United States, and our senior management are required to devote substantial time to new compliance initiatives and corporate governance practices.**

As a U.S. public company, and particularly after we no longer qualify as an emerging growth company, we will continue to incur significant legal, accounting and other expenses that we did not incur prior to becoming a U.S. public company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of Nasdaq and other applicable securities rules and regulations impose various requirements on non-U.S. reporting public companies, including the establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our senior management and other personnel have devoted and will need to continue to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will continue to increase our legal and financial compliance costs and will make some activities more time-consuming and costly.

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

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we 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 time frame or at all, that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

**The dual listing of our ordinary shares and our ADSs may adversely affect the liquidity and value of our ordinary shares and ADSs.**

Our ADSs are listed on Nasdaq, and our ordinary shares are 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 trading market or price for our ADSs or ordinary shares .

**Certain of our shareholders, members of our board of directors, and senior management own a majority of our ordinary shares (including ordinary shares represented by ADSs) and as a result, are be able to exercise significant control over us.**

As of February 27, 2018, our senior management, board of directors and greater than 5% shareholders and their respective affiliates, in the aggregate, owned approximately 61% of our ordinary shares (including ordinary shares represented by ADSs) assuming no exercise of outstanding options or warrants, and approximately 55% of our ordinary shares, assuming exercise of all options available for exercise and outstanding warrants. Depending on the level of attendance at our general meetings of shareholders, these shareholders either alone or voting together as a group may be in a position to determine or significantly influence the outcome of decisions taken at any such general meeting. Any shareholder or group of shareholders controlling more than 50% of the share capital present and voting at our general meetings of shareholders may control any shareholder resolution requiring a simple majority, including the appointment of board members, certain decisions relating to our capital structure, 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 the perception that such sales will occur, could cause a decline in the market price of our ADSs and ordinary shares. Sales in the United States of our ADSs and ordinary shares held by our directors, officers and affiliated shareholders are subject to restrictions. If these shareholders sell substantial amounts of ordinary shares or ADSs in the public market, or the market perceives that such sales may occur, the market price of our ADSs or ordinary shares and our ability to raise capital through an issue of equity securities in the future could be adversely affected.

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

Under current 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 our ADS holders and shareholders' sole source of gains for the foreseeable future, and they will suffer a loss on their investment if they are unable to sell their ADSs or ordinary shares at or above the price at which they were purchased. Investors seeking cash dividends should not purchase our ADSs or ordinary shares.

**Securities traded on AIM may carry a higher risk than securities traded on other exchanges, which may impact the value of our investors' investments.**

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. 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.

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

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

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

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

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

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

**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 our final prospectus filed with the Securities and Exchange Commission on April 28, 2017 relating to our Registration

Statement on Form F-1 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 are subject to reporting obligations under the Securities Exchange Act of 1934, as amended, or the Exchange Act, that, to some extent, are more lenient and less frequent than those of a U.S. domestic public company.**

We report under the Exchange Act as a non-U.S. company with foreign private issuer status. Because we qualify as a foreign private issuer, 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 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, our investors may not have the same protections afforded to shareholders of companies that are not foreign private issuers.

**As a foreign private issuer and as permitted by the listing requirements of Nasdaq, we rely on certain home country governance practices rather than the corporate governance requirements of Nasdaq.**

As a foreign private issuer, in accordance with the listing requirements of Nasdaq, we follow our home country governance requirements and certain exemptions thereunder rather than the corporate governance requirements of Nasdaq.

For example, we are exempt from Nasdaq regulations that require a listed U.S. company to:

- have a majority of the board of directors consist of independent directors;

- require non-management directors to meet on a regular basis without management present;
- promptly disclose any waivers of its code of conduct for directors or executive officers;
- have an independent nominating committee and compensation committee;
- solicit proxies and provide proxy statements for all shareholder meetings; and
- seek shareholder approval for the implementation of certain equity compensation plans and issuances of ordinary shares.

For an overview of our corporate governance principles, see "Description of Share Capital and Articles of Association — Articles of Association" in our final prospectus filed with the Securities and Exchange Commission on April 28, 2017 relating to our Registration Statement on Form F-1.

Our Audit Committee is required to comply with the provisions of Section 301 of the Sarbanes-Oxley Act of 2002 and Rule 10A-3 of the Exchange Act, both of which also are applicable to Nasdaq-listed U.S. companies. Because we are a foreign private issuer, however, our Audit Committee is not subject to additional Nasdaq requirements applicable to listed U.S. companies, including an affirmative determination that all members of the Audit Committee are "independent" using more stringent criteria than those applicable to us as a foreign private issuer.

Because we are exempt from certain Nasdaq governance requirements, our ADS holders may not have the same protections afforded to shareholders of companies that are subject to these Nasdaq requirements.

**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. 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, not being required to present selected financial data for any period prior to the earliest audited period presented in our first registration statement, and exemptions from the requirement of holding a shareholder nonbinding advisory vote on executive compensation and golden parachute payments. 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 the initial public offering of our ADSs, 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 have taken steps that we believe address the underlying causes of the material weakness by the hiring of our new chief financial officer, enhancing our financial reporting team's technical accounting knowledge associated with the accounting rules for business combinations, implementing additional internal controls and engaging expert external consultants for additional technical support. However, we cannot be certain that these efforts will be sufficient to 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 publish inaccurate or unfavorable research, about our business, the price of our ADSs and ordinary shares and our trading volume could decline.**

The trading market for our ADSs and ordinary shares depends in part on the research and reports that securities or industry analysts publish about us or our business. 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 in "Item 10.E— Taxation") 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 "Item 10.E— Taxation—Passive Foreign Investment Company Rules."

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

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

#### **ITEM 4 INFORMATION ON THE COMPANY**

##### **A. History and Development of the Company.**

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, 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. The principal legislation under which we operate is the Companies Act 2006. Our website address is [www.veronapharma.com](http://www.veronapharma.com). Information contained on, or that can be accessed through, our website does not constitute a part of this Annual Report. We have included our website address in this Annual Report solely as an inactive textual reference.

Our agent for service of process in the United States is Cogency Global Inc. National Corporate Research, Ltd. was acquired by Cogency, whose address is 10 E. 40<sup>th</sup> Street, 10<sup>th</sup> floor, New York, New York 10016.

In February 2017, we effected a 50-for-one share consolidation in which we consolidated every 50 of our existing ordinary shares, nominal value £0.001 per share, in our issued share capital into one ordinary share, nominal value £0.05 per share. In May 2017, we completed the initial public offering of our American Depositary Shares ("ADSs") in the United States as well as a private placement of our ordinary shares in Europe. Our ADSs were listed on The Nasdaq Global Market under the symbol "VRNA."

Our principal capital expenditures for the year ended December 31, 2017 were £0.2 million. These capital expenditures primarily consisted of patent costs. We expect our expenditure on patent costs to increase in the near term as we continue to advance our research and development programs for RPL554 and grow our operations. .



We anticipate our capital expenditure in 2018 to be financed from the proceeds of our initial public offering of ADSs and private placement of ordinary shares. For more information on our capital expenditures, see the section of this Annual Report titled “Item 5.B. Liquidity and Capital Resources-Capital Expenditures.”

## **B.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 patient enrollment in twelve Phase 1 and 2 clinical trials for RPL554 with over 700 subjects enrolled; ten of these studies have been reported, one study is expected to report late in the first quarter of 2018 and one study is expected to report early in the second quarter of 2018. 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 commonly used short- and long-acting 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.

We also are developing RPL554 in both dry powder inhaler, or DPI, and metered dose inhaler, or pMDI, formulations for the maintenance treatment of COPD. Handheld DPI and pMDI 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 pMDI 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.

To evaluate RPL554 in a nebulized formulation for the maintenance treatment of COPD, we commenced a four-week Phase 2b dose-ranging clinical trial in July 2017, which is evaluating RPL554 as a single agent as compared to placebo in approximately 400 patients with moderate to severe COPD (trial RPL554-CO-203). We have now completed dosing in this study and expect to report top-line data from this trial early in the second quarter of 2018. Depending on the data from all clinical trials conducted with RPL554 to date, future interactions with regulatory authorities and our commercial assessment of different development options for RPL554 we will consider any opportunity to focus and accelerate our development plans for RPL554, including proceeding more rapidly towards Phase 3 clinical trials. The previously planned 12-week Phase 2b dose-ranging clinical trial may therefore be shortened or deemed unnecessary. Earlier entry into Phase 3 clinical trials with nebulized RPL554 for the maintenance treatment of COPD could require us to focus our resources and funding initially on the maintenance market as a priority in the short term, over progressing our planned trials to evaluate nebulized RPL554 as a treatment for acute exacerbations of COPD in hospitalized patients and as a treatment for CF patients.

We also plan to evaluate RPL554 in a nebulized formulation as an add-on therapy to two commonly used bronchodilators administered together, in up to 100 patients, beginning in the second half of 2018. In addition, following the completion of our DPI and pMDI formulation process, we plan to commence pre-clinical studies for RPL554 in these formulations in 2018, to be followed by the first clinical trials in healthy subjects or patients with COPD. We do not expect the timing of these trials to be affected by any decision to progress more rapidly into Phase 3 clinical trials with our nebulized maintenance treatment for COPD.

In February 2017, we commenced a Phase 2a double blind, placebo-controlled, three way cross-over trial in 30 subjects with COPD, which included two different doses of RPL554, 1.5 mg and 6 mg, or placebo, dosed twice-daily for three days, in addition to tiotropium, a commonly used long-acting anti-muscarinic bronchodilator, dosed once daily. This clinical trial was conducted in the United Kingdom. We reported positive top-line data from this trial earlier than expected, in September 2017. The data from this Phase 2a trial demonstrated significantly improved peak lung function when RPL554 was added to tiotropium in patients with moderate-to-severe COPD.

- Primary outcome measures:

RPL554, compared to placebo, produced a statistically significant (1.5 mg,  $p=0.002$ ; 6 mg,  $p<0.001$ ) and a clinically meaningful ( $>100$  ml) peak  $FEV_1$  on the third day of dosing (additional bronchodilation) when administered on top of the standard bronchodilator tiotropium (Spiriva®);

Average  $FEV_1$  on the third day of dosing (0 - 12 hours) of RPL554 when added on top of tiotropium was larger than that of tiotropium alone (1.5mg,  $p=0.099$ ; 6 mg,  $p<0.001$ );

In the study, a  $p$ -value $<0.05$  is regarded as statistically significant.

- Secondary outcome measures:

Both doses of RPL554 produced a statistically significant faster onset of action (defined as  $FEV_1$  improvement by  $\geq 10\%$ ; 1.5 mg, 4.2 min; 6 mg, 4.6 min) when added to tiotropium compared to tiotropium alone (37.6 min;  $p<0.001$ );

The administration of RPL554 as an add-on treatment to tiotropium caused a marked reduction in Functional Residual Capacity (1.5 mg,  $p<0.01$ ; 6 mg,  $p<0.05$ ) and in Residual Volume (1.5 mg,  $p=0.07$ ; 6 mg,  $p<0.01$ ), both measures of trapped air in the lung, as compared to tiotropium alone, suggesting that RPL554 treatment may reduce dyspnea, a major debilitating symptom of COPD.

In June 2017 we commenced an IND-opening single-dose pharmacokinetic, or PK, trial in 12 healthy volunteers in the US. We reported top-line data from this trial earlier than expected in September 2017. A PK trial involves the study of the process of bodily absorption, distribution, metabolism and excretion of a drug. With any inhaled or nebulized medication, a portion of the substance is deposited in the mouth and then swallowed by the patient. The results showed that in the study subjects only 10.4 percent of the inhaled dose entered the bloodstream via the gastrointestinal tract. The low oral bioavailability of nebulized RPL554, as demonstrated in the study, is consistent with optimal inhaled delivery of medications for the treatment of COPD and asthma. Therefore, the results from this study confirm that inhalation is an appropriate form of administration of RPL554 for 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 late in the first quarter of 2018. A PD trial involves the study of the biochemical and physiological effects of a drug and its mechanism of action, including the correlation of the drug's actions and effects with its chemical structure. The results of this clinical trial will support dose selection for a proof-of-concept Phase 2b trial in approximately 100 patients with CF, which we plan to commence 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 expected to become the third leading cause of death globally by 2030, 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 about half of whom have been diagnosed. Of those diagnosed with COPD in the United States, more than 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. Whereas the number of patients diagnosed with COPD in the US continues to increase annually, the growth in numbers in countries like China is significantly higher. The prevalence of COPD in China is estimated to be about 8% of the population aged over 40, and this percentage is expected to increase in coming years. Global sales of drugs currently indicated for COPD in major markets were approximately \$15 billion in 2015 and are expected to grow to \$20 billion by 2025.

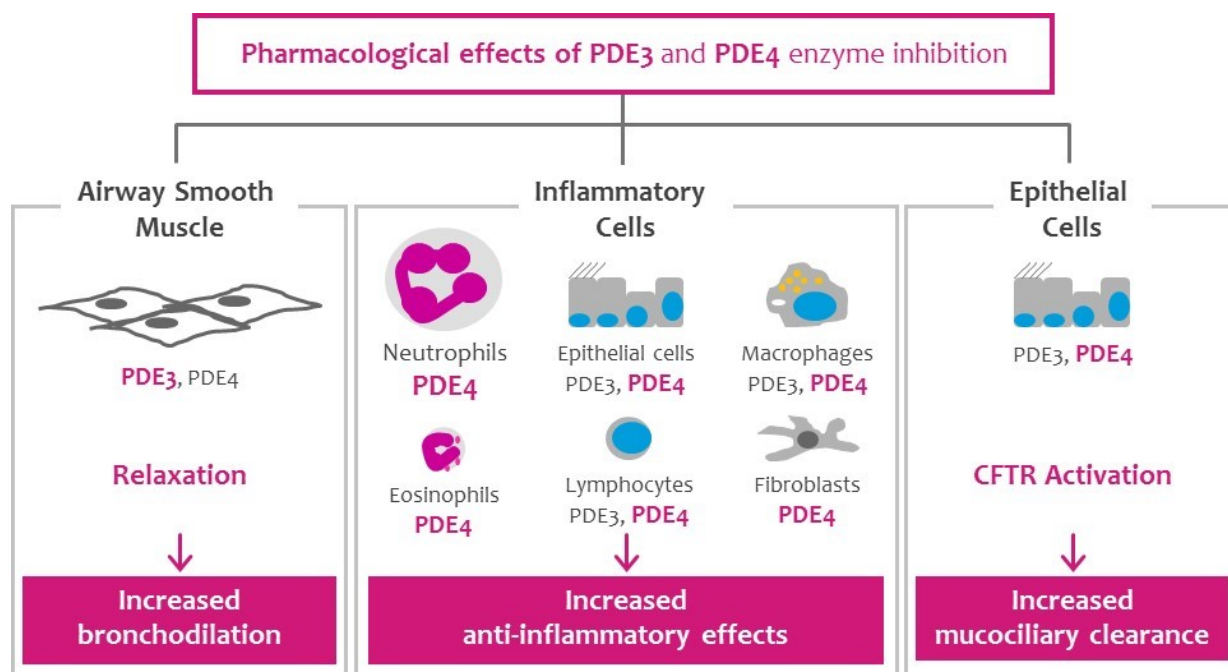
COPD patients are commonly treated with bronchodilators, which seek to relieve airway constriction and make it easier to breathe, and inhaled corticosteroids, which seek to reduce lung inflammation. For patients with more severe disease who experience recurrent exacerbations, and for whom inhaled corticosteroids 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 although current therapies are leading to longer lifespans the median age of death for CF patients is still only around 40 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. Phosphodiesterases, 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 or asthma 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. In 2017 we announced the results of a Phase 2a clinical trial of RPL554 in 30 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 minute, FEV<sub>1</sub>, and the duration of action of RPL554. We evaluated RPL554 administered as an add-on therapy to a commonly used bronchodilator tiotropium, marketed as Spiriva. We observed clinically meaningful and statistically significant improvement in lung function, as measured by FEV<sub>1</sub>, when RPL554 was administered as an add-on therapy to a standard dose of tiotropium as compared to a standard dose of tiotropium alone. In this clinical trial, we observed the effect size, or peak improvement was 127 ml and 104 ml for 1.5mg and 6mg doses respectively over tiotropium alone. 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. In addition, RPL554 administered as an add-on therapy to tiotropium resulted in a statistically significant reduction in time of onset of bronchodilation as compared to tiotropium alone. The data from this study was highly consistent with the results of a previous Phase 2a clinical trial we announced in 2016 of RPL554 in 36 patients with COPD. Our primary objective in that clinical trial was to evaluate the improvement in lung function, as measured by FEV<sub>1</sub>, 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<sub>1</sub>, 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. We also observed clinically meaningful and statistically significant improvement in lung function, as measured by FEV<sub>1</sub>, 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 sputum samples from a model of COPD-like lung inflammation in human subjects. 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 September 2017 we reported top-line data from an IND-opening single-dose pharmacokinetic, or PK, trial in 12 healthy volunteers in the United States. A PK trial involves the study of the process of bodily absorption, distribution, metabolism and excretion of a drug. With any inhaled or nebulized medication, a portion of the substance is deposited in the mouth and then swallowed by the patient. The results showed that in the study subjects only 10.4 percent of the inhaled dose entered the bloodstream via the gastrointestinal tract. The low oral bioavailability of nebulized RPL554, as demonstrated in the study, suggests that inhalation delivers an optimal dose of RPL554 and is consistent with inhaled delivery of medications commonly used for the treatment of COPD and asthma. Therefore, the results from this study confirmed that inhaled RPL554 is an appropriate form of administration for patients.

In addition, based on our pre-clinical studies, we believe that RPL554 has the potential to reduce the deleterious inflammation in CF patients, which seems to be 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. As of February 6, 2018 our intellectual property portfolio includes seven issued U.S. patents, four pending U.S. patent applications, 20 issued foreign patents in countries including China, Canada, Brazil, Japan, Mexico and Australia, and also including four issued European patents that have been validated in many European countries, including Germany, Italy, Spain, France and the United Kingdom, and 52 pending foreign applications in regions including Canada, Mexico, Asia and Europe, and also including one patent application 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 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 approximately £145 million in gross proceeds from investors since such listing, of which approximately £70 million was raised in our Nasdaq listing and the accompanying private offering in Europe and the shareholder private placement; we raised a further £45 million raised in our July 2016 private placement of equity securities 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	Delivery	Pre-Clinical	Phase 1	Phase 2	Phase 3	Addressable Market Opportunity
COPD Maintenance (Home)	 Nebulizer					
COPD Acute (Hospital)						
Cystic Fibrosis						
COPD Maintenance (Home)	MDI 					
COPD Maintenance (Home)	DPI 					

*RPL554 also has applications in other significant respiratory diseases such as asthma.*

## 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 pMDI 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 enrollment of patients in twelve Phase 1 and 2 clinical trials for RPL554 with over 700 subjects enrolled; ten of these studies have been reported, one study is expected to report late in the first quarter of 2018 and one study is expected to report early in the second quarter of 2018. 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 several commonly used bronchodilators as compared to such bronchodilators 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 these bronchodilators. 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<sub>1</sub> 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 are conducting an ongoing four-week Phase 2b dose ranging clinical trial to evaluate RPL554 for the maintenance treatment of COPD. In this trial, we are comparing the use of RPL554 in a nebulized formulation to placebo in approximately 400 patients. This trial has completed patient enrollment and we expect to report top-line data early in the second quarter of 2018.
- Depending on the data from all clinical trials conducted with RPL554 to date, future interactions with regulatory authorities and our commercial assessment of different development options for RPL554 we will consider any opportunity to focus and accelerate our development plans for RPL554, including proceeding more rapidly towards Phase 3 clinical trials, particularly with nebulized RPL554 for the maintenance treatment of COPD. This could possibly avoid or shorten the previously planned 12-week Phase 2b dose-ranging clinical trial. Earlier entry into Phase 3 clinical trials with nebulized RPL554 for the maintenance treatment of COPD could require us to focus our resources and funding initially on the maintenance market as a priority in the short term over progressing our planned trials to evaluate nebulized RPL554 as a treatment for acute exacerbations of COPD hospitalized patients and as a treatment for CF patients.
- We plan on studying RPL554 on top of two commonly used long acting bronchodilators in a dose ranging, three way cross-over trial involving up to 100 patients with moderate to severe COPD. We plan on starting this trial in the fourth quarter of 2018.

- **Adapt the current nebulized formulation and presentation of RPL554.** RPL554 for nebulized administration is currently presented in a glass vial with a flip, tear-up cap. This format is adequate for clinical trials but patient acceptance in a commercial setting is expected to be improved by a switch to presenting the suspension formulation of RPL554 in plastic ampules. We will investigate the feasibility to manufacture and supply RPL554 nebulized suspension formulation in plastic ampules. In addition to patient acceptance, switching to plastic ampules may also be more cost-effective for manufacturing in larger volumes. A decision on presentation form will be made before the start of Phase 3 clinical trials; during this evaluation process we will also review and optimize the nebulized suspension formulation as part of a quality by design program.
- **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 late in the second half of 2018. Depending on the data from all clinical trials conducted with RPL554 to date, future interactions with regulatory authorities and our commercial assessment of different development options for RPL554 we will consider any opportunity to focus and accelerate our development plans for RPL554, including proceeding more rapidly towards Phase 3 clinical trials, particularly with nebulized RPL554 for the maintenance treatment of COPD. Earlier entry into Phase 3 clinical trials with nebulized RPL554 for the maintenance treatment of COPD could require us to focus our resources and funding initially on the maintenance market as a priority in the short term over progressing our planned trials to evaluate nebulized RPL554 as a treatment for acute exacerbations of COPD in hospitalized patients and as a treatment for CF patients.
- **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 late in the first quarter 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 late in the second half of 2018. Depending on the data from all clinical trials conducted with RPL554 to date, future interactions with regulatory authorities and our commercial assessment of different development options for RPL554 we will consider any opportunity to focus and accelerate our development plans for RPL554, including proceeding more rapidly towards Phase 3 clinical trials, particularly with nebulized RPL554 for the maintenance treatment of COPD. Earlier entry into Phase 3 clinical trials with nebulized RPL554 for the maintenance treatment of COPD could require us to focus our resources and funding initially on the maintenance market as a priority in the short term over progressing our planned trials to evaluate nebulized RPL554 as a treatment for acute exacerbations of COPD in hospitalized patients and as a treatment for CF patients.
- **Develop DPI and MDI formulations of RPL554.** In addition to our nebulized formulation of RPL554, we are developing RPL554 in both DPI and pMDI formulations for the maintenance treatment of COPD. We believe the development of DPI and pMDI formulations has the potential to significantly increase the market opportunity for RPL554, if approved, for the maintenance treatment of COPD. Following the progression of our DPI and pMDI formulation process, we plan to commence pre-clinical studies for RPL554 in these formulations in 2018, to be followed by the first clinical trials in healthy subjects or patients with COPD. In addition, we may explore the development of RPL554 in these formulations for the treatment of asthma and other respiratory diseases.
- **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 of 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 inhaled 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<sub>1</sub>. 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 pMDI 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 perhaps 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 corticosteroid is not effective in all patients. In addition, inhaled corticosteroids (fluticasone) have been shown to decrease the immune response in some patients, which results in an increased incidence of pneumonia.

Recently, inhalers have been approved containing two long acting bronchodilators (one LAMA and one LABA) and an inhaled corticosteroid. These so-called triple therapies are combinations of medications that are already available in the market place as either single or dual agents. Triple therapy may offer advantages over double therapy (two bronchodilators) in some patients with COPD.

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 several 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 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.

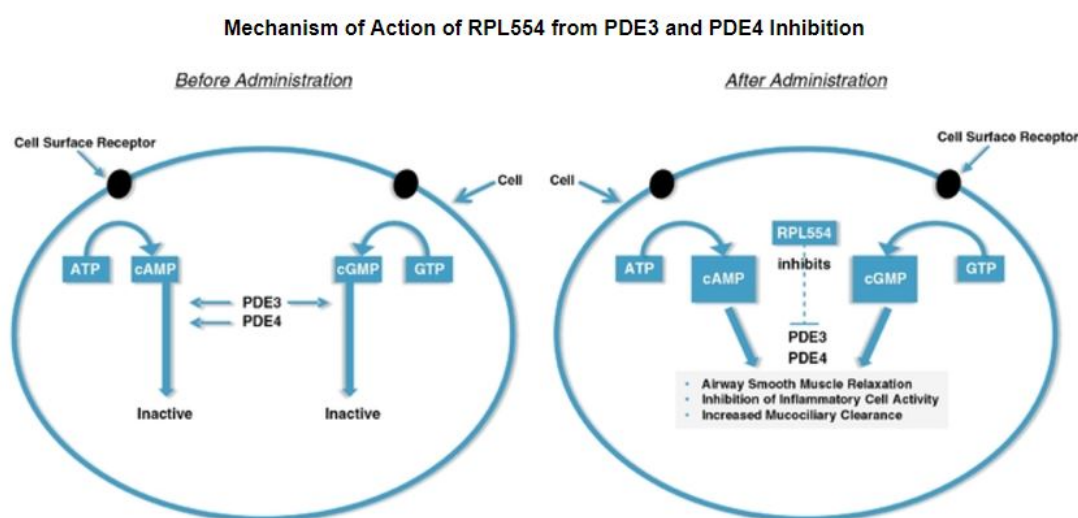
### ***Our Solution***

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.



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.** We have completed patient enrollment in twelve Phase 1 and 2 clinical trials for RPL554 with over 700 subjects enrolled; ten of these studies have been reported, one study is expected to report late in the first quarter of 2018 and one study is expected to report early in the second quarter of 2018. 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 a number of commonly used bronchodilators as compared to all such bronchodilators administered as single agents. 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 the typical 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 trials for RPL554, we have observed a rapid onset of bronchodilation when RPL554 was administered as an add-on therapy to a range of currently marketed short-acting and long-acting bronchodilators: ipratropium, tiotropium and albuterol. The time of onset of action of ipratropium was 18.4 minutes, while the time of onset of action for RPL554 was approximately 14.6 minutes. When RPL554 was administered as an add-on therapy to ipratropium, the time of onset was reduced by 75% to 4.8 minutes as compared to ipratropium alone, which is similar to albuterol alone, albuterol being one of the fastest acting bronchodilators. The time of onset of action of tiotropium was approximately 37 minutes; when RPL554 was administered as an add-on therapy to tiotropium, the time of onset was reduced by 86% to approximately five minutes as compared to tiotropium alone, which again 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- and long-acting bronchodilators in both the maintenance treatment, and 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 lung function, reduce symptoms and potentially also exacerbations, 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 pMDI 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 pMDI 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 pMDI formulations has the potential to significantly increase the market opportunity for RPL554, if approved, for the maintenance treatment of COPD. Following the progression of our DPI and pMDI formulation process, we plan to commence pre-clinical studies for RPL554 in these formulations in 2018, to be followed by the first clinical trials in healthy subjects or patients with COPD.

### ***Clinical Development***

We completed five Phase 1 and Phase 2a trials for RPL554 in Europe, dosing 105 subjects with an initial proof-of-concept solution 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<sub>1</sub>, 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 suspension 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 suspension formulation of RPL554; our IND-opening PK clinical trial was conducted in the United States, and the other studies have been conducted outside of the United States:

## Summary of Completed RPL554 Clinical Trials with New Nebulized Suspension Formulation

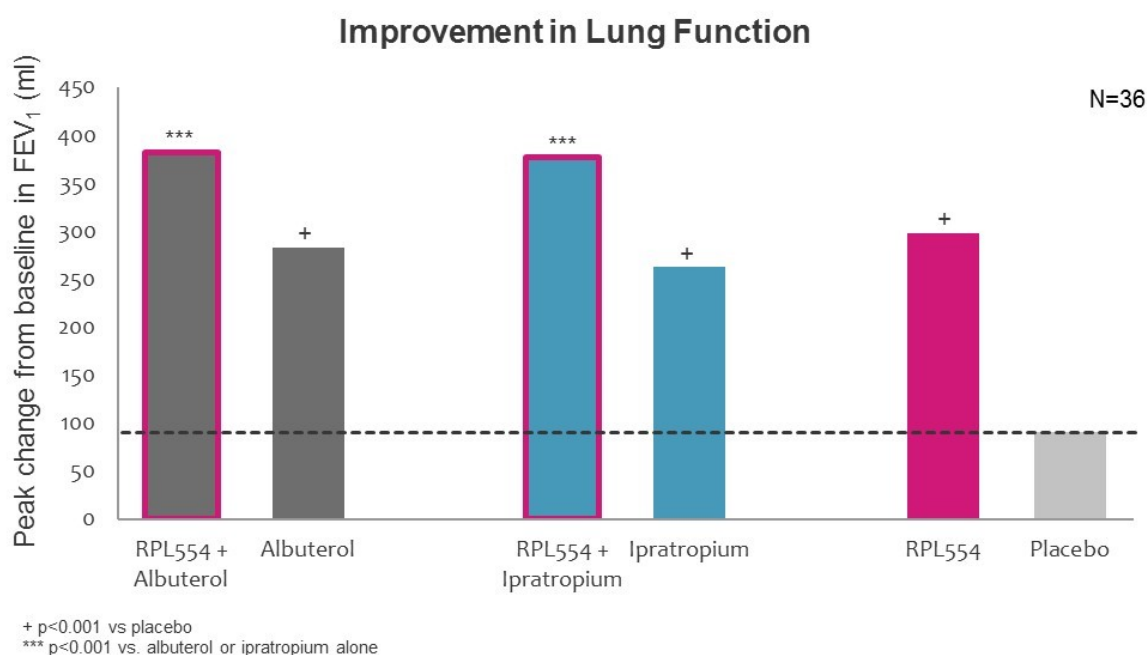
Trial Description	Patient Population	RPL554 Dosage	Key Findings
Phase 2a trial to assess the improvement in lung function, as measured by FEV <sub>1</sub> , of RPL554 as an add-on treatment to each of albuterol and ipratropium Completion date: February 2016	36 moderate-to-severe COPD patients, males 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 ig) or ipratropium (40 ig) and was statistically significant as compared to placebo RPL554 produced significant additive bronchodilation (>50% increase) when dosed with either albuterol (200 ig) or ipratropium (40 ig) 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 ig) or ipratropium (40 ig) was more rapid than with albuterol or ipratropium, respectively, alone
Phase 2a trial to assess the improvement in lung function, as measured by FEV <sub>1</sub> , of RPL554 as an add on treatment to tiotropium Completion date: September 2017	30 moderate to severe COPD patients, males and females, age [52 - 70] 1 location; United Kingdom	Multiple dose (twice daily for 3 days) of 1.5mg and 6mg	Well tolerated following multiple doses of 1.5mg and 6 mg of RPL554 alone and as add-on treatment RPL554 produced significant additive bronchodilation (>100ml increase) when dosed with tiotropium (18 mcg) as compared to tiotropium alone, and caused an additive and significant reduction in lung volumes and airway resistance The time to onset of RPL554 when dosed with tiotropium (18 mcg) 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 <sub>1</sub> , 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 Part A: 50 (35 RPL554 / 15 placebo) healthy subjects, males, age 19 - 48	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 <sub>1</sub> , 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 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 <sub>1</sub> , 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 <sub>1</sub> , of up to 360 mL (9%) from baseline Part B: RPL554 was well tolerated and there was a sustained increase in FEV <sub>1</sub> Part C: RPL554 was well tolerated and there was a significant increase in lung function, as measured by FEV <sub>1</sub> , of up to 360 mL (24%) from baseline, with a duration of action of 12 hours
Phase 1 trial to assess the relative oral bioavailability of RPL554	12 healthy male volunteers. 1 location in US	Single dose of RPL554 6mg given with, or without, a charcoal block to prevent absorption of RPL554 from the GI tract	Demonstrated a low oral bioavailability (GI absorption) of RPL554 of 10.4%. The terminal serum half life of RPL554 was 11.9 hours. RPL554 was well tolerated in this study.

### Phase 2a Clinical Trials

We have completed two Phase 1 and four Phase 2a clinical trials using our new nebulized suspension 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<sub>1</sub>, of RPL554 as an add-on therapy to albuterol (200 mg), as an add-on therapy to ipratropium (40 mg) 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<sub>1</sub>, 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<sub>1</sub>, as compared to albuterol or ipratropium alone, and statistically significant improvements as compared to placebo. These results are illustrated by the figure below.



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.

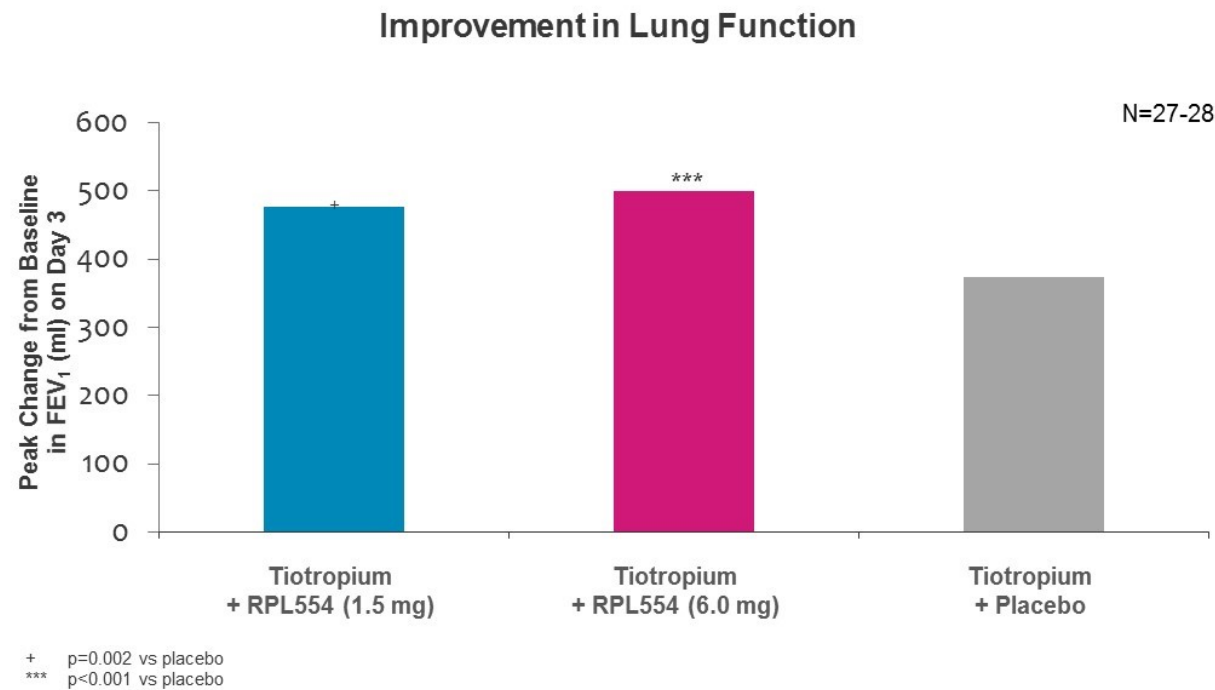
Another important parameter in COPD is the resistance of the airways to airflow. The inverse of this is airway conductance. Similar to the effect on residual lung volume, patients treated with RPL554 as a single agent experienced numerically greater increases in airway conductance as compared to each 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.



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.

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 September 2017, we completed a multiple-dose, double-blinded, placebo-controlled, three-way cross-over Phase 2a clinical trial for RPL554 conducted in the United Kingdom. A total of 30 patients were randomized to receive each of the three treatments, which were in each case tiotropium 18 mcg dosed once a day, administered together with an add-on of placebo, RPL554 dosed at 1.5 mg or RPL554 dosed at 6.0 mg (all three add-on treatments were dosed twice per day). The primary objective of this trial was to establish the improvement in lung function, as measured by FEV<sub>1</sub>, of RPL554 as an add-on therapy to tiotropium 18 mcg as compared to placebo and tiotropium. The testing dose levels for RPL554 were 1.5 mg and 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<sub>1</sub>, as an add-on therapy to standard doses of tiotropium as compared to standard doses of tiotropium alone. In this clinical trial, we observed the peak improvement was 104 ml higher for the add-on therapy of 1.5 mg RPL554 and 127 ml higher for the add-on therapy of 6 mg RPL554, in each case as compared to tiotropium alone. These results are illustrated by the figure below.

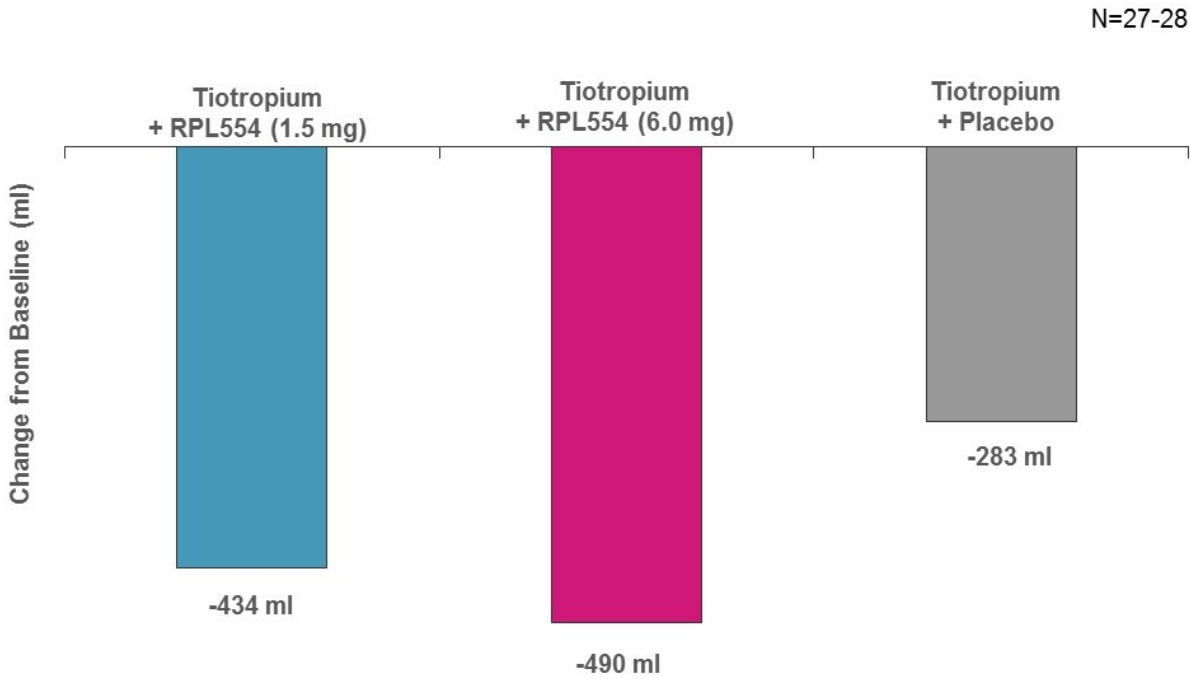


**Improvement in Lung Function**

In addition, patients treated with both 1.5 mg or 6 mg RPL554 as an add-on to tiotropium experienced statistically significant improvements in residual lung volume as compared to placebo, 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.

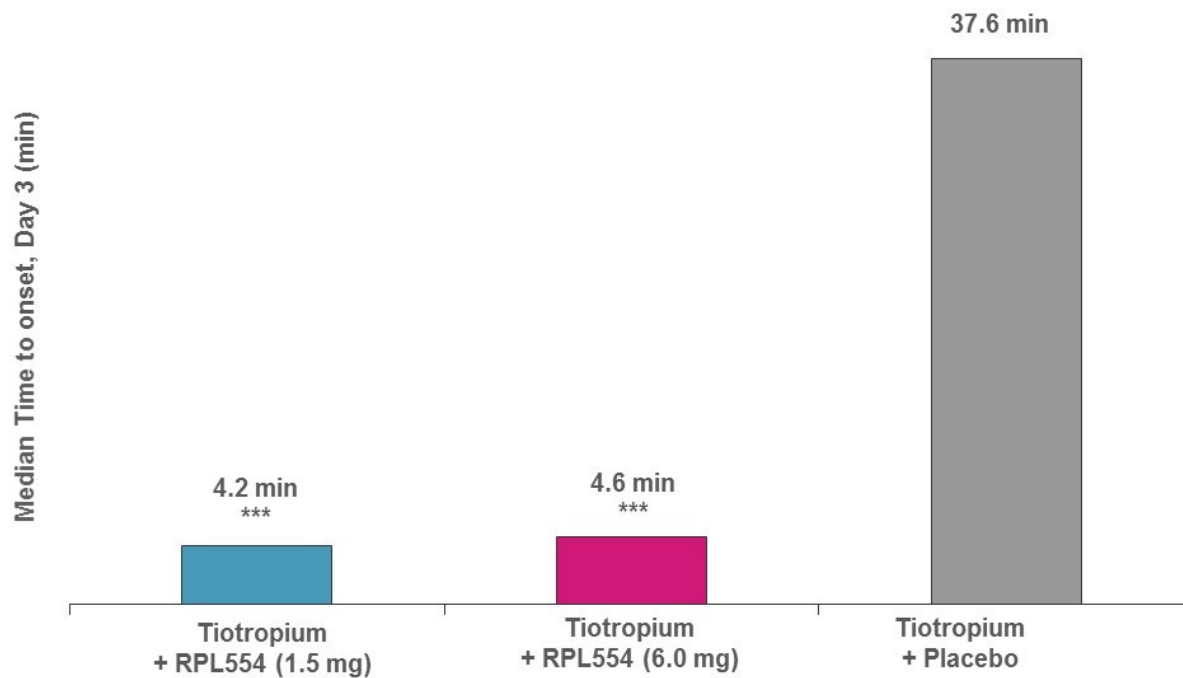
Change in Residual Volume (ml)



In this trial, the time of onset of action of tiotropium was approximately 37 minutes. When RPL554 was administered, either at 1.5 mg or at 6 mg, as an add-on therapy to tiotropium, the time of onset was reduced to less than 5 minutes. In both cases, RPL554 as an add-on therapy resulted in a statistically significant reduction in time of onset as compared to tiotropium alone. The time of onset in minutes is shown in the figure below.

## Median Time to Onset ( $\geq 10\%$ improvement in FEV<sub>1</sub>; mins) on Day 3

N=27-28



\*\*\* p<0.001 vs placebo

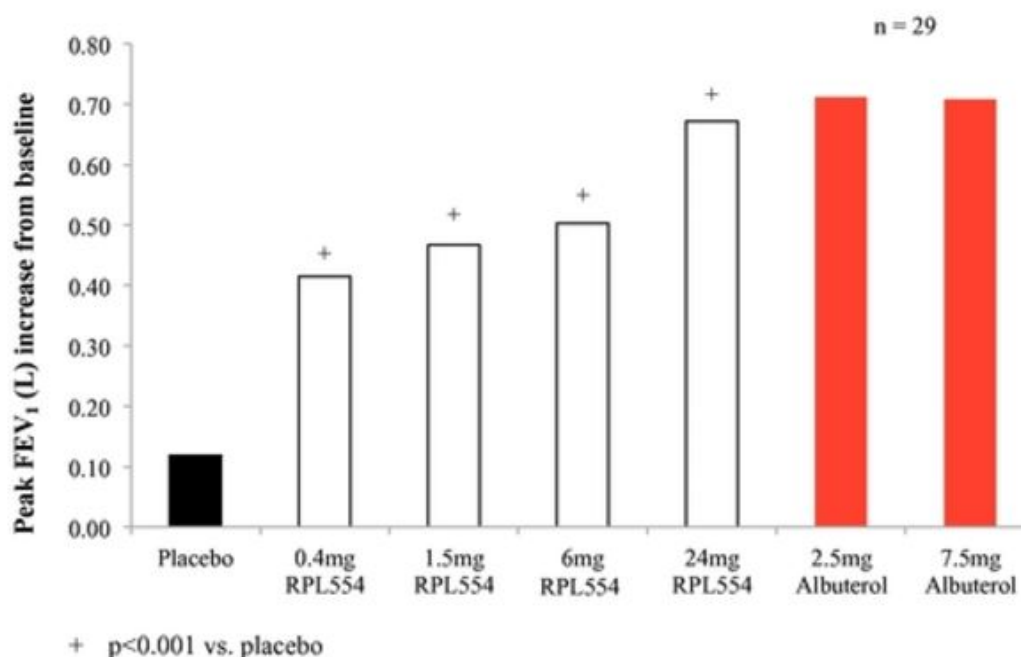
Consistent with prior trials,

RPL554 was well tolerated as an add-on therapy and was not observed to increase the incidence of any adverse event over tiotropium 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 tiotropium.

In January 2016, we completed a single-dose, double-blind, placebo-controlled, seven-way cross-over Phase 2a dose-finding trial of nebulized 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<sub>1</sub>, 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<sub>1</sub>, with a p-value of less than 0.001, as compared to placebo. The maximum improvement in lung function, as measured by FEV<sub>1</sub>, 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<sub>1</sub>, as compared to albuterol and placebo.

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



### Phase 1 Clinical Trials

In September 2017 we reported top-line data from an IND-opening single-dose pharmacokinetic, or PK, trial in 12 healthy volunteers in the United States. A PK trial involves the study of the process of bodily absorption, distribution, metabolism and excretion of a drug. With any inhaled or nebulized medication, a portion of the substance is deposited in the mouth and then swallowed by the patient. The results showed that in the study subjects only 10.4 percent of the inhaled dose entered the bloodstream via the gastrointestinal tract. The low oral bioavailability of nebulized RPL554, as demonstrated in the study, is consistent with optimal inhaled delivery of medications for the treatment of COPD and asthma. The half life of the drug was found to be 11.9 hours, which is consistent with prior studies, and demonstrates that RPL554 is appropriate to be studied as a twice daily medication. Therefore, the results from this study confirmed that inhaled RPL554 is an appropriate form of administration for patients.

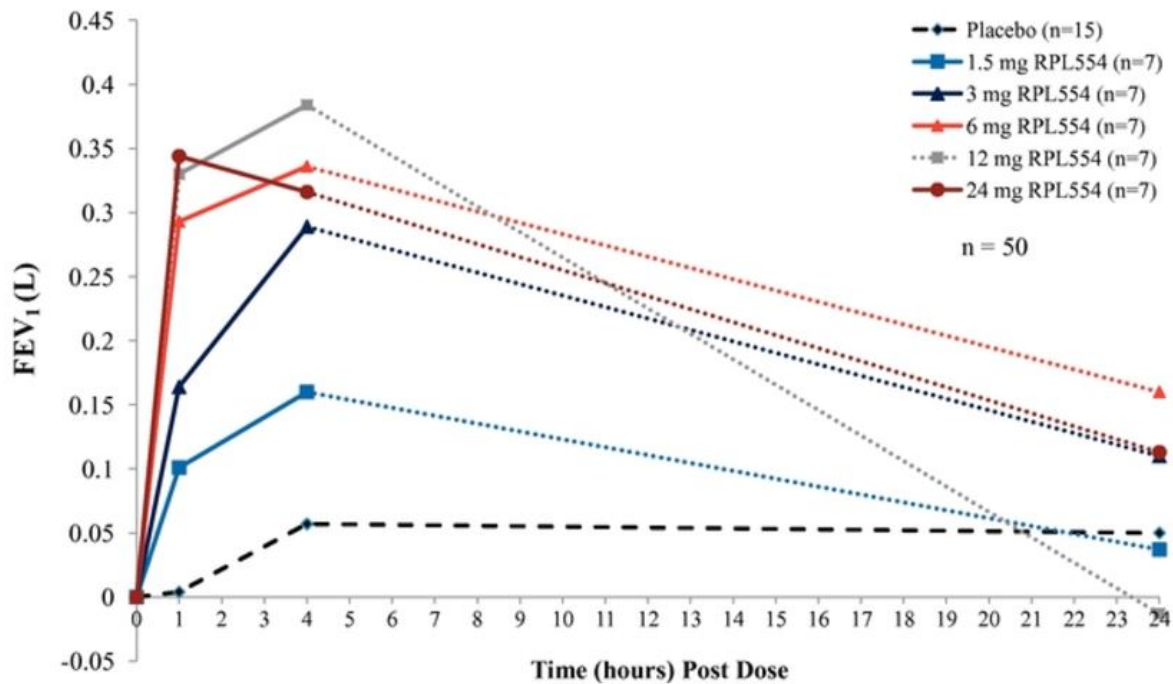
In September 2015, we completed a Phase 1 clinical trial that had three parts consisting of a single ascending dose, or SAD, trial in 50 healthy male subjects, a multiple ascending dose, or MAD, trial in 30 healthy male subjects and a MAD trial in 32 male and female patients with COPD. Doses in the SAD 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<sub>1</sub>, 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<sub>1</sub>, in these healthy individuals, despite none of them having asthma or COPD, as illustrated in the figure below.

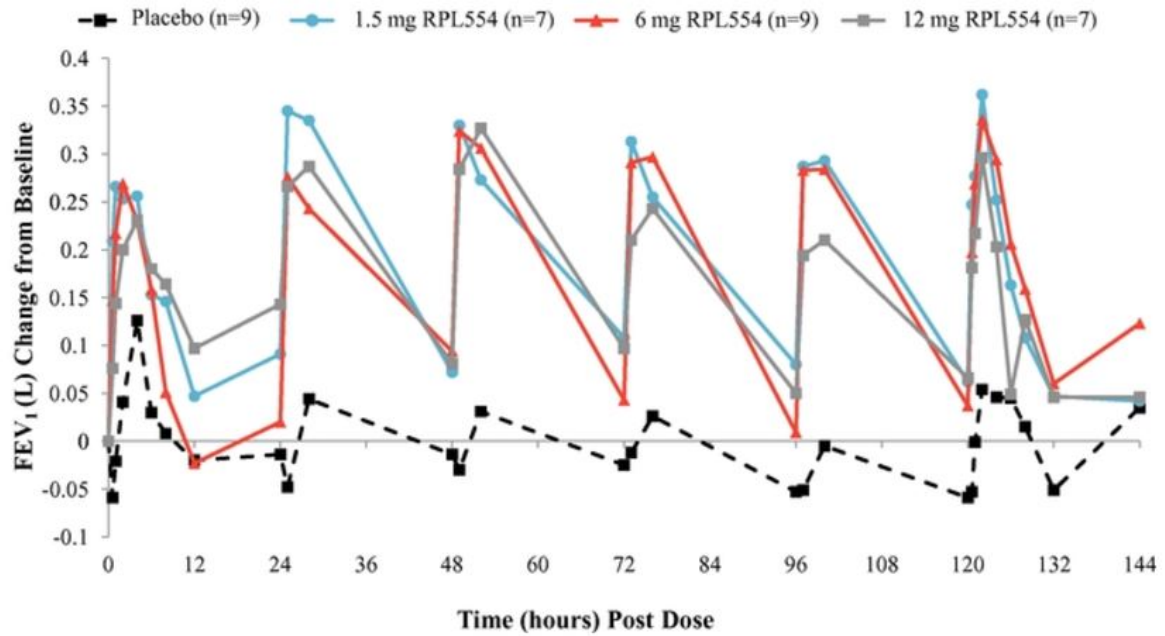
### Improvement in Lung Function (FEV<sub>1</sub>) in Healthy Subjects (SAD part)



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<sub>1</sub>, in these healthy individuals, despite none of them having asthma or COPD.

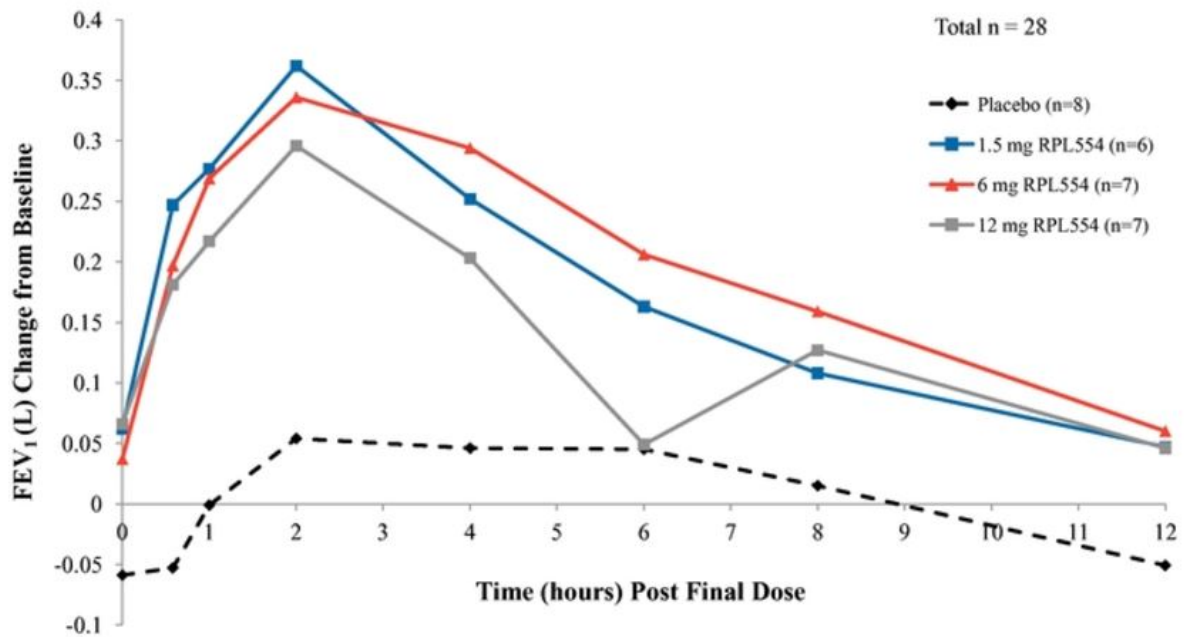
The primary objective of the third part of the trial, which was a MAD trial in 32 patients with moderate COPD, was to assess safety and tolerability and measure the PK profile of RPL554 in COPD patients receiving RPL554 as compared to placebo. The secondary objective was to assess the improvement in lung function, as measured by FEV<sub>1</sub>, 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<sub>1</sub>, 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<sub>1</sub>, on each day of the study.

Improvement in Lung Function (FEV<sub>1</sub>) over Six Days of Dosing

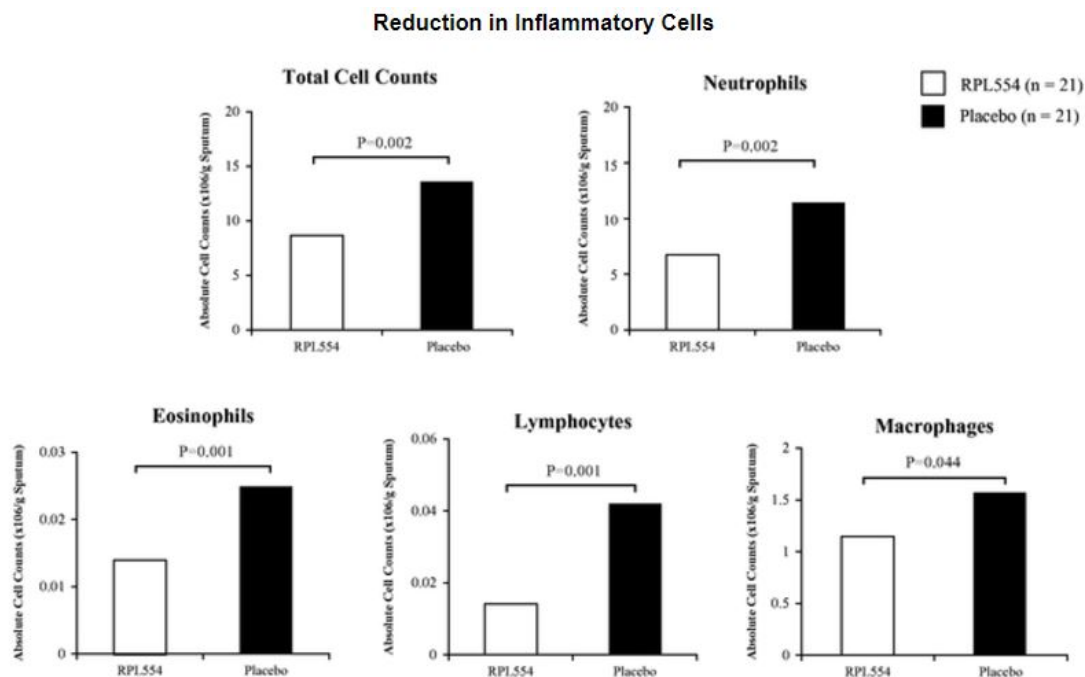


The figure below, which represents the effects of the final dose after five and a half days of treatment with RPL554, shows that patients with moderate COPD that were administered RPL554 experienced an improvement in lung function, as measured by FEV<sub>1</sub>, and that the improvement peaked at two hours and continued through the 12-hour measurement period.

Improvement in Lung Function (FEV<sub>1</sub>) 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.



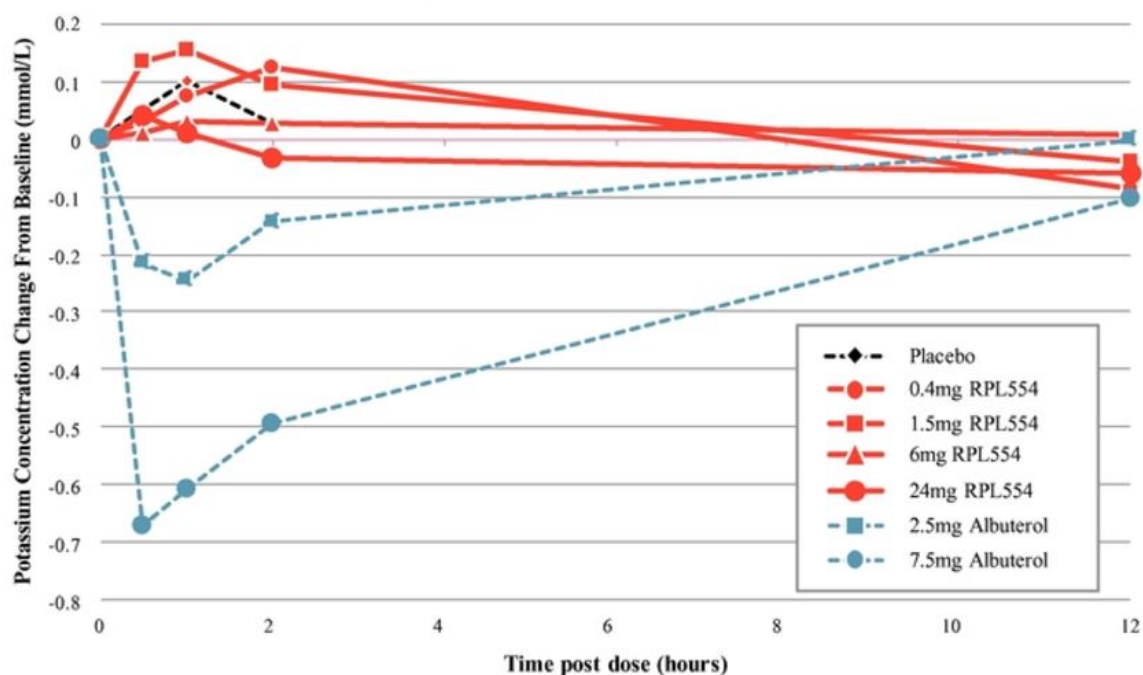
### Summary of Safety Results

RPL554 was well tolerated in each of our ten Phase 1 and 2a clinical trials that has been reported, 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.

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



### Effect on Serum Levels of Potassium



### Clinical Development Plans

We plan to conduct further 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 pMDI 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.** In July 2017 we announced the commencement of a Phase 2b dose-ranging study for RPL554 for the maintenance treatment in approximately 400 patients with COPD in Europe. The Phase 2b clinical trial is a four-week double-blind placebo-controlled parallel group trial. The primary endpoint is improvement in lung function, as measured by FEV<sub>1</sub>, after dosing with RPL554 or placebo. We expect to report top-line data from the Phase 2b trial early in the second quarter of 2018.
- The study investigates the effect of 4 weeks of twice daily treatment of four different doses of RPL554 (0.75mg, 1.5mg, 3mg and 6mg) or placebo, each administered twice per day, in patients with moderate to severe COPD. Patients will be instructed to wash out any long-acting bronchodilators but can continue with an inhaled corticosteroid if maintained at the same dose throughout the study. Albuterol may be used as rescue medication.
- The primary outcome measure is the effect of RPL554 or placebo on change from baseline in peak FEV1 over 4 weeks.
- Secondary outcome measures include various additional measurements of lung function, COPD symptoms based on a range of different scales and methodologies, and tolerability.
- Following completion of this ongoing 4-week Phase 2b clinical trial we will evaluate and possibly adjust the overall and near-term development plans for RPL554. Depending on the data from all clinical trials conducted with RPL554 to date, future interactions with regulatory authorities and our commercial assessment of different development options for RPL554 we will consider any opportunity to focus and accelerate our development plans for RPL554, including proceeding more rapidly towards Phase 3 clinical



trials, particularly with nebulized RPL554 for the maintenance treatment of COPD. Earlier entry into Phase 3 clinical trials with nebulized RPL554 for the maintenance treatment of COPD could require us to focus our resources and funding initially on the maintenance market as a priority in the short term over progressing our planned trials to evaluate nebulized RPL554 as a treatment for acute exacerbations of COPD in hospitalized patients and as a treatment for CF patients.

- **pMDI and DPI development for treatment of COPD patients.** In addition to our nebulized formulation of RPL554, we are developing RPL554 in both DPI and pMDI 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 pMDI 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 pMDI formulations has the potential to significantly increase the market opportunity for RPL554, if approved, for the maintenance treatment of COPD. Following the progression of our DPI and pMDI formulation process, we plan to commence pre-clinical studies for RPL554 in these formulations in 2018, to be followed by the first clinical trials in healthy subjects or patients with COPD.
- **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. We plan this Phase 2 clinical trial as 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. Depending on the data from all clinical trials conducted with RPL554 to date, future interactions with regulatory authorities and our commercial assessment of different development options for RPL554 we will consider any opportunity to focus and accelerate our development plans for RPL554, including proceeding more rapidly towards Phase 3 clinical trials, particularly with nebulized RPL554 for the maintenance treatment of COPD. Earlier entry into Phase 3 clinical trials with nebulized RPL554 for the maintenance treatment of COPD could require us to focus our resources and funding initially on the maintenance market as a priority in the short term over progressing our planned trials to evaluate nebulized RPL554 as a treatment for acute exacerbations of COPD in hospitalized patients and as a treatment for CF patients.

### **Additional Development Programs**

#### **RPL554 for the Treatment of Cystic Fibrosis**

##### **Overview**

We are evaluating 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 bronchodilator and anti-inflammatory 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<sub>1</sub>. 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 novel targeted therapies 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.

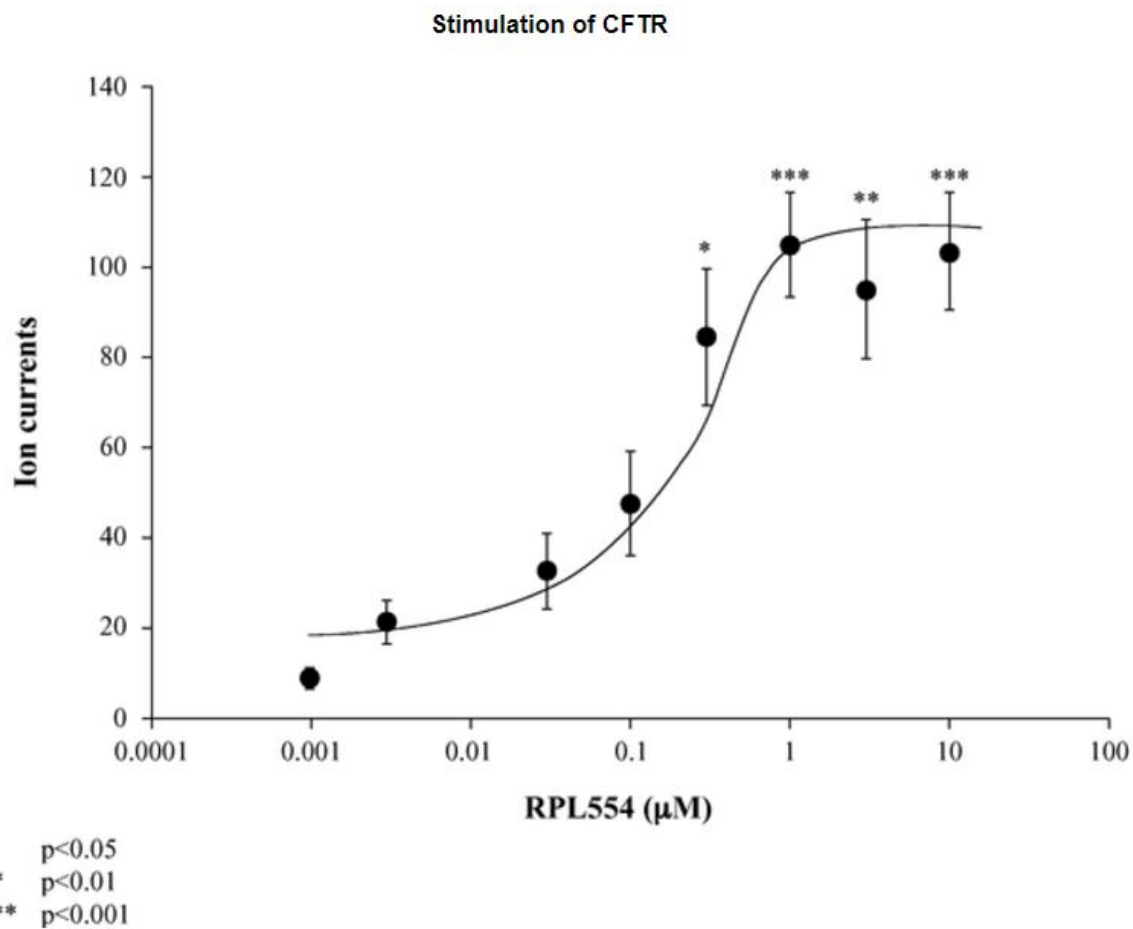
### ***Our Solution***

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.

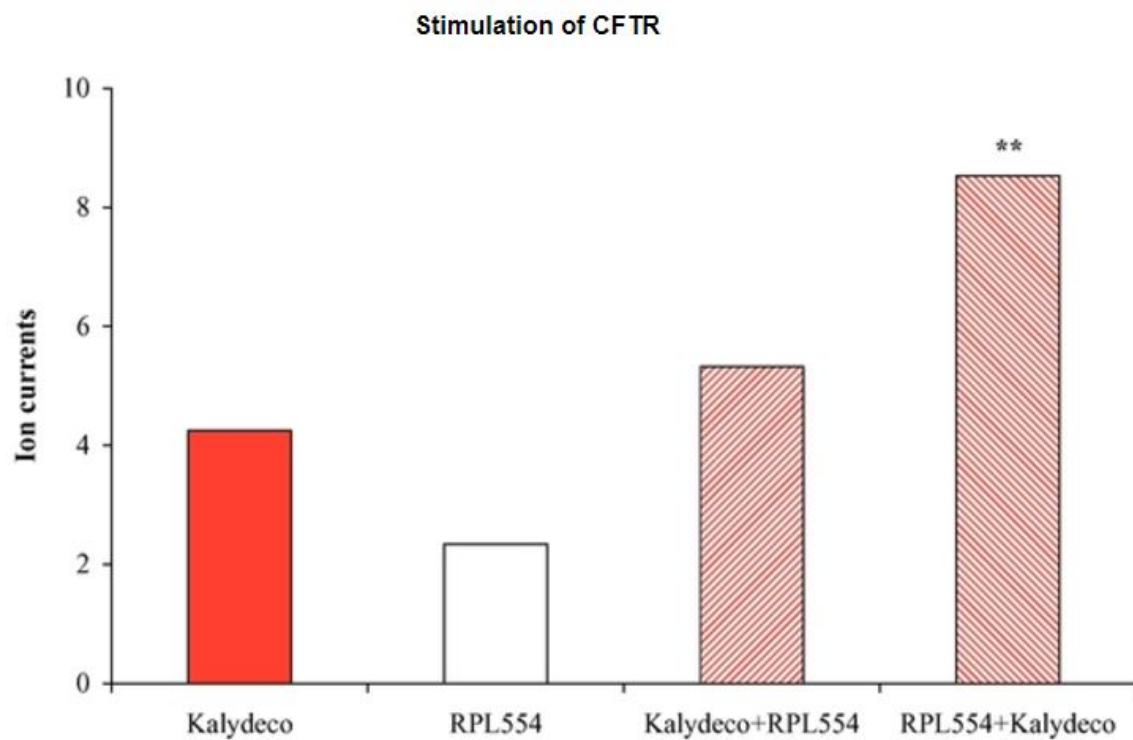
In our pre-clinical studies, RPL554 has been observed to stimulate the CFTR, as well as increase ciliary beat frequency, a key parameter determining the rate of mucus clearance, in primary airway cells and to improve electrolyte balance in the lung. Based on available data, we believe that RPL554 has 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.

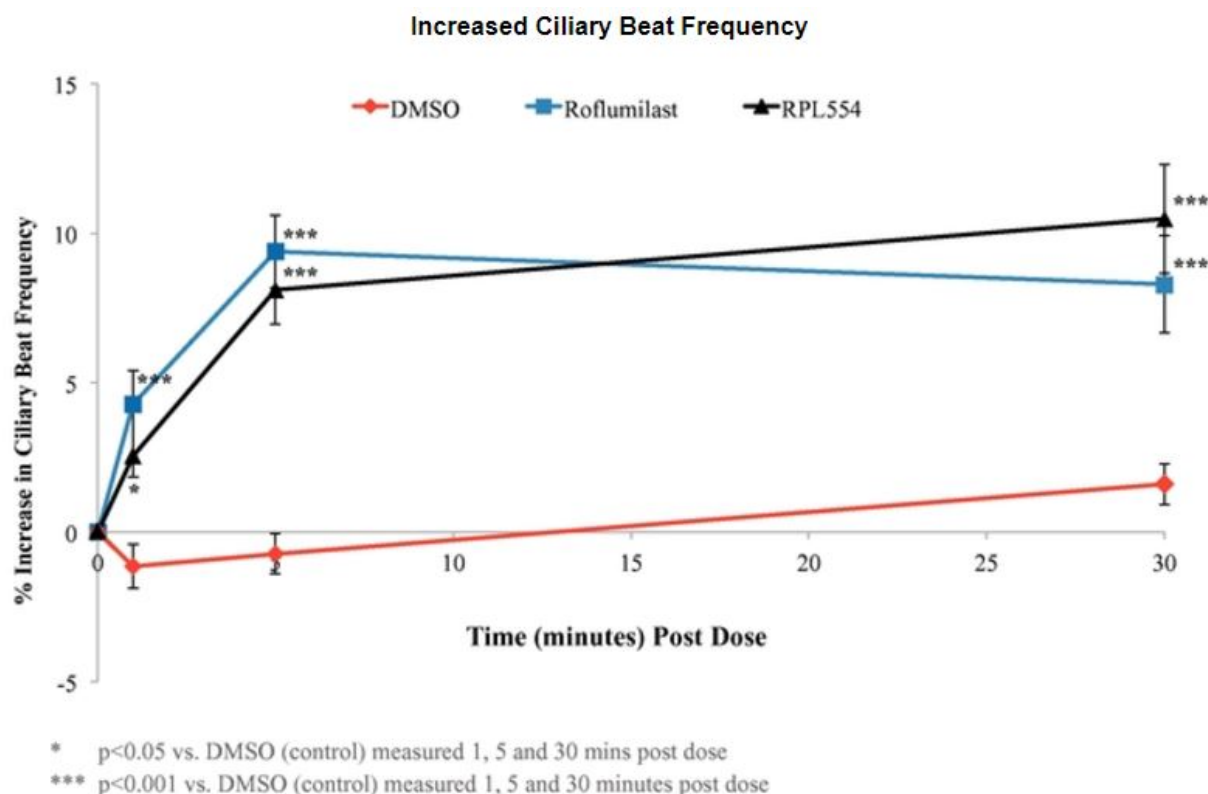


Furthermore, in a pre-clinical study comparing RPL554 to Kalydeco, both compounds increased CFTR activity in cells from a CF patient with the mutation that is appropriate for treatment with Kalydeco. When RPL554 was administered before Kalydeco, it had an additive effect, which was smaller when the compounds were delivered in the reverse order. This stimulatory effect on the CFTR, as measured by ion currents, is shown in the figure below.



\*\*  $p < 0.01$  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.



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 February 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 will evaluate the PK and PD profile and tolerability of RPL554 in patients with CF, as well as the tolerability of the compound. We expect to report top-line data from this trial in the first quarter of 2018. The results of this trial will support dose selection for a proof-of-concept Phase 2b trial in Europe in patients with CF. Currently we plan to commence this proof-of-concept trial in 2018.{add more details about the trial design and dosing}

Depending on the data from all clinical trials conducted with RPL554 to date, future interactions with regulatory authorities and our commercial assessment of different development options for RPL554 we will consider any opportunity to focus and accelerate our development plans for RPL554, including proceeding more rapidly towards Phase 3 clinical trials, particularly with nebulized RPL554 for the maintenance treatment of COPD. Earlier entry into Phase 3 clinical trials with nebulized RPL554 for the maintenance treatment of COPD could require us to focus our resources and funding initially on the maintenance market as a priority in the short term over progressing our planned trials to evaluate nebulized RPL554 as a treatment for acute exacerbations of COPD hospitalized patients and as a treatment for CF patients.

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

<b>Trial Description</b>	<b>Trial Design</b>	<b>Patient Population</b>	<b>Primary Endpoints</b>	<b>Secondary Endpoints</b>	<b>Anticipated Milestones</b>
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 <sub>1</sub> > 40% of expected levels	<ul style="list-style-type: none"> <li>PK profile</li> <li>Safety</li> </ul>	<ul style="list-style-type: none"> <li>FEV<sub>1</sub>: peak and AUC</li> </ul>	Commenced in March 2017, with top-line data expected late in the first quarter 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)	CF patients, age 18 and older, with FEV <sub>1</sub> of > 40% of expected levels All CFTR mutations	<ul style="list-style-type: none"> <li>FEV<sub>1</sub>: peak</li> </ul>	<ul style="list-style-type: none"> <li>FEV<sub>1</sub> trough</li> <li>Inflammation biomarkers</li> <li>Exacerbations</li> <li>Safety</li> </ul>	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 little experience in product candidate formulation or manufacturing, and no in-house manufacturing capability. 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 , 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 one CMO. Similarly, we currently have one CMO for our DPI development and manufacturing program and one CMO for our

pMDI development and manufacturing program. We believe that the RPL554 manufacturing processes 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 record-keeping, 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.

RPL554 for nebulized administration is currently presented in a glass vial with a flip, tear-up cap. This format is adequate for clinical trials but patient acceptance in a commercial setting is expected to be improved by a switch to presenting the suspension formulation of RPL554 in plastic ampules. We will investigate the feasibility to manufacture and supply RPL554 nebulized suspension formulation in plastic ampules. In addition to patient acceptance, switching to plastic ampules may also be more cost-effective for manufacturing in larger volumes. A decision on presentation form will be made before the start of Phase 3 clinical trials; during this evaluation process we will also review and optimize the nebulized suspension formulation as part of a quality by design program.

### **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. Additional new therapies in development or recently approved include triple combinations of existing therapies such as a long-acting anti-muscarinic bronchodilator, a long-acting beta2-agonist bronchodilator and an inhaled corticosteroid; such triple combinations have been developed by GlaxoSmithKline and Chiesi and are approved in US and EU. AstraZeneca has a triple combination product in development.

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

side 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 or be priced at a level that makes it difficult for us to supply product in a cost-efficient and profitable way.

## 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 February 6, 2018, our patent portfolio consisted of seven issued U.S. patents, four pending U.S. patent applications, 20 issued foreign patents and 52 pending foreign applications including one patent application 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 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 February 6, 2018, 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 February 6, 2018, this patent family included granted patents in Australia, Canada, China, Europe, Indonesia, Japan, Malaysia, Mexico, Philippines, Russia, the United States and Taiwan and patent applications in Israel, Japan, South Korea, 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 February 6, 2018, this patent family included granted patents Europe and the United States and a patent application in Canada. We expect patents in this family to expire in March 2034.
- The fourth of these patent families relates to the combination of RPL554 with a muscarinic receptor antagonist. As of February 6, 2018, this patent family included granted patents in Europe and the United States and patent applications in Australia, Canada, China, Israel, India, Japan, South Korea, Mexico, Russia, Thailand and the United States (continuation application). 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 February 6, 2018, this patent family included patent applications in Australia, Canada, China, Europe, Israel, Japan, Mexico, New Zealand, the United States and South Africa. 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 February 6, 2018, this patent family included patent applications in Australia, Canada, Europe (parent and divisional applications), 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 February 6, 2018, this patent family included patent applications in Australia, Brazil, Canada, China, Europe (parent and divisional applications), Indonesia, Israel, India, Japan, South Korea, Mexico, Malaysia, New Zealand, the Philippines, Singapore, South Africa, Thailand, and the United States. A notice of allowance issued on the United States application on January 11, 2018. A Communication under Rule 71(3) EPC (notice of allowance) issued on the European parent application on November 15, 2017. . 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 February 6, 2018, this patent family included a PCT application and a patent application in Taiwan. 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](http://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 under which NDA applicants must pay a substantial "program fee" for each prescription drug product approved in an NDA.

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. In addition, Congress could consider subsequent legislation to replace those elements of the ACA if so repealed. The ultimate content, timing or effect of any healthcare reform legislation on the U.S. healthcare industry is unclear.

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

Additionally, on August 2, 2011, the Budget Control Act of 2011 created measures for spending reductions was enacted, which, among other things, included aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will stay in effect through 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 December 31, 2017, we had 15 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 EC2N 1DW, United Kingdom, where we lease office space under leases that terminate in 2018 and early 2019. We also lease office space in White Plains, New York, under leases that terminate in 2018. 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.

## C. Organizational Structure.

We have two wholly-owned subsidiaries, Verona Pharma Inc., which is incorporated in the United States in the State of Delaware, and Rhinopharma Ltd., which is incorporated in Canada.

## D. Property, Plants and Equipment.

Our principal office is located at 3 More London Riverside, London SE1 2RE, United Kingdom, where we lease office space. We also lease office space in White Plains, New York. The office space in these two locations is held under four leases that terminate between August 2018 and January 2020. 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.

## Environmental Issues

For information on environmental issues that may affect our utilization of our facilities, please see the section of this Annual Report titled “Item 3.D. Risk Factors - Risks Related to Healthcare Laws and Other Legal Compliance Matters - *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.*”

## ITEM 4A: UNRESOLVED STAFF COMMENTS

Not applicable.

## ITEM 5: OPERATING AND FINANCIAL REVIEW AND PROSPECTS

### A. OPERATING RESULTS

#### 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 patient enrollment in twelve Phase 1 and 2 clinical trials for RPL554 with over 700 subjects enrolled; ten of these studies have been reported, one study is expected to report late in the first quarter of 2018 and one study is expected to report early in the second quarter of 2018. 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 commonly used short- and long-acting 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.

To evaluate RPL554 in a nebulized formulation for the maintenance treatment of COPD, in July 2017 we commenced a four week Phase 2b dose-ranging clinical trial in Europe, which is evaluating RPL554 as a single agent as compared to placebo in approximately 400 patients with moderate to severe COPD. We have now completed dosing in this study and we expect to report top-line data from this trial early in the second quarter of 2018, earlier than previously guidance of mid-2018 and original guidance of second half of 2018.

In September 2017, we reported our Phase 2a clinical trial of nebulized RPL554 for the maintenance treatment of COPD in the United Kingdom. This trial evaluated RPL554 compared to placebo as an add-on therapy to tiotropium in 30 patients. In September 2017 we also reported data from our IND-opening single-dose pharmacokinetic, or PK, trial of RPL554 in approximately 12 healthy volunteers in the US.

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 late in the first quarter of 2018. A PD trial involves the study of the biochemical and physiological effects of a drug and its mechanism of action, including the correlation of the drug's actions and effects with its chemical structure. The results of this clinical trial will 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, 2016 and 2017 we incurred net losses of £5.0 million and £20.5 million, respectively. As of December 31, 2017, we had an accumulated loss of £49.3 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.

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 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 approximately £145 million in gross proceeds from investors since such listing, of which approximately £70 million was raised in our Nasdaq listing and the accompanying private offering in Europe and the shareholder private placement; we raised a further £45 million raised in our July 2016 private placement of equity securities 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 2.12 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 2016 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 2016 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 "patent box" initiative that allows profits attributable to revenues from patents or patented products to be taxed at a lower rate than other revenue of 10%.

### **Critical Accounting Judgments and Estimates**

Our 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 Annual Report.

Our significant accounting policies are more fully described in the notes to our financial statements appearing elsewhere in this Annual Report. 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,” “Item 4.B. Business Overview - Vernalis Agreement” and Note 18 to our Annual Consolidated Financial Statements included elsewhere in this Annual Report. 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 the Black-Scholes 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 2016 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 became exercisable 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 2016 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.

### ***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.

### ***Recent Accounting Pronouncements***

We refer to Note 2.18 to our Annual Consolidated Financial Statements for the year ended December 31, 2017 included elsewhere in this Annual Report 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.

### **Internal Control Over Financial Reporting**

In connection with the preparation for our listing on Nasdaq, 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 historical 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 have remediated this material weakness by the hiring of our chief financial officer in September 2016 and enhancing our financial reporting team. We have instituted a program of controls over financial reporting that will ensure we manage our financial reporting in accordance with good business practice and Sarbanes-Oxley legislation. However, we cannot be certain that these efforts will prevent future material weaknesses or significant deficiencies from occurring.

## Results of Operations

### Comparison of Operations for the Years ended December 31, 2017 and 2016

The following table sets forth our results of operations for the periods indicated. For the convenience of the reader, we have translated pound sterling amounts as of December 31, 2017 at the noon buying rate of the Federal Reserve Bank of New York on December 29, 2017, which was £1.00 to \$1.3529. 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,		
	2016		2017
	£000's	£000's	\$000's
Research and development costs	£ (4,522)	£ (23,717)	\$ (32,087)
General and administrative costs	(2,498)	(6,039)	(8,170)
Operating loss	(7,020)	(29,756)	(40,257)
Finance income	1,841	7,018	9,495
Finance expense	(794)	(2,465)	(3,335)
Loss before taxation	(5,973)	(25,203)	(34,097)
Taxation — credit	954	4,706	6,367
Loss for the year	(5,019)	(20,497)	(27,730)
Other comprehensive income / (loss):			
Exchange differences on translating foreign operations	43	(29)	(39)
Total comprehensive loss attributable to owners of the company	£ (4,976)	£ (20,526)	\$ (27,769)



### ***Comparison of Operations for the Years ended December 31, 2017 and 2016***

The operating loss for the year ended December 31, 2017 was £29.8 million (2016: £7.0 million) and the loss after tax for the year ended December 31, 2017 was £20.5 million (2016: £5.0 million).

#### ***Research and Development Costs***

Research and development costs were £23.7 million for the year ended December 31, 2017 as compared to £4.5 million for the year ended December 31, 2016, an increase of £19.2 million. The increase was attributable to a £12.3 million increase in clinical trial expenses related to the initiation of four, and completion of two, Phase 2 clinical trials of RPL554. In addition we increased spending on contract manufacturing and other formulation work by £2.7 million and toxicology and other pre-clinical development by £1.2m. Our salary costs increased by £0.3m and our share-based payment charge by £1.2 million as we expanded our team and initiated a new long term incentive plan to drive development of RPL 554. Furthermore, our spend on third party consultants increased by £0.8 million and patent and other costs by £0.3 million.

#### ***General and Administrative Costs***

General and administrative costs were £6.0 million for the year ended December 31, 2017 as compared to £2.5 million for the year ended December 31, 2016, an increase of £3.5 million. The increase was attributable to £0.8 million increase in our salary costs and a £1.1 million increase in our share-based payment charge as we built the team to support the activities of the Company. There was an increase of £1.3 million of costs in preparation for and relating to the Global Offering, as well as ongoing compliance and other costs due to listing our ADSs on the Nasdaq stock market. We also incurred costs of £0.4 million developing our commercial strategy for RPL 554.

#### ***Finance Income and Expense***

Finance income was £7.0 million for the year ended December 31, 2017 and £1.8 million for the year ended December 31, 2016. The increase in finance income was primarily due to a decrease in the fair value of the warrant liability of £6.6 million caused by changes in the underlying assumptions for measuring the liability of the warrants issued in the July 2016 Placement, including the price and volatility of our ordinary shares and the unwinding of the expected life of the warrants.

Finance expense was £2.5 million for the year ended December 31, 2017 as compared to £0.8 million for the year ended December 31, 2016. The increase was primarily due to the foreign exchange loss on translation of foreign currency denominated cash and cash equivalents and short term investments.

As at December 31, 2017 the Company had approximately £31.4 million in cash and cash equivalents (2016: £39.8 million) and £48.8 million in short term investments (2016: £nil).

#### ***Taxation***

Taxation for the year ended December 31, 2017 amounted to a credit of £4.7 million as compared to a credit of £1.0 million for the year ended December 31, 2016, an increase in the credit amount of £3.7 million. The credits are obtained at a rate of 14.5% of 230% of our qualifying research and development expenditure, and the increase in the credit amount was primarily attributable to our increased expenditure on research and development.

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

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

	Year Ended December 31,	
	2015	2016
	£000's	£000's
Research and development costs	(7,270)	(4,522)
General and administrative costs	(1,706)	(2,498)
Operating loss	(8,976)	(7,020)
Finance income	45	1,841
Finance expense	(73)	(794)
Loss before taxation	(9,004)	(5,973)
Taxation — credit	1,509	954
Loss for the year	(7,495)	(5,019)
Other comprehensive income:		
Exchange differences on translating foreign operations	4	43
Total comprehensive loss attributable to owners of the company	(7,491)	(4,976)

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

### 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 2016 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 2016 Placement which related to the issue of warrants, and which were recorded as a finance expense (the remainder of the July 2016 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.

## B. 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 approximately £145 million from private placements of equity securities, of which approximately £70 million was raised in April 2017 through our Nasdaq listing and the accompanying private offering in Europe and the shareholder private placement; we raised a further £45 million raised in our July 2016 private placement of equity securities with a number of European and U.S.-based healthcare specialist investment firms. As of December 31, 2017, we had cash and cash equivalents of £31.4 million. As of December 31, 2017 we also held short term investments (representing bank deposits with maturities of greater than 3 months at inception) of £48.8 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,			
	2016		2017	
	£000's		£000's	
				\$000's
Net cash used in operating activities	£	(5,588)	£	(20,696)
Net cash used in investing activities		(41)		(49,469)
Net cash from financing activities		41,203		63,246
Net increase / (decrease) in cash and cash equivalents	£	35,574	£	(6,919)

The decrease in net cash used in operating activities to £20.7 million for the year ended December 31, 2017 from £5.6 million for the year ended December 31, 2016 was primarily due to an increase in loss before taxation driven by higher research and development costs.

The increase in net cash used in investing activities to £49.5 million for the year ended December 31, 2017 from £41 thousand for the year ended December 31, 2016 was due to placing funds raised in the Global Offering on term deposits with maturities of more than three months at inception.

The net cash of £63.2 million received from financing activities to for the year ended December 31, 2017 was the cash raised from the Global Offering. The £41.2 million received for the year ended December 31, 2016 was the cash received from the sale of our equity securities and warrants in connection with the July 2016 Placement.

### Operating and Capital Expenditure Requirements

As of December 31, 2017, we had an accumulated loss of £49.3 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 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 pMDI 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, cash equivalents and short-term investments will enable us to fund our operating expenses and capital expenditure requirements through the end of our Phase 2 development of nebulized RPL554 and our proof-of-concept development with DPI and pMDI formulations of RPL554 for the treatment of COPD, as well as our Phase 2 development of nebulized 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.

### C. Research and Development, Patent and Licenses, etc.

For a discussion of our research and development activities, including amounts spent on company-sponsored research and development activities for the last three financial years, see "Item 4.B. Business Overview" and "Item 5.A. Operating Results."

### D. Trend Information

Other than as disclosed elsewhere in this Annual Report, we are not aware of any trends, uncertainties, demands, commitments or events that are reasonably likely to have a material adverse effect on our net revenues, income from continuing operations, profitability, liquidity or capital resources, or that would cause the disclosed financial information to be not necessarily indicative of future operating results or financial conditions. For more information, see "Item 4.B. Business Overview," "Item 5.A. Operating Results," and "Item 5.B. Liquidity and Capital Resources."

### E. Off-Balance Sheet Arrangements

During the periods presented, we did not and do not currently have any off-balance sheet arrangements.

### F. Contractual Obligations and Commitments

The table below summarizes our contractual obligations at December 31, 2017.

	Payments Due by Period				
	Total	Less than 1 year	1 - 3 years	3 - 5 years	More than 5 years
	(£000's)				
Operating lease obligations	568	291	277	£—	£—
Total	568	291	277	£—	£—

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 contract research organizations ("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.

### Selected Quarterly Financial Data (unaudited)

Selected quarterly results from operations for the year ended December 31, 2017 and 2016 are as follows (in thousands, except per share amounts).

	Fiscal 2017 Quarter Ended			
	December 31, 2017	September 30, 2017	June 30, 2017	March 31, 2017
	£'000s	£'000s	£'000s	£'000s
Research and development costs	9,689	6,085	4,838	3,105
General and administrative costs	998	2,040	1,969	1,032

	Fiscal 2016 Quarter Ended			
	December 31, 2016	September 30, 2016	June 30, 2016	March 31, 2016
	£'000s	£'000s	£'000s	£'000s
Research and development costs	1,868	1,409	522	723
General and administrative costs	1,085	752	350	311

### ITEM 6: DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES

#### Executive Officers and Directors

The following table presents information about our executive officers and directors, including their ages as of February 27, 2017:

Name	Age	Position
<b>Executive Officers</b>		
Jan-Anders Karlsson, Ph.D.	63	Chief Executive Officer and Director
Piers Morgan	51	Chief Financial Officer
Kenneth Newman, M.D.	60	Chief Medical Officer
Peter Spargo, Ph.D.	56	Senior Vice President, Chemistry Manufacturing and Controls
Claire Poll	51	Legal Counsel
Richard Hennings	48	Commercial Director
Desiree Luthman	58	Vice President, Regulatory Affairs
<b>Non-Executive Directors</b>		
David Ebsworth, Ph.D. <sup>(1,2,3)</sup>	63	Chairman of the Board
Ken Cunningham, M.D. <sup>(2)</sup>	65	Non-executive Director
Rishi Gupta <sup>(2)</sup>	40	Non-executive Director
Mahendra Shah, Ph.D. <sup>(3)</sup>	73	Non-executive Director
Andrew Sinclair, Ph.D. <sup>(1)</sup>	46	Non-executive Director
Vikas Sinha <sup>(1)</sup>	54	Non-executive Director
Anders Ullman, Ph.D. <sup>(3)</sup>	62	Non-executive 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.

**Desiree Luthman, DDS.** Dr. Luthman has served as our Vice President, Regulatory Affairs since June 2017. Dr. Luthman has over 20 years of regulatory experience including both large and small pharmaceutical companies across different regions and different therapeutic areas. From 2015 to 2017, Dr. Luthman served as Senior Regulatory Director, Global Inflammation - Immunocology Therapeutic Area at Sanofi. From 2013 to 2015, Dr. Luthman was a Director, Global Regulatory Strategy and Science at Bristol, Meyers & Squibb. Dr. Luthman received a doctorate in dentistry from the Karolinska Institute, Stockholm, Sweden.

**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 of Medherant Ltd. Dr. Cunningham received a degree in medicine 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 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., a specialty pharmaceuticals company, Crinetics Pharmaceuticals, Inc., Soleno Therapeutics, Inc., Impel Neuropharma, Inc., and several other 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. Since January 2018, Mr. Sinha has served as an Executive Partner of MPM Capital, Inc., a life sciences investment company. From 2005 to 2016, Mr. Sinha was 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. Since 2016, he has served as Head of the COPD Centre at Sahlgrenska University Hospital,



Sweden. From 2013 to 2014, Dr. Ullman was 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 a M.D. and a Ph.D. in clinical pharmacology from the University of Gothenburg.

## Family Relationships

There are no family relationships among any of the members of our board of directors and executive officers.

## Compensation

### Executive Officer Remuneration

The following table sets forth the approximate remuneration paid during the year ended December 31, 2017 our current executive officers.

Name and Principal Position	Salary (£)	Bonus <sup>(1)</sup> (£)	Option Awards <sup>(2)</sup> (£)	All Other Compensation (£)	Total (£)
Jan-Anders Karlsson, Ph.D. Chief Executive Officer	290,000	254,000	1,632,055	29,165 <sup>(3)</sup>	2,205,220
Piers Morgan <sup>(4)</sup> Chief Financial Officer	210,000	73,500	945,464	12,600 <sup>(3)</sup>	1,241,564
Kenneth Newman, M.D. Chief Medical Officer	273,221	53,581	937,718	21,987 <sup>(4)</sup>	1,286,508
Peter Spargo, Ph.D. Senior Vice President of Chemistry, Manufacturing and Controls	190,000	46,550	641,564	—	878,114
Claire Poll Legal Counsel	170,000	59,650	574,033	4,517 <sup>(3)</sup>	808,200
Richard Hennings Commercial Director	119,231	36,200	198,258	7,154 <sup>(3)</sup>	360,843
Desiree Luthman <sup>(5)</sup> Vice President, Regulatory Affairs	113,743	22,884	126,756	—	263,383
<b>Total</b>	<b>1,366,195</b>	<b>546,365</b>	<b>5,055,849</b>	<b>75,422</b>	<b>7,043,832</b>

<sup>(1)</sup> Amount shown reflects bonuses awarded for achievement of performance goals in 2017.

<sup>(2)</sup> Amount shown represents the aggregate grant date fair value of option and restricted stock units awards granted in 2017 measured using the Black Scholes model. For a description of the assumptions used in valuing these awards, see note 16 to our Annual Consolidated Financial Statements included elsewhere in this prospectus.

<sup>(3)</sup> Amount shown represents health benefits payments and pension contributions made by us.

<sup>(4)</sup> Amount shown represents health benefits payments made by us.

<sup>(5)</sup> Mrs Luthman began her employment with us on June 12, 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 £290,000 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 was 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 at an exercise price of £1.25 per ordinary share, 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, effective September 26, 2016. This agreement entitles Mr. Morgan to receive an annual base salary of £210,000, 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. Mr. Morgan 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 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 £190,000 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. Dr. Spargo 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 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, effective September 1, 2016. This agreement, as amended, entitles Ms. Poll to receive an annual base salary of £170,000, 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. Ms. Poll is also entitled to participate in a workplace pension scheme that we contribute to on her behalf. See "— Pension, Retirement or Similar Benefits" below.

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, pursuant to which he agreed to serve as our Commercial Director, effective 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. Pursuant to his employment agreement, Mr. Hennings is also entitled to receive (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 (£1.32) and (b) restricted share units with a grant date fair value of approximately £40,000. 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.

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 US and UK 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 UK 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.

#### *Desiree Luthman, DDS.*

We entered into an employment agreement with Ms Luthman on May 1, 2017, pursuant to which she agreed to serve as our Vice-President Regulatory Affairs, effective June 15, 2017. This agreement entitles Ms Luthman to receive an annual base salary of \$265,000, or such higher rate as may be agreed in writing, and a target annual bonus opportunity of up to 25% of her annual base salary, with the amount of any such bonus based on annual performance criteria to be agreed between us and Ms Luthman. Pursuant to her employment agreement, Ms Luthman is also entitled to receive an option to purchase a total of 20,000 of our ADSs under the terms of the

Company's equity incentive plan. The ADSs relate to 160,000 ordinary shares and the exercise price is £1.32 per ordinary share.

If Ms Luthman's employment is terminated by us without "Cause" or by Ms Luthman for "Good Reason" (as each such term is defined in her offer agreement), then, subject to her signing and not revoking a general release of claims, she is entitled to receive (i) eight weeks of base salary continuation, (ii) eight weeks of continued payment of premiums for continued medical coverage under COBRA, and (iii) a pro-rated portion of the annual bonus that she otherwise would have earned in the year of termination based on actual performance in such year.

## **Equity Compensation Arrangements**

In May 2017, we closed the initial public offering of our American Depositary Shares in the United States and a private placement of our ordinary shares in Europe, together the global offering. Prior to the global offering, we 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. Since the adoption of the 2017 Incentive Plan (as defined below), no further awards are being made under either the Unapproved Scheme or the EMI Scheme.

### *EMI Option Scheme*

Under the EMI Scheme, eligible employees were granted tax-efficient options to purchase our ordinary shares. Options were granted to eligible employees who were 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 granted non-tax-qualifying options to purchase our ordinary shares. Options were 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., M.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	—	—	—	—
David Ebsworth	—	—	—	—
Anders Ullman	—	—	—	—
Ken Cunningham	—	—	—	—
Rishi Gupta	—	—	—	—
Mahendra Shah	—	—	—	—
Vikas Sinha	—	—	—	—
Andrew Sinclair	—	—	—	—

### **2017 Incentive Plan**

We have adopted the 2017 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 2017 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 2017 Incentive Plan. The 2017 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 2017 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 2017 Incentive Plan, to interpret the 2017 Incentive Plan and award agreements and to adopt, amend and repeal rules for the administration of the 2017 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 2017 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 2017 Incentive Plan.

### **Sub-Plan**

The 2017 Incentive Plan authorized the administrator to establish one or more sub-plans. Immediately after the 2017 Incentive Plan had been established, the administrator established a sub-plan. The sub-plan incorporated all of the terms of the 2017 Incentive Plan, except that only employees of ours (or our subsidiaries) were eligible to receive awards under the sub-plan. Awards under the sub-plan counted towards the total number of shares available for issuance under the 2017 Incentive Plan. The sub-plan is an "employees' share scheme" for the purposes of the UK Companies Act 2006.

## **Shares Available for Awards**

An aggregate of 6,333,000 of our ordinary shares were initially made available for issuance under the 2017 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 2017 Incentive Plan, awards may be issued under the 2017 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 2017 Incentive Plan upon the exercise of incentive options. Shares issued under the 2017 Incentive Plan may be authorized but unissued shares, shares purchased on the open market, treasury shares or ADSs.

If an award under the 2017 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 2017 Incentive Plan. Awards granted under the 2017 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 2017 Incentive Plan, but will count against the maximum number of shares that may be issued upon the exercise of incentive options.

## **Awards**

The 2017 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 2017 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 2017 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 2017 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 2017 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 2017 Incentive Plan and replacing or terminating awards under the 2017 Incentive Plan. In addition, in the event of certain non-reciprocal transactions with our shareholders, the plan administrator will make equitable adjustments to the 2017 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 2017 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 2017 Incentive Plan at any time; however, no amendment, other than an amendment that increases the number of shares available under the 2017 Incentive Plan, may materially and adversely affect an award outstanding under the 2017 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 2017 Incentive Plan with an exercise price per share that is less than the exercise price per share of the original option or SAR. The 2017 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 2017 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 2017 Incentive Plan are generally non-transferable, 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 2017 Incentive Plan, and exercise price obligations arising in connection with the exercise of options under the 2017 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

The following table summarizes the options that we granted to our directors and executive officers under the 2017 Incentive Plan in 2017:

Name	Ordinary Shares Underlying Options	Exercise Price Per Share (£)	Grant Date	Expiration Date
Jan-Anders Karlsson, Ph.D., M.D.	1,385,598	1.32	April 26, 2017	April 26, 2027
Piers Morgan	802,690	1.32	April 26, 2017	April 26, 2027
Kenneth Newman, M.D.	796,128	1.32	April 26, 2017	April 26, 2027
Peter Spargo, Ph.D.	544,681	1.32	April 26, 2017	April 26, 2027
Claire Poll	487,347	1.32	April 26, 2017	April 26, 2027
Richard Hennings	160,000	1.32	April 26, 2017	April 26, 2027
Desiree Luthman	160,000	1.32	April 26, 2017	April 26, 2027
Vikas Sinha	120,384	1.32	April 26, 2017	April 26, 2027
David Ebsworth	—	—	—	—
Anders Ullman	—	—	—	—
Ken Cunningham	—	—	—	—
Rishi Gupta	—	—	—	—
Mahendra Shah	—	—	—	—
Andrew Sinclair	—	—	—	—

The following table summarizes the RSUs that we granted to our directors and executive officers under the 2017 Incentive Plan in 2017:

Name	Restricted Share Units Granted
Jan-Anders Karlsson, Ph.D., M.D.	346,395
Piers Morgan	200,669
Kenneth Newman, M.D.	199,016
Peter Spargo, Ph.D.	136,168
Claire Poll	121,835
Richard Hennings	48,153
David Ebsworth	—
Anders Ullman	—
Ken Cunningham	—
Rishi Gupta	—
Mahendra Shah	—
Vikas Sinha	—
Andrew Sinclair	—

The options and RSUs (other than those granted to Messrs. Hennings and Sinha) 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 vest in three substantially equal annual installments following the grant date. This description relates to the options and RSUs granted in connection with the global offering.

## Non-Employee Directors Remuneration

The following table sets forth the remuneration paid during 2017 to our current non-employee directors:

Name	Annual Fees (£)	Total (£)
David Ebsworth	108,000	108,000
Anders Ullman	30,000	30,000
Ken Cunningham	40,000	40,000
Rishi Gupta	30,000	30,000
Mahendra Shah	30,000	30,000
Vikas Sinha	42,000	42,000
Andrew Sinclair	30,000	30,000
Patrick Humphrey	8,750	8,750

## 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 UK 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 2017 was £41,671, which represents contributions made by us in 2017 in respect of a defined contribution scheme in which Dr. Karlsson, Ms. Poll, Mr. Hennings and Mr. Morgan participated.

## C. Board Practices

### Composition of our Board of Directors

Our Board is comprised of eight members. 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.

The expiration of the current terms of the members of our board of directors and the period each member has served in that term are as follows:

Name	Year Current Term Began	Next year of re-election
Jan-Anders Karlsson, Ph.D.	2012	2020
David Ebsworth, Ph.D.	2014	2018
Ken Cunningham, M.D.	2015	2019
Rishi Gupta	2016	2021
Mahendra Shah, Ph.D.	2016	2020
Andrew Sinclair, Ph.D.	2016	2019
Vikas Sinha	2016	2021
Anders Ullman, M.D., Ph.D.	2015	2018

There are no arrangements or understanding between us and any of the members of our board of directors providing for benefits upon termination of their service.

## **Committees of our Board of Directors**

Our Board has three standing committees: an Audit Committee, a Remuneration Committee and a Nomination and Governance Committee.

### ***Audit Committee of the Board***

The Audit Committee, which consists of Vikas Sinha, Dr. David Ebsworth and Dr. Andrew Sinclair, 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 Audit Committee. The Audit Committee consists of members of our Board who are financially literate and are also considered to be "audit committee financial experts" as defined by applicable SEC rules and have 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 include:

- recommending the appointment of the independent auditor to the general meeting of shareholders;
- the appointment, compensation, retention and oversight of the independent auditor;
- 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 our Board on at least an annual basis;
- reviewing and discussing with the executive officers, our Board and the independent auditor our financial statements and our financial reporting process; and
- considering and recommending to our Board whether the audited financial statements be approved.

The Audit Committee will meet as often as one or more members of the 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 auditor, without our executive officers being present.

### ***Remuneration Committee of the Board***

The Remuneration Committee, which consists of Dr. Ken Cunningham, Dr. David Ebsworth and Rishi Gupta, assists the Board in determining directors' and senior executives' compensation. Dr Cunningham serves as Chairman of the Committee.

The Remuneration Committee's responsibilities include:

- identifying, reviewing and proposing policies relevant to the compensation of the Company's directors and executive officers;
- 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;
- appointing and setting the terms of reference for any remuneration consultants who advise the Committee and obtain benchmarking data with respect to the directors' and executive officers' compensation; and
- reviewing and assessing risks arising from our compensation policies and practices.

### ***Nomination and Governance Committee of the Board***

The Nomination and Governance Committee, which consists of Dr. David Ebsworth, Dr. Mahendra Shah and Dr. Anders Ullman, assists our Board in identifying individuals qualified to become executive and non-executive directors of our Company consistent with criteria established by our Board and in developing our corporate governance principles. Dr Ebsworth serves as Chairman of the Committee.

The Nomination and Governance Committee's responsibilities include:

- reviewing and evaluating the structure, size and composition of our Board and making recommendations with regard to any adjustments considered necessary;
- drawing up selection criteria and appointment procedures for Board members;
- identifying and nominating, for the approval of our Board, candidates to fill vacancies on the Board and its corresponding committees;
- keeping under review the leadership needs of the Company, both executive and non-executive, and planning the orderly succession of such appointments; and
- assessing the functioning of our Board and individual members and reporting the results of such assessment to the Board.

#### **D. Employees**

As of December 31, 2017, 2016 and 2015, we had 15, 11, and 9 employees, respectively. All of our employees were based in the United Kingdom, except that, as of December 31, 2017, 2016 and 2015, we had one to four employees based outside of the United Kingdom. All of our employees were engaged in either administrative or research and development functions. None of our employees are covered by a collective bargaining agreement.

#### **E. Share Ownership**

For information regarding the share ownership of members of our board and executive officers and arrangements involving our employees in our share capital, see “Item 6.B. Compensation,” Item 7.A. Major Shareholders” and “Item 7.B. Related Party Transactions.”

## ITEM 7: MAJOR SHAREHOLDERS AND RELATED PARTY TRANSACTIONS

### A. MAJOR SHAREHOLDERS

The following table sets forth information relating to the beneficial ownership of our ordinary shares as of December 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 February 27, 2018 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 is computed on the basis of 105,017,400 of our ordinary shares outstanding as of February 1, 2018. Ordinary shares that a person has the right to acquire within 60 days of December 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. As of February 1, 2018, 55,931,336 ordinary shares, representing 53% of our issued and outstanding ordinary shares, were held by 14 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.

<u>Name and address of beneficial owner</u>	Number of Shares Beneficially Owned	
	Number	Percentage
<b>3% or Greater Shareholders:</b>		
Novo A/S <sup>(1)</sup>	14,159,611	13%
Vivo Capital affiliates <sup>(2)</sup>	13,811,584	13%
OrbiMed Private Investments VI, LP <sup>(3)</sup>	11,871,114	11%
Growth Equity Opportunities Fund IV, LLC <sup>(4)</sup>	11,527,019	11%
Abingworth Bioventures VI, LP <sup>(5)</sup>	8,619,774	8%
venBio Select Advisor <sup>(6)</sup>	7,000,000	7%
Biodiscovery 4 FCPI <sup>(7)</sup>	6,652,398	6%
Foresite <sup>(8)</sup>	5,000,000	5%
Tekla Capital affiliates <sup>(9)</sup>	5,296,845	5%
Aisling Capital IV, LP <sup>(10)</sup>	4,138,643	4%
Arix Bioscience Holdings Ltd affiliates <sup>(11)</sup>	3,916,493	4%
Canaccord Genuity Group, Inc. <sup>(12)</sup>	3,255,792	3%
<b>Executive Officers and Directors:</b>		
Jan-Anders Karlsson, Ph.D. <sup>(13)</sup>	749,142	1%
Piers Morgan <sup>(14)</sup>	100,000	—%
Kenneth Newman, M.D. <sup>(15)</sup>	356,665	1%
Claire Poll <sup>(16)</sup>	236,663	—%
Richard Hennings	—	—%
Peter Spargo, Ph. D. <sup>(17)</sup>	139,663	—%
Ken Cunningham, M.D.	—	—%
David Ebsworth, Ph.D. <sup>(18)</sup>	140,703	—%
Rishi Gupta	—	—%
Mahendrah Shah, Ph.D.	—	—%
Andrew Sinclair, Ph.D. <sup>(19)</sup>	—	—%
Vikas Sinha <sup>(20)</sup>	22,222	—%
Anders Ullman, Ph.D.	—	—%
All executive officers and directors as a group (13 persons)	1,745,058	2%

(1) Consists of (a) 12,389,985 ordinary shares held directly by Novo A/S, or Novo, and (b) warrants to purchase 1,769,626 ordinary shares. 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 June 6, 2017. Novo's mailing address is Tuborg Havnevej 19, Hellerup, G7 2900, Denmark.

(2) Consists of (a) 2,388,728 ordinary shares held directly by Vivo Ventures Fund VI, L.P., or Vivo VI, of which 1,126,760 are held in the form of ADSs, (b) warrants to purchase 370,871 ordinary shares held directly by Vivo VI, (c) warrants to purchase 2,717 ordinary shares held directly by Vivo Ventures VI Affiliates Fund, L.P., or Vivo Affiliates VI, (d) 9,554,917 ordinary shares held directly by Vivo Ventures Fund VII L.P., or Vivo VII, of which 4,507,040 are held in the form of ADSs, (e) warrants to purchase 1,462,477 ordinary shares held directly by Vivo VII, (f) warrants to purchase 31,874 ordinary shares held directly by Vivo Ventures VII Affiliates Fund, L.P., or 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 May 30, 2017. Vivo Capital's mailing address is 505 Hamilton Avenue, Suite 200, Palo Alto, CA 94301.

- (3) Consists of (a) 10,003,175 ordinary shares held directly by OrbiMed Private Investments VI, LP, or OrbiMed VI, of which 5,333,328 are held in the form of ADSs and (b) warrants to purchase 1,867,939 ordinary shares 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 May 25, 2017. OrbiMed Advisors' mailing address is 601 Lexington Avenue, 54th Floor, New York, NY 10022.
- (4) Consists of (a) 9,757,393 ordinary shares held directly by Growth Equity Opportunities Fund IV, LLC, or GEO, of which 5,333,328 are held in the form of ADSs, and (c) warrants to purchase 1,769,626 ordinary shares 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 May 8, 2017. GEO's mailing address is 1954 Greenspring Drive, Suite 600, Timonium, MD 21093-4135.
- (5) Consists of (a) 7,215,553 ordinary shares held directly by Abingworth Bioventures VI, LP, or Abingworth VI, of which 3,705,000 are held in the form of ADSs, and (b) warrants to purchase 1,404,221 ordinary shares 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 May 9, 2017. Abingworth VI's mailing address is 38 Jermyn Street, London SW1Y 6DN, United Kingdom.
- (6) Consists of 7,000,000 ordinary shares held in the form of ADSs by VenBio Select Advisor. This information is based on information known to us. The mailing address for VenBio Select Advisor is 120 W 45th St #2802, New York, NY 10036
- (7) Consists of (a) 5,767,585 ordinary shares held in the form of ADSs by Biodiscovery 4 FCPI, or Biodiscovery, and (b) warrants to purchase 884,813 ordinary shares held directly by Biodiscovery. Beneficial ownership information is based on information known to us and a Form TR-1 provided to us on May 5, 2017. The mailing address for Biodiscovery is 47 rue du Faubourg Saint-Honoré 75401 Cedex 08 Paris France
- (8) Consists of 5,000,000 ordinary shares held in the form of ADSs by Foresight Capital Management. This information is based on information known to us. The mailing address for Foresight Capital Management is 600 Montgomery Street, Suite 4500, San Francisco, CA 94111
- (9) Consists of (a) 4,412,031 ordinary shares held directly by Tekla World Healthcare Fund, or Tekla World, of which 2,200,000 are held in the form of ADSs, (b) warrants to 513,192 purchase ordinary shares held directly by Tekla World, and (c) warrants to purchase 371,622 ordinary shares 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) 3,548,768 ordinary shares held directly by Aisling Capital IV, LP, or Aisling, of which 2,074,080 are held in the form of ADSs, and (b) warrants to purchase 589,875 ordinary shares held directly by Aisling. This information is based on information known to us and a TR-1 provided to us on June 6, 2017. The mailing address of Aisling is Aisling Capital, 888 Seventh Avenue, 12th Floor, New York, NY 10106
- (11) 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 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.

- (12) Canaccord Genuity Group Inc. is the beneficial owner of an aggregate of 3,255,792 ordinary shares held directly by (a) Hargreave Hale which holds 2,941,250 ordinary shares and (b) Canaccord Genuity Wealth Management which holds 314,542 ordinary shares. This information is based on information known to us. The mailing address for Canaccord Genuity Group Inc. is 88 Wood Street, London, UK, EC2V 7QR.
- (13) Consists of (a) 89,150 ordinary shares and (b) 659,992 options to purchase ordinary shares that are or will be immediately exercisable within 60 days of February 1, 2018.
- (14) Consists of 100,000 options to purchase ordinary shares that are or will be immediately exercisable within 60 days of February 1, 2018.
- (15) Consists of 356,665 options to purchase ordinary shares that are or will be immediately exercisable within 60 days of February 1, 2018.
- (16) Consists of (a) 95,000 ordinary shares and (b) 141,663 options to purchase ordinary shares that are or will be immediately exercisable within 60 days of February 1, 2018.
- (17) Consists of (a) 13,000 ordinary shares and (b) 126,663 options to purchase ordinary shares that are or will be immediately exercisable within 60 days of February 1, 2018.
- (18) Consists of (a) 135,787 ordinary shares, and (b) warrants to purchase 4,916 ordinary shares.
- (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.
- (20) Consists of 22,222 options to purchase ordinary shares that are or will be immediately exercisable within 60 days of February 1, 2018.

To our knowledge, and other than changes in percentage ownership as a result of the shares issued in connection with our initial public offering of our ADSs, there has been no significant change in the percentage ownership held by the major shareholders listed above since January 1, 2017, except as discussed under the heading "Related Party Transactions."

The major shareholders listed above do not have voting rights with respect to their ordinary shares that are different from the voting rights of other holders of our ordinary shares.

## Participation in the Global Offering

In April 2017, the holders of 3% or more of our common shares participated in the global offering as follows:

Investor	Number of ADSs or shares subscribed for	Aggregate purchase price
Novo A/S	740,740 ADSs	USD 9,999,990
Vivo Capital affiliates	563,380 ADSs	USD 7,605,630
OrbiMed Private Investments VI, LP	666,666 ADSs	USD 8,999,991
New Enterprise Associates, LP	666,666 ADSs	USD 8,999,991
Abingworth Bioventures VI, LP	463,125 ADSs	USD 6,252,188
venBio Select Advisor	875,000 ADSs	USD 11,812,500
Biodiscovery 4 FCPI	444,444 ADSs	USD 5,999,994
Foresite	600,000 ADSs	USD 8,100,000
Tekla Capital affiliates	275,000 ADSs	USD 3,712,500
Aisling Capital IV, LP	259,260 ADSs	USD 3,500,010
Arix Bioscience Holdings Ltd affiliates	170,228 ADSs	USD 2,298,078
Canaccord Genuity Group, Inc.	1,255,001 shares	GBP 1,656,601

## Shareholder Private Placement

In May 2017, we issued and sold 13,373 ordinary shares to our Chairman, Dr. David Ebsworth, for aggregate gross proceeds to us of £18,000.



**Registration Rights Agreement**

In July 2016, we entered into a registration rights agreement that provided certain 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 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, with respect to the ordinary shares and any ADSs held by them.

**Demand Registration Rights**

At any time, the holders of at least a majority of the registrable securities as defined in the registration rights agreement have the right to demand that we effect an underwritten public offering of their 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, and Abingworth, 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, and Abingworth to our board of directors, who are Dr. Mahendra Shah, Mr. Rishi Gupta, and Dr. Andrew Sinclair, respectively. The appointment rights under the 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.

**Indemnification Agreements**

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 have also entered into a deed of indemnity with each of our directors and executive officers and this has been in place since March 31, 2017. In addition to such indemnification, we provide our directors and executive officers with directors' and officers' liability insurance.

**B. Related Party Transactions.**

The following is a description of related party transactions we have entered into since January 1, 2017 or currently in effect with any member of our board of directors and executive officers.

**Agreements with Our Executive Officers and Directors**

We have entered into employment agreements with certain of our executive officers and service agreements with our non-employee directors. See Item 6B and note 8 of the financial statements.

**Participation in U.S. Initial Public Offering**

As part of the global offering our Chairman, Dr. David Ebsworth, purchased 13,373 shares at £1.32 per share generating gross proceeds of £18 thousand. The transaction was on the same terms as third parties.

**C. Interests of Experts and Counsel**

Not applicable.

## ITEM 8: FINANCIAL INFORMATION

### A. Consolidated Statements and Other Financial Information.

#### Consolidated Financial Statements

Our consolidated financial statements are appended at the end of this Annual Report, starting at page F-1, and are incorporated herein by reference.

#### Legal Proceedings

We are not subject to any material legal proceedings.

#### Dividend Distribution 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.

### B. Significant Changes.

There have been no significant changes since December 31, 2017.

## ITEM 9: THE OFFER AND THE LISTING

### A. Offer and Listing Details.

Our ADSs have been listed on The Nasdaq Global Market under the symbol “VRNA” since April 27, 2017. The initial public offering price of our ADSs was \$13.50 per ADS. The following table sets forth for the periods indicated the high and low sales prices per common share as reported on The Nasdaq Global Market:

	Price Per Common ADS (\$)	
	High	Low
<b>Year Ended December 31,</b>		
2017 (from April 27 through December 31)	16.95	10.80
<b>Quarter Ended</b>		
Second Quarter 2017 (beginning April 27)	16.26	11.40
Third Quarter 2017	16.95	11.54
Fourth Quarter 2017	15.75	10.80
First Quarter 2018 (through February 16)	13.25	11.69
<b>Month of</b>		
August 2017	12.70	11.80
September 2017	16.95	11.96
October 2017	15.75	13.35
November 2017	14.13	10.80
December 2017	12.10	11.30
January 2018	13.25	12.21
February 2018 (through February 16)	12.80	11.693

Our ordinary shares have been trading on AIM, a market operated by the London Stock Exchange plc, under the symbol “VRP” since September 2006. The following table sets forth, for the periods indicated, the reported high and low closing sale prices of our ordinary shares on AIM in pounds sterling.

	Price Per Share (£)	
	High	Low
<b>Year Ended December 31,</b>		
2013	2.58	0.88
2014	2.18	0.53
2015	3.36	0.60
2016	2.16	1.19
2017	1.69	1.04
<b>Quarter Ended</b>		
First Quarter 2016	2.16	1.19
Second Quarter 2016	1.86	1.41
Third Quarter 2016	1.73	1.48
Fourth Quarter 2016	2.06	1.55
First Quarter 2017	1.69	1.25
Second Quarter 2017	1.61	1.11
Third Quarter 2017	1.53	1.12
Fourth Quarter 2017	1.48	1.04
First Quarter 2018 (through February 16)	1.21	1.02
<b>Month of</b>		
August 2017	1.24	1.16
September 2017	1.53	1.12
October 2017	1.48	1.33
November 2017	1.34	1.06
December 2017	1.11	1.04
January 2018	1.21	1.06
February 2018 (through February 16)	1.21	1.02

**B. Plan of Distribution.**

Not applicable.

**C. Markets.**

Our Ordinary Shares have been listed on the AIM market of the London Stock Exchange since September 19, 2006, and our ADSs have been listed on The Nasdaq Global Market under the symbol “VRNA” since April 27, 2017.

**D. Selling Shareholders.**

Not applicable.

**E. Dilution.**

Not applicable.

**F. Expenses of the Issue.**

Not applicable.

**ITEM 10: ADDITIONAL INFORMATION****A. Share Capital.**

Not applicable.

**B. Memorandum and Articles of Association.**

The information in response to this item is contained under the caption “Description of Share Capital and Articles of Association” in our final prospectus filed with the Securities and Exchange Commission on April 28, 2017 and is incorporated herein by reference.

**C. Material Contracts.**

The following are summaries of each material contract to which we are a party for the two years preceding the date of this Annual Report.

**Underwriting Agreement**

On April 26, 2017, we entered into an underwriting agreement with Jefferies LLC and Stifel, Nicolaus & Company, Incorporated, as representatives of the underwriters, on April 26, 2017, for the initial public offering of 5,768,000 American Depositary Shares in the United States and the private placement of 1,255,001 ordinary shares in Europe. Pursuant to the underwriting agreement, we paid underwriting discounts and commissions of \$0.9450 per ADS and £0.0924 per ordinary shares. The underwriting agreement contained customary representations and warranties. We also agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, and to contribute to payments the underwriters may be required to make in respect of such liabilities.

**Employment Agreements**

We have entered into employment agreements with our executive officers. Information on the employment agreements may be found in this Annual Report under “Item 6.B. Compensation-Executive Officer Remuneration-Executive Officer Employment Agreements” and is incorporated herein by reference.

**Indemnification Agreements**

We have entered into indemnification agreements with our executive officers and board members. Information on the indemnification agreements may be found in this Annual Report under “Item 7-Major Shareholders and Related Party Transactions-Indemnification Agreements” and is incorporated herein by reference.

**Registration Rights Agreements**

We have entered into registration rights agreement with certain of our existing shareholders. Information on the registration rights agreements may be found in this Annual Report under “Item 7-Major Shareholders and Related Party Transactions-Registration Rights Agreement” and is incorporated herein by reference.

**Relationship Agreements**

We have entered into relationship agreements with certain of our existing shareholders. Information on these relationship agreements may be found in this Annual Report under “Item 7-Major Shareholders and Related Party Transactions-Relationship Agreements” and is incorporated herein by reference.

**Lease**

Our principal office is located at 3 More London Riverside, London SE1 2RE, United Kingdom, where we lease office space. We also lease office space in White Plains, New York. The office space in these two locations is held under four leases that terminate between August 2018 and January 2020 and under these leases we pay £0.3m per year. 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.

## D. 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 our Articles of Association on the right of non-residents to hold or vote shares.

## E. Taxation

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 subject to special tax accounting rules as a result of any item of gross income with respect to ordinary shares or ADSs being taken into account in an applicable financial statement;
- persons that own or are deemed to own ten percent or more of our shares by vote or value; 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 ("PFIC") 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.

## **F. Dividends and Paying Agents.**

Not applicable.

## **G. Statement by Experts.**

Not applicable.

## **H. Documents on Display.**

We maintain a corporate website at [www.veronapharma.com](http://www.veronapharma.com). We make available free of charge on our website our Reports on Form 6-K and we intend make available our Annual Reports on Form 20-F, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. Information contained on, or that can be accessed through, our website does not constitute a part of this Annual Report. We have included our website address in this Annual Report solely as an inactive textual reference.

You may also review a copy of this Annual Report, including exhibits and any schedule filed herewith, and obtain copies of such materials at prescribed rates, at the SEC's Public Reference Room in Room 1580, 100 F Street, N.E., Washington, D.C. 20549. You may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. The SEC maintains a website ([www.sec.gov](http://www.sec.gov)) that contains reports, proxy and information statements and other information regarding registrants that file electronically, such as us, with the SEC.

References made in this Annual Report to any contract or other document of Verona Pharma plc are not necessarily complete and you should refer to the exhibits attached or incorporated by reference into this Annual Report for copies of the actual contract or document.

**I. Subsidiary Information.**

Not applicable.

## ITEM 11: 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.

### ***Currency 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***

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.

See note 3.1 of the financial statements for quantitative disclosures about market risk.

## ITEM 12: DESCRIPTION OF SECURITIES OTHER THAN EQUITY SECURITIES

### **A. Debt Securities.**

Not applicable.

### **B. Warrants and Rights.**

Not applicable.

### **C. Other Securities.**

Not applicable.

### **D. American Depositary Shares.**

#### **Fees and Charges**

Holders of our ADSs are 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

Holders of our ADSs are also 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 American Depositary Receipts; 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 the Depositary Trust Company, or 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. Note that the fees and charges holders of our ADSs may be required to pay may vary over time and may be changed by us and by the depositary. Holders of our ADSs 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.

## PART II

### ITEM 13: DEFAULTS, DIVIDEND ARREARAGES AND DELINQUENCIES

None.

### ITEM 14: MATERIAL MODIFICATIONS TO THE RIGHTS OF SECURITY HOLDERS AND USE OF PROCEEDS

- A. Not applicable
- B. Not applicable
- C. Not applicable
- D. Not applicable

#### E. Use of Proceeds.

In May 2017, we completed the initial public offering of our American Depositary Shares in the United States and a private placement of our ordinary shares in Europe, or the global offering. In the global offering we issued and sold 6,501,738 ADSs, including 733,738 ADSs issued and sold upon the partial exercises of the underwriters pursuant to their overallotment option to purchase additional ADSs, at a public offering price of \$13.50 per ADS and 1,225,001 ordinary shares at an offering price of £1.32 per share.

The offer and sale of all of the ADSs and ordinary shares in the global offering was registered under the Securities Act pursuant to a registration statement on Form F-1 (File No. 333-217124), which was declared effective by the SEC on April 26, 2017, and a registration statement on Form F-1 to register additional securities (File No. 333-217487), which was immediately effective upon filing on April 26, 2017, or, together, the Registration Statement. Under the Registration Statement, we registered 5,768,000 ADSs, 1,225,001 ordinary shares, and 865,200 ADSs issuable upon exercise of the underwriters' option to purchase additional ADSs at a public offering price of \$13.50 per ADS and £1.32 per ordinary share, for a registered aggregate offering price of approximately \$89.9 million including the 733,738 ADSs issued and sold upon the partial exercises of the underwriters' option to purchase additional ADSs. Following the sale of the ADSs and ordinary shares in connection with the closing of the global offering, the offering terminated. The offering commenced on April 18, 2017 and did not terminate until the sale of all of the shares offered. Jefferies LLC and Stifel, Nicolaus & Company, Incorporated acted as joint book-running managers of the offering, and Wedbush Securities Inc. and SunTrust Robinson Humphrey, Inc. acted as co-managers of the offering.

In addition, a further 254,099 shares were issued to private investors for proceeds of \$0.4m.

We received aggregate gross proceeds from the offering of approximately \$90.3 million, or aggregate net proceeds of approximately \$80.8 million after deducting underwriting discounts and commissions of approximately \$6.3 million and offering expenses of \$3.2 million. No payments for such expenses were made directly or indirectly to (i) any of our officers, members of our board of directors, or their associates, (ii) any persons owning 10% or more of any class of our equity securities or (iii) any of our affiliates.

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

### ITEM 15: CONTROLS AND PROCEDURES

#### Disclosure Controls and Procedures.

Our management, with the participation of our principal executive officer and principal financial officer, has evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a- 15(e) and 15d- 15(e) under the Securities Exchange Act of 1934, as amended), as of the end of the period covered by this Annual Report on Form 20-F. Based on such evaluation, our principal executive officer and principal financial officer have concluded that as of such date, our disclosure controls and procedures were effective at the reasonable assurance level as of December 31, 2017.

This annual report does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of the company's registered public accounting firm due to a transition period established by rules of the Securities and Exchange Commission for newly public companies.

#### **Material Weaknesses in Internal Control Over Financial Reporting.**

This Annual Report on Form 20-F does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of our registered public accounting firm due to a transition period established by rules of the Securities and Exchange Commission for newly public companies.

In connection with the preparation for the initial public offering of our ADSs, 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 Ltd. 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

We have remediated this material weakness by the hiring of our chief financial officer in September 2016 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 prevent future material weaknesses or significant deficiencies from occurring. Review updated remediation language.

#### **Changes in Internal Control Over Financial Reporting.**

Other than as discussed above, there has been no change in our internal control over financial reporting (as defined in Rule 13a-15(f) under the Exchange Act) during the period covered by this annual report that has materially affected, or is reasonably likely to materially affect, internal control over financial reporting.

#### **ITEM 16A: AUDIT COMMITTEE FINANCIAL EXPERT**

Our board of directors has determined that Vikas Sinha, Dr. David Ebsworth and Dr. Andrew Sinclair each qualify as an audit committee financial expert as defined by the rules of the Securities and Exchange Commission and has the requisite financial sophistication under the applicable rules and regulations of Nasdaq. Mr. Sinha and Drs. Ebsworth and Sinclair are each independent as such term is defined in Rule 10A-3 under the Securities Exchange Act of 1934, as amended, and under the listing standards of Nasdaq.

#### **ITEM 16B: CODE OF ETHICS**

##### **Code of Business Conduct and Ethics**

We have adopted a Code of Business Conduct and Ethics, or the Code of Conduct, that is applicable to all of our employees, executive officers, members of our board of directors, and consultants. The Code of Conduct is available on our website at [www.veronapharma.com](http://www.veronapharma.com). We intend to satisfy the disclosure requirement under Item 16B(e) of Form 20-F regarding amendment to, or waiver from, a provision of our Code of Conduct, as well as Nasdaq's requirement to disclose waivers with respect to directors and executive officers, by posting such information on our website at the address and location specified above. Our executive officers are responsible for administering the Code of Conduct. Amendment, alteration or termination of the Code of Conduct requires the approval of our board of directors.

## ITEM 16C: PRINCIPAL ACCOUNTANT FEES AND SERVICES

The following table summarizes the fees of PricewaterhouseCoopers LLP, our independent registered public accounting firm, billed to us for each of the last two fiscal years for audit and other services:

Fee Category	2016	2017
	£'000s	£'000s
Audit Fees	80	117
Audit-Related Fees	525	333
Other Services	—	150
Total Fees	605	600

### Audit-Related Fees

For the year ended December 31, 2017, audit related services include fees for quarterly interim reviews, advice on compliance with Sarbanes-Oxley legislation and assurance on information included in the Company's U.S. registration statement for the April 2017 initial public offering in the United States (the "Global Offering"). For the year ended December 31, 2017, an amount of £256 thousand in relation to these services was offset against share premium on completion of the Global Offering.

For the year ended December 31, 2016, audit related services include assurance reporting on historical financial information included in the Company's U.S. registration statement for the Global Offering. As at December 31, 2016 an amount of £466 thousand in relation to these services was booked in deferred IPO costs that was offset against share premium on completion of the Global Offering.

### Tax Fees

We did not incur any tax fees for services from PricewaterhouseCoopers LLP in 2016 or 2017.

### All Other Fees

We did not incur any other fees in 2017 or 2016.

### Audit Committee Pre-Approval Policy and Procedures

The Audit Committee has adopted a policy, or the Pre-Approval Policy, which sets forth the procedures and conditions pursuant to which audit and non-audit services proposed to be performed by the independent auditor may be pre-approved. The Pre-Approval Policy generally provides that we will not engage PricewaterhouseCoopers LLP to render any audit, audit-related, tax or permissible non-audit service unless the service is either (i) explicitly approved by the Audit Committee, or specific pre-approval, or (ii) entered into pursuant to the pre-approval policies and procedures described in the Pre-Approval Policy, or general pre-approval. Unless a type of service to be provided by PricewaterhouseCoopers LLP has received general pre-approval under the Pre-Approval Policy, it requires specific pre-approval by the Audit Committee or by a designated member of the Audit Committee to whom the committee has delegated the authority to grant pre-approvals. Any proposed services exceeding pre-approved cost levels or budgeted amounts will also require specific pre-approval. For both types of pre-approval, the Audit Committee will consider whether such services are consistent with the SEC's rules on auditor independence. The Audit Committee will also consider whether the independent auditor is best positioned to provide the most effective and efficient service, for reasons such as its familiarity with our business, people, culture, accounting systems, risk profile and other factors, and whether the service might enhance our ability to manage or control risk or improve audit quality. All such factors will be considered as a whole, and no one factor should necessarily be determinative. The Audit Committee may also review and generally pre-approve the services (and related fee levels or budgeted amounts) that may be provided by PricewaterhouseCoopers LLP without first obtaining specific pre-approval from the Audit Committee. The Audit Committee may revise the list of general pre-approved services from time to time, based on subsequent determinations.



**ITEM 16D: EXEMPTIONS FORM THE LISTING STANDARDS FOR AUDIT COMMITTEES**

None

**ITEM 16E: PURCHASES OF EQUITY SECURITIES BY THE ISSUER AND AFFILIATED PURCHASERS**

None

**ITEMS 16F: CHANGE IN REGISTRANT'S CERTIFYING ACCOUNTANT**

There has been no change in our independent accountant during our two most recent fiscal years.

**ITEM 16G: CORPORATE GOVERNANCE**

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 follow U.K. corporate governance practices in lieu of Nasdaq corporate governance rules as follows:

We do not 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 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.

**ITEM 16H: MINE SAFETY DISCLOSURE**

None

**PART III****ITEM 17: FINANCIAL STATEMENTS**

We have elected to provide financial statements pursuant to Item 18.

**ITEM 18: FINANCIAL STATEMENTS**

The financial statements are filed as part of this Annual Report beginning on page F-1.

**ITEM 19: EXHIBITS**

The Exhibits listed in the Exhibit Index at the end of this Annual Report are filed as Exhibits to this Annual Report.

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**Incorporated by Reference to Filings Indicated**

Exhibit Number	Exhibit Description	Form	File No.	Exhibit No. No.	Filing date Date	Filed / Furnished Furnished
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1.1	Articles of Association, as amended and as currently in effect	F-1	333-217124	3.1	4/3/2017	
<a href="#">2.1</a>	Deposit Agreement					*
2.2	Form of American Depositary Receipt (included in Exhibit 2.1)					*
2.3	Form of Warrant issued to each of the investors named in Schedule A thereto	F-1	333-217124	4.3	4/3/2017	
2.4	Warrant Instrument issued to NPlus1 Singer LLP	F-1	333-217124	4.4	4/3/2017	
4.1	Registration Rights Agreement, dated July 29, 2016, by and among Verona Pharma plc and the investors set forth therein	F-1	333-217124	10.1	4/3/2017	
4.2†	Intellectual Property Assignment and Licence Agreement between Vernalis Development Limited and Rhinopharma Limited, as predecessor to Verona Pharma plc, dated February 7, 2005	F-1	333-217124	10.2	4/3/2017	
4.3	Lease by and between the Verona Pharma plc and Regus Management (UK) Limited dated October 17, 2014 and related Renewal Agreements dated September 30, 2015 and October 1, 2016	F-1	333-217124	10.3	4/3/2017	
4.3.1	Lease by and between the Verona Pharma plc and Regus Management (UK) Limited dated October 26, 2016	F-1	333-217124	10.3.1	4/3/2017	
4.3.2	Lease by and between the Verona Pharma plc and Regus Management (UK) Limited dated October 26, 2016	F-1	333-217124	10.3.2	4/3/2017	
<a href="#">4.3.3</a>	Renewal Agreement to Lease by and between the Verona Pharma plc and Regus Management (UK) Limited dated October 17, 2014 (exhibit 4.3)					*
<a href="#">4.3.4</a>	Renewal Agreement to Lease by and between the Verona Pharma plc and Regus Management (UK) Limited dated October 26, 2016 (exhibits 4.3.1 and 4.3.2)					*
4.4#	EMI Option Scheme	F-1	333-217124	10.4	4/3/2017	

4.5#	Unapproved Share Option Scheme, as amended	F-1	333-217124	10.5	4/3/2017
<a href="#">4.6#</a>	2017 Incentive Award Plan and forms of award agreements thereunder				
4.7#	Employment Agreement, dated April 30, 2012, as amended, between Verona Pharma plc and Jan-Anders Karlsson	F-1	333-217124	10.6	4/3/2017
4.8#	Offer Letter, dated December 15, 2014, as amended, between Verona Pharma plc and Kenneth Newman	F-1	333-217124	10.7	4/3/2017
4.9#	Employment Agreement, dated September 24, 2016, between Verona Pharma plc and Piers John Morgan	F-1	333-217124	10.8	4/3/2017
4.10#	Employment Agreement, dated October 1, 2016, between Verona Pharma plc and Claire Poll	F-1	333-217124	10.9	4/3/2017
4.11#	Employment Agreement, dated October 1, 2016, as amended, between Verona Pharma plc and Peter Spargo	F-1	333-217124	10.10	4/3/2017
4.12#	Employment Agreement, dated October 1, 2016, as amended, between Verona Pharma plc and Peter Spargo	F-1	333-217124	10.16	4/3/2017
<a href="#">4.13#</a>	Employment Agreement, dated May 1, 2017, between Verona Pharma plc and Desiree Luthman[2]				
4.14	Form of Indemnification Agreement for board members	F-1/A	333-217124	10.11.1	4/18/2017
4.15	Form of Indemnification Agreement for executive officers	F-1/A	333-217124	10.11.2	4/18/2017
4.16	Relationship Agreement relating to Verona Pharma plc, dated July 29, 2016, by and among the Verona Pharma plc, OrbiMed Private Investments VI, LP and NPlus1 Singer Advisory LLP	F-1	333-217124	10.12	4/3/2017
4.17	Relationship Agreement relating to Verona Pharma plc, dated July 29, 2016, by and among the Verona Pharma plc, Abingworth Bioventures VI LP and NPlus1 Singer Advisory LLP	F-1	333-217124	10.13	4/3/2017
4.18	Relationship Agreement relating to Verona Pharma plc, dated July 29, 2016, by and among the Verona Pharma plc, Vivo Ventures Fund VII, L.P., Vivo Ventures VII Affiliates Fund, L.P., Vivo Ventures Fund VI, L.P., Vivo Ventures VI Affiliates Fund, L.P. and NPlus1 Singer Advisory LLP	F-1	333-217124	10.14	4/3/2017
8.1	List of Subsidiaries	F-1	333-217124	10.14	4/3/2017

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<a href="#"><u>12.1</u></a>	Rule 13a-14(a)/15d-14(a) Certification of Chief Executive Officer	*
<a href="#"><u>12.2</u></a>	Rule 13a-14(a)/15d-14(a) Certification of Chief Financial Officer	*
<a href="#"><u>13.1</u></a>	Section 1350 Certification of Chief Executive Officer	**
<a href="#"><u>13.2</u></a>	Section 1350 Certification of Chief Financial Officer	**
<a href="#"><u>15.1</u></a>	Consent of PricewaterhouseCoopers LLP	*
101.INS	XBRL Instance Document	*
101.SCH	XBRL Taxonomy Extension Schema Document	*
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document	*
101.LAB	XBRL Taxonomy Extension Label Linkbase Document	*
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document	*
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document	*

\* Filed herewith.

\*\* Furnished herewith.

# Indicates management contract or compensatory plan.

† Confidential treatment granted as to portions of the exhibit. Confidential materials omitted and filed separately with the Securities and Exchange Commission.

## INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

### Consolidated financial statements

as of and for the years ended December 31, 2016 and 2017

<a href="#">Report of Independent Registered Public Accounting Firm</a>	<a href="#">F-2</a>
<a href="#">Consolidated Statement of Financial Position as at December 31, 2016 and 2017</a>	<a href="#">F-3</a>
<a href="#">Consolidated Statement of Comprehensive Income for the years ended December 31, 2015, 2016 and 2017</a>	<a href="#">F-4</a>
<a href="#">Consolidated Statement of Cash Flows for the years ended December 31, 2015, 2016 and 2017</a>	<a href="#">F-5</a>
<a href="#">Consolidated Statement of Changes in Equity for the years ended December 31, 2015, 2016 and 2017</a>	<a href="#">F-6</a>
<a href="#">Consolidated Notes to the Financial Statements</a>	<a href="#">F-7</a>



## Report of Independent Registered Public Accounting Firm

To the Board of Directors and Shareholders of Verona Pharma Plc

### ***Opinion on the Financial Statements***

We have audited the accompanying consolidated statement of financial position of Verona Pharma Plc and its subsidiaries as of December 31, 2017 and December 31, 2016 and the related consolidated statements of comprehensive income, of changes in equity and of cash flows for each of the three years in the period ended December 31, 2017 including the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2017 and December 31, 2016, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2017 in conformity with International Financial Reporting Standards as issued by the International Accounting Standards Board.

### ***Basis for Opinion***

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

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

Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ PricewaterhouseCoopers LLP  
Reading, United Kingdom  
February 27, 2018

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

PricewaterhouseCoopers LLP, 3 Forbury Place, 23 Forbury Road, Reading, Berkshire, RG1 3JH  
T: +44 (0) 118 597 111, F: +44 (0) 1189 383 020, [www.pwc.co.uk](http://www.pwc.co.uk)

PricewaterhouseCoopers LLP is a limited liability partnership registered in England with registered number OC303525. The registered office of PricewaterhouseCoopers LLP is 1 Embankment Place, London WC2N 6RH. PricewaterhouseCoopers LLP is authorised and regulated by the Financial Conduct Authority for designated investment business.

**VERONA PHARMA PLC**  
**CONSOLIDATED STATEMENT OF FINANCIAL POSITION**  
**AS OF DECEMBER 31, 2016 AND 2017**

	Notes	As of December 31, 2016 £'000s	As of December 31, 2017 £'000s
<b>ASSETS</b>			
<b>Non-current assets:</b>			
Goodwill	11	441	441
Intangible assets	12	1,877	1,969
Property, plant and equipment	13	14	16
<b>Total non-current assets</b>		<b>2,332</b>	<b>2,426</b>
<b>Current assets:</b>			
Prepayments and other receivables	14	2,959	1,810
Current tax receivable		1,067	5,006
Short term investments	3	—	48,819
Cash and cash equivalents		39,785	31,443
<b>Total current assets</b>		<b>43,811</b>	<b>87,078</b>
<b>Total assets</b>		<b>46,143</b>	<b>89,504</b>
<b>EQUITY AND LIABILITIES</b>			
<b>Capital and reserves attributable to equity holders:</b>			
Share capital	15	2,568	5,251
Share premium		58,526	118,862
Share-based payment reserve		2,103	5,022
Accumulated loss		(28,728)	(49,254)
<b>Total equity</b>		<b>34,469</b>	<b>79,881</b>
<b>Current liabilities:</b>			
Derivative financial instrument	19	7,923	1,273
Trade and other payables	17	2,823	7,154
Tax payable—U.S. Operations		126	169
<b>Total current liabilities</b>		<b>10,872</b>	<b>8,596</b>
<b>Non-current liabilities:</b>			
Assumed contingent obligation	18	802	875
Deferred income		—	152
<b>Total non-current liabilities</b>		<b>802</b>	<b>1,027</b>
<b>Total equity and liabilities</b>		<b>46,143</b>	<b>89,504</b>

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

**VERONA PHARMA PLC**  
**CONSOLIDATED STATEMENT OF COMPREHENSIVE INCOME**  
**FOR THE YEARS ENDED DECEMBER 31, 2015, 2016 AND 2017**

	Notes	Year Ended December 31, 2015	Year ended December 31, 2016	Year ended December 31, 2017
		£'000s	£'000s	£'000s
Research and development costs		(7,270)	(4,522)	(23,717)
General and administrative costs		(1,706)	(2,498)	(6,039)
<b>Operating loss</b>	7	(8,976)	(7,020)	(29,756)
Finance income	9	45	1,841	7,018
Finance expense	9	(73)	(794)	(2,465)
<b>Loss before taxation</b>		(9,004)	(5,973)	(25,203)
Taxation — credit	10	1,509	954	4,706
<b>Loss for the year</b>		(7,495)	(5,019)	(20,497)
<b>Other comprehensive income / (loss) :</b>				
<b>Items that might be subsequently reclassified to profit or loss</b>				
Exchange differences on translating foreign operations		4	43	(29)
<b>Total comprehensive loss attributable to owners of the Company</b>		(7,491)	(4,976)	(20,526)
Loss per ordinary share — basic and diluted (pence)	5	(37.1)	(15.0)	(23.4)

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, 2016 AND 2017**

	Year ended December 31, 2015	Year ended December 31, 2016	Year ended December 31, 2017
	£'000s	£'000s	£'000s
<b>Cash used in operating activities:</b>			
Loss before taxation	(9,004)	(5,973)	(25,203)
Finance income	(45)	(1,841)	(7,018)
Finance expense	73	794	2,465
Share-based payment charge	399	577	2,919
Decrease / (increase) in prepayments and other receivables	59	(1,809)	(161)
Increase in trade and other payables	1,274	1,068	5,363
Depreciation of property, plant and equipment	10	10	7
Loss on disposal of property, plant and equipment	—	3	—
Loss on disposal of intangible assets	135	—	—
Amortization of intangible assets	43	52	116
Cash used in operating activities	(7,056)	(7,119)	(21,512)
Cash inflow from taxation	700	1,533	816
<b>Net cash used in operating activities</b>	<b>(6,356)</b>	<b>(5,586)</b>	<b>(20,696)</b>
<b>Cash flow from investing activities:</b>			
Interest received	51	87	128
Purchase of plant and equipment	(1)	(13)	(9)
Payment for patents and computer software	(142)	(115)	(208)
Transfer to short term investments	—	—	(54,465)
Maturity of short term investments	—	—	5,085
<b>Net cash used in investing activities</b>	<b>(92)</b>	<b>(41)</b>	<b>(49,469)</b>
<b>Cash flow from financing activities:</b>			
Gross proceeds from issue of shares and warrants	—	44,750	—
Gross proceeds from the April 2017 Global Offering	—	—	70,032
Transaction costs on issue of shares and warrants	—	(2,910)	—
Transaction costs on April 2017 Global Offering	—	(636)	(6,786)
<b>Net cash generated from financing activities</b>	<b>—</b>	<b>41,204</b>	<b>63,246</b>
<b>Net (decrease) / increase in cash and cash equivalents</b>	<b>(6,448)</b>	<b>35,577</b>	<b>(6,919)</b>
Cash and cash equivalents at the beginning of the year	9,968	3,524	39,785
Effect of exchange rates on cash and cash equivalents	4	684	(1,423)
<b>Cash and cash equivalents at the end of the period</b>	<b>3,524</b>	<b>39,785</b>	<b>31,443</b>

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, 2016 AND 2017**

	Share Capital	Share Premium	Share-based Expenses	Total Accumulated Losses	Total Equity
	£'000s	£'000s	£'000s	£'000s	£'000s
<b>Balance at January 1, 2015</b>	1,010	26,650	1,127	(16,261)	12,526
Loss for the year	—	—	—	(7,495)	(7,495)
Other comprehensive income for the year:					
Exchange differences on translating foreign operations	—	—	—	4	4
Total comprehensive loss for the period	—	—	—	(7,491)	(7,491)
Share-based payments	—	—	399	—	399
<b>Balance at December 31, 2015</b>	1,010	26,650	1,526	(23,752)	5,434
<b>Balance at January 1, 2016</b>	1,010	26,650	1,526	(23,752)	5,434
Loss for the year	—	—	—	(5,019)	(5,019)
Other comprehensive income for the year:					
Exchange differences on translating foreign operations	—	—	—	43	43
Total comprehensive loss for the period	—	—	—	(4,976)	(4,976)
New share capital issued	1,556	34,151	—	—	35,707
Transaction costs on share capital issued	—	(2,325)	—	—	(2,325)
Share options exercised during the period	2	50	—	—	52
Share-based payments	—	—	577	—	577
<b>Balance at December 31, 2016</b>	2,568	58,526	2,103	(28,728)	34,469
<b>Balance at January 1, 2017</b>	2,568	58,526	2,103	(28,728)	34,469
Loss for the year	—	—	—	(20,497)	(20,497)
Other comprehensive loss for the year:					
Exchange differences on translating foreign operations	—	—	—	(29)	(29)
Total comprehensive loss for the period	—	—	—	(20,526)	(20,526)
New share capital issued	2,677	67,648	—	—	70,325
Transaction costs on share capital issued	—	(7,453)	—	—	(7,453)
Share options exercised during the period	6	141	—	—	147
Share-based payments	—	—	2,919	—	2,919
<b>Balance at December 31, 2017</b>	5,251	118,862	5,022	(49,254)	79,881

The currency translation reserve for 2015, 2016 and 2017 is not considered material and as such is not presented in a separate reserve but is included in the total accumulated losses reserve.

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

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS

FOR THE YEAR ENDED DECEMBER 31, 2017

1. General information

Verona Pharma plc and its subsidiaries (the "Company") 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 dual listed on the Alternative Investment Market of the London Stock Exchange and on April 27, 2017, American Depositary Shares began trading on Nasdaq Global Market. The company is incorporated and domiciled in the United Kingdom. The address of the registered office is 1 Central Square, Cardiff, CF10 1FS, United Kingdom.

The Company has two subsidiaries, Verona Pharma Inc. and Rhinopharma Limited ("Rhinopharma"), both of which are wholly owned.

On February 10, 2017 the Company effected a 50-for-1 consolidation of its shares. All references to ordinary shares, options and warrants, as well as share, per share and related information in these consolidated financial statements have been adjusted to reflect the consolidation as if it had occurred at the beginning of the earliest period presented.

On April 26, 2017, the Company announced the closing of its global offering of an aggregate of 47,399,001 new ordinary shares, consisting of the initial public offering in the United States of 5,768,000 American Depositary Shares ("ADSs") at a price of \$13.50 per ADS and the private placement in Europe of 1,255,001 ordinary shares at a price of £1.32 per ordinary share, for gross proceeds of \$80 million (the "Global Offering"). Each ADS offered represents eight ordinary shares of the Company. The ordinary shares offered were allotted and issued in a concurrent private placement in Europe and other countries outside of the United States and Canada.

In addition, the Chairman of Verona Pharma's board of directors, Dr David Ebsworth, and an existing shareholder agreed to subscribe for 254,099 new ordinary shares at a price of £1.32 per ordinary share in a shareholder private placement separate from the Global Offering (the "Shareholder Private Placement"), contingent on and concurrent with the Global Offering and generating additional gross proceeds of £0.3 million.

On May 15 and May 23, 2017, pursuant to the Global Offering, the underwriters purchased an additional 733,738 ADSs, representing 5,869,904 ordinary shares, at a price of \$13.50 per ADS, for additional gross proceeds of \$9.9 million bringing the total gross proceeds in the Global Offering to \$89.9 million (£70.0 million). Including the Shareholder Private Placement, the total gross proceeds of the capital raising amounted to \$90.3 million (£70.3 million).

The ADSs began trading on the Nasdaq Global Market under the ticker symbol "VRNA" on April 27, 2017. Verona Pharma's ordinary shares continue to trade on the AIM market of the London Stock Exchange ("AIM") under the symbol "VRP".

**VERONA PHARMA PLC****NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)****FOR THE YEAR ENDED DECEMBER 31, 2017****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 Company have been prepared in accordance with International Financial Reporting Standards ("IFRSs") as issued by the International Accounting Standards Board and IFRS Interpretations Committee and with the Companies Act 2006 applicable to companies reporting under IFRS.

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 Company'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, 2017, the Company had a loss of £20.5 million (2016: £5.0 million). As of December 31, 2017, the Company had net assets of £79.9 million (2016: £34.5 million) of which £80.3 million (2016: £39.8 million) was cash and cash equivalents and short term investments.

The operation of the Company is currently being financed from funds that the Company raised from share placings. On May 2nd, 2017, the company raised \$89.9 million (£70 million) from the initial public offering in the United States. On July 29, 2016, the Company raised gross proceeds of £44.7 million from a placing, subscription and open offer (the "July 2016 Placement"). These funds are expected to be used primarily to support the development of RPL554 in chronic obstructive pulmonary disease ("COPD"), other chronic respiratory diseases as well as corporate and general administrative expenditures.

The Directors believe that the Company 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 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 Company applies the acquisition method to account for business combinations. The consideration transferred for the acquisition of a subsidiary is the fair value of the assets transferred, the liabilities incurred to the former owners of the acquiree and the equity interests issued by the Company. The consideration transferred includes the fair value of any asset or liability resulting from a contingent consideration arrangement 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 Company'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.

**VERONA PHARMA PLC****NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)****FOR THE YEAR ENDED DECEMBER 31, 2017****Accounting policies (Continued)**

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 Foreign currency translation**

Items included in the Company's consolidated financial statements are measured using the currency of the primary economic environment in which the Entity 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 Company.

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.

**2.3 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.

**2.4 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 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.

**2.5 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 Company 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 Company'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.

**2.6 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

**VERONA PHARMA PLC****NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)****FOR THE YEAR ENDED DECEMBER 31, 2017****Accounting policies (Continued)**

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

**2.7 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 ("IPR&D")**

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 subject to impairment testing until completion, abandonment of the projects or when the research findings are commercialized through a revenue generating project. The Company 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 Company 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.

**2.8 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 (cash generating units "CGUs").

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 Company 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.

**VERONA PHARMA PLC****NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)****FOR THE YEAR ENDED DECEMBER 31, 2017****Accounting policies (Continued)**

Non-financial assets, other than goodwill, that have been previously impaired are reviewed for possible reversal of the impairment at each subsequent reporting date.

**2.9 Employee Benefits****(a) Pension**

The Company 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 Company has no further payment obligation once the contributions have been paid.

**(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.

**2.10 Share-based payments**

The Company 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 Company'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 16.

**2.11 Provisions**

Provisions are recognized when the Company 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.

**2.12 Assumed contingent obligation related to the business combinations**

On September 19, 2006, the Company acquired Rhinopharma for a total consideration of £1.52 million payable in ordinary shares. In addition, the Company 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 midtwenty percent of any consideration received from any sub-licensees for the Vernalis Patents and for Vernalis know-how. On the date of

**NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)****FOR THE YEAR ENDED DECEMBER 31, 2017****Accounting policies (Continued)**

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 an assessment of the probability of success using standard market probabilities for respiratory drug development. The risk-weighted value of the assumed contingent arrangement was then discounted back to its net present value applying an effective interest rate 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 difficult to predict and subject to estimate, which is inherently uncertain. 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, when the probability of success changes. 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.

**2.13 Government and other grants**

The Company 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 Company would include such income under "Other income" in the Consolidated Statement of Comprehensive Income. Grants or investment credits may be repayable if the Company 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 Company would not make any provision for repayment.

**2.14 Financial instruments — initial recognition and subsequent measurement**

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.

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 and subsequent measurement**

All financial assets not recorded at fair value through profit or loss, such as receivables and deposits, are recognized initially at fair value plus transaction costs. 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.



**VERONA PHARMA PLC****NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)****FOR THE YEAR ENDED DECEMBER 31, 2017****Accounting policies (Continued)**

The measurement of financial assets depends on their classification. 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.

**(b) Financial liabilities, initial recognition and measurement and subsequent 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 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

The Company's financial liabilities include trade and other payables and derivative financial instruments.

**(c) 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 2.15.

The full fair value of the derivative is classified as a non-current liability when the warrants are exercisable in more than 12 months and as a current liability when the warrants are exercisable in 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.

**2.15 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. The financial liability component is remeasured depending on its classification. Equity is not remeasured.

**2.16 Short Term Investments**

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

**2.17 Transaction costs**

Qualifying transaction costs might be 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 recognized. Deferred costs are subsequently reclassified as a deduction from equity when the equity instruments are recognized, as 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.

**NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)****FOR THE YEAR ENDED DECEMBER 31, 2017****Accounting policies (Continued)**

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 Company**

The following amendments have been adopted by the Company for the first time for the financial year beginning on or after 1 January, 2017. It did not materially impact the Company's results:

- Annual Improvements to IFRS Standards 2014-2016 Cycle,
- Disclosure initiative - amendments to IAS 7, and
- Recognition of Deferred Tax Assets for Unrealized Losses - Amendments to IAS 12.

The amendments to IAS 7 require disclosure of changes in liabilities arising from financing activities, see note 3.3.

**2.19 New standards, amendments and interpretations issued but not effective for the financial year beginning January 1, 2017 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 will have no material impact on the accounting or measurement of any of the financial instruments the Company currently holds.

IFRS 15 will have no impact on the financial statements of the Company as it is not currently revenue generating.

IFRS 16 is effective for accounting periods beginning on or after 1 January 2019 and will replace IAS 17 'leases'. It will eliminate the classification of leases as either operating leases or finance leases and, instead, introduce a single lessee accounting model. The adoption of IFRS 16 will result in the Company recognizing lease liabilities and corresponding 'right to use' assets for agreements that are currently classified as operating leases. See note 20 for further details on operating leases held.

**VERONA PHARMA PLC**
**NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)**
**FOR THE YEAR ENDED DECEMBER 31, 2017**
**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 Company's net assets will be negatively impacted due to fluctuations in exchange rates. The Company has not entered into foreign exchange contracts to hedge against gains or losses from foreign exchange fluctuations.

The summary quantitative data about the Company's exposure to currency risk is as follows. Figures are the sterling values of balances in each currency:

	Year Ended December 31, 2016		Year Ended December 31, 2017	
	USD	EUR	USD	EUR
	£'000s	£'000s	£'000s	£'000s
Cash and cash equivalents	10,631	242	16,806	301
Short term Investments	—	—	19,718	—
Trade and other payables	305	180	276	403

**Sensitivity Analysis**

A reasonably possible strengthening (weakening) of the Euro, US dollar, or Sterling against all other currencies at 31 December would have affected the measurement of the financial instruments denominated in a foreign currency and affected equity and profit and loss by the amounts shown below. This analysis assumes that all other variables remain constant.

	Profit or loss and equity	
	Strengthening	Weakening
	£'000s	£'000s
<b>December 31, 2017</b>		
EUR (5% movement)	35	(35)
USD (5% Movement)	1,840	(1,840)
<b>December 31, 2016</b>	£'000s	£'000s
EUR (5% movement)	21	(21)
USD (5% Movement)	547	(547)

Foreign currency denominated trade payables are short term in nature (generally 30 to 45 days). The Company has a U.S. operation, the net assets of which are exposed to foreign currency translation risk.

**(b) Credit risk**

Credit risk reflects the risk that the Company may be unable to recover contractual receivables. As the Company is still in the development stage no policies are currently required to mitigate this risk.

**VERONA PHARMA PLC**
**NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)**
**FOR THE YEAR ENDED DECEMBER 31, 2017**
**Financial Instruments (continued)**

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 Company become exposed to further financial risks as the business develops.

As of December 31, 2017, and December 31, 2016, cash and cash equivalents and short term investments were placed at the following banks:

<b>Cash and Cash Equivalents</b>	<b>Year ended December 31, 2016</b>	<b>Credit rating</b>	<b>Year ended December 31, 2017</b>	<b>Credit rating</b>
	<b>£'000</b>		<b>£'000</b>	
<b>Banks</b>				
Royal Bank of Scotland	11,287	A3	16,623	A2
Lloyds Bank	28,447	A1	13,448	Aa3
Standard Chartered	—	—	1,242	A1
Wells Fargo	51	Aa1	130	Aa1
Total	<u>39,785</u>		<u>31,443</u>	

<b>Short Term Investments</b>	<b>Year ended December 31, 2016</b>	<b>Credit rating</b>	<b>Year ended December 31, 2017</b>	<b>Credit rating</b>
	<b>£'000</b>		<b>£'000</b>	
<b>Banks</b>				
Royal Bank of Scotland	—	—	15,316	A2
Lloyds Bank	—	—	11,036	Aa3
Standard Chartered	—	—	22,467	A1
Wells Fargo	—	—	—	Aa1
Total	<u>—</u>		<u>48,819</u>	

**(c) Management of capital**

The Company considers capital to be its equity reserves. At the current stage of the Company's life cycle, the Company's objective in managing its capital is to ensure funds raised meet the research and operating requirements until the next development stage of the Company's suite of projects.

The Company 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, 2017, the Company had cash deposits of £31.4 million (2016: £39.8 million) and short term investments of £48.8 million (2016: nil). The rates of interest received during 2017 ranged between 0.0% and 1.73%. A 0.25% increase in interest rates would not have a material impact on finance income. The Company'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:

**VERONA PHARMA PLC**
**NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)**
**FOR THE YEAR ENDED DECEMBER 31, 2017**
**Financial Instruments (continued)**

	December 31, 2016		December 31, 2017	
	Floating interest rate	Fixed Interest rate	Floating interest rate	Fixed Interest rate
	£'000s	£'000s	£'000s	£'000s
<b>Financial asset</b>				
Cash deposits	11,338	28,447	25,720	5,723
Short Term Investments	—	—	—	48,819
<b>Total</b>	<u>11,338</u>	<u>28,447</u>	<u>25,720</u>	<u>54,542</u>

(e) Liquidity risk

The Company prepares periodic working capital forecasts for the foreseeable future, allowing an assessment of the cash requirements of the Company, to manage liquidity risk. The following table provides an analysis of the Company's financial liabilities. The carrying value of all balances is equal to their fair value. The Company's maturity analysis for the derivative financial instrument from the issue of warrants is given in note 19.

	LESS THAN 1 YEAR	BETWEEN 1 AND 2 YEARS	BETWEEN 2 AND 5 YEARS	OVER 5 YEARS <sup>(1)</sup>
	£'000s	£'000s	£'000s	£'000s
<b>At December 31, 2016</b>				
Trade payables	719	—	—	—
Other payables	54	—	—	—
Accruals	2,050	—	—	—
Contingent obligation	—	—	—	1,807
<b>Total</b>	<u>2,823</u>	<u>—</u>	<u>—</u>	<u>1,807</u>

(1) This table includes the undiscounted amount of the assumed contingent obligation. See note 18.

	LESS THAN 1 YEAR	BETWEEN 1 AND 2 YEARS	BETWEEN 2 AND 5 YEARS	OVER 5 YEARS <sup>(1)</sup>
	£'000s	£'000s	£'000s	£'000s
<b>At December 31, 2017</b>				
Trade payables	1,214	—	—	—
Other payables	74	—	—	—
Accruals	5,866	—	—	—
Contingent obligation	—	—	—	1,807
<b>Total</b>	<u>7,154</u>	<u>—</u>	<u>—</u>	<u>1,807</u>

(1) This table includes the undiscounted amount of the assumed contingent obligation. See note 18.

**NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)**
**FOR THE YEAR ENDED DECEMBER 31, 2017**
**Financial Instruments (continued)**
**3.2 Fair value estimation**

The carrying amounts of cash and cash equivalents, receivables, accounts payable and accrued liabilities approximate to fair value due to their short-term nature. The carrying amount of the assumed contingent liability approximates to fair value as the underlying assumptions are currently similar.

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, 2017, and 2016, fair value adjustments to financial instruments through profit and loss resulted in the recognition of finance income of £6.7 million and £1.1 million 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.

	Level 3	Total
	£'000s	£'000s
<b>At December 31, 2017</b>		
Derivative financial instrument	1,273	1,273
<b>Total</b>	<b>1,273</b>	<b>1,273</b>

Movements in Level 3 items during the years ended December 31, 2016, and 2017 are as follows:

<b>Derivative financial instrument</b>	2016	2017
	£'000s	£'000s
<b>At January 1</b>	—	7,923
Initial recognition of derivative financial instrument	8,991	—
Fair value adjustments recognized in profit and loss	(1,068)	(6,650)
<b>At December 31</b>	<b>7,923</b>	<b>1,273</b>

Further details relating to the derivative financial instrument are set out in notes 4 and 19 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 19.

## NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)

FOR THE YEAR ENDED DECEMBER 31, 2017

## Financial Instruments (continued)

## 3.3 Change in liabilities arising from financing activities

The Company has provided a reconciliation so that changes in liabilities arising from financing activities, including both changes arising from cash flows and non-cash changes can be evaluated.

	December 31, 2017
	Derivative financial instrument
	£'000s
At January 1	7,923
Fair value adjustments - non cash	(6,650)
At December 31	1,273

See note 19 for information relating to the derivative financial instrument.

## 4. Critical accounting estimates and judgments

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 judgment in the process of applying the Company's accounting policies.

The areas involving a higher degree of judgment or complexity, or areas where assumptions and estimates are significant to the consolidated financial statements are as follows:

## (a) Assumed contingent obligation

The Company 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 on acquisition requires the selection of an appropriate valuation model, consideration as to the inputs necessary for the valuation model chosen, the estimation of the likelihood that the regulatory approval milestone will be achieved and estimates of the future cash flows and their timing (for further detail see note 19). The estimates for the assumed contingent obligation are based on a discounted cash flow model. Key assessments and judgments included in the fair value 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 expected cash flows, the assumed contingent obligation is re-measured with the change in value

**NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)****FOR THE YEAR ENDED DECEMBER 31, 2017****Critical accounting estimates and judgments (continued)**

going through the Consolidated Statement of Comprehensive Income. Cash flow estimates are revised when the probability of success changes. 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, 2017 amounts to £0.9 million. (2016: £0.8 million). The increase in value of the assumed contingent obligation during 2017 amounted to £0.1 million (2016: £0.2 million) and the movement relates to unwinding the discount on the liability and retranslating for changes in US\$ exchange rates. The increase was recorded in finance expense. There was no change in the year to the probability of success and consequently cash flow estimates were not revised.

The discount percentage applied is 12%.

**(b) Valuation of the July 2016 warrants**

Pursuant to the July 2016 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 2.15, 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 see note 19.

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.

**(c) Recognition of research and development expenditure**

The Company incurs research and development expenditure from third parties. The Company recognizes this expenditure in line with the management's best estimation of the stage of completion of each research and development project. This includes the calculation of accrued costs at each period end to account for expenditure that has been incurred. This requires management to estimate full costs to complete for each project and also to estimate its current stage of completion. The costs related to the Clinical Research Organization expenses in the year was £18.5 million. The related accruals and prepayments were £4.6 million and £0.5 million respectively.

**(d) Transaction costs related the Global Offering**

The Company incurred various transaction costs relating to the Global Offering, including commissions, professional advisor fees, financial advice, listing fees and other costs. When management judged them to be incremental costs directly attributable to the transaction they were accounted for as a deduction from equity. Otherwise the costs were expensed to the consolidated income statement as incurred.

**5. Earnings per share**

Basic loss per ordinary share of 23.4p (2016: 15.0p and 2015: 37.1p) for the Company is calculated by dividing the loss for the year ended December 31, 2017 by the weighted average number of ordinary shares in issue of 87,748,031 as of December 31, 2017 (2016: 33,499,413 and 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.



**NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)**
**FOR THE YEAR ENDED DECEMBER 31, 2017**
**6. Segmental reporting**

The Company's activities are covered by one operating and reporting segment: Drug Development. There have been no changes to management's assessment of the operating and reporting segment of the Company during the period.

All non-current assets are based in the United Kingdom.

**7. Operating loss**

	Year ended December 31, 2015	Year ended December 31, 2016	Year ended December 31, 2017
	£'000s	£'000s	£'000s
<b>Operating Loss is stated after charging:</b>			
<b>Research and development costs:</b>			
Employee benefits (note 8)	1,322	2,037	3,435
Amortization of patents (note 12)	43	51	111
Legal, professional consulting and listing fees	—	—	331
Loss on disposal of patents	136	—	—
Other research and development expenses	5,769	2,434	19,840
Total research and development costs	7,270	4,522	23,717
<b>General and administrative costs:</b>			
Employee benefits (note 8)	625	865	2,857
Legal, professional consulting and listing fees	608	884	2,045
Amortization of computer software (note 12)	—	1	5
Loss on disposal of property, plant and equipment (note 13)	—	3	—
Depreciation of property, plant and equipment (note 13)	10	10	7
Operating lease charge — land and buildings	157	169	294
Loss on variations in foreign exchange rate	21	139	36
Other general and administrative expenses	285	427	795
Total general and administrative costs	1,706	2,498	6,039
Operating loss	8,976	7,020	29,756

**VERONA PHARMA PLC**
**NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)**
**FOR THE YEAR ENDED DECEMBER 31, 2017**
**8. Directors' emoluments and staff costs**

	Year ended December 31, 2015	Year ended December 31, 2016	Year ended December 31, 2017
The average number of employees (excluding directors) of the Company during the year:			
Research and Development	5	5	7
General and Administrative	3	2	5
Total	8	7	12
	Year ended December 31, 2015	Year ended December 31, 2016	Year ended December 31, 2017
	£'000s	£'000s	£'000s
<b>Aggregate emoluments of directors:</b>			
Salaries and other short-term employee benefits	722	951	897
Social security costs	132	118	103
Incremental payment for additional services	89	44	—
Other pension costs	38	19	17
Total directors' emoluments	981	1,132	1,017
Share-based payment charge	232	257	1,037
Directors' emoluments including share-based payment charge	1,213	1,389	2,054
	Year ended December 31, 2015	Year ended December 31, 2016	Year ended December 31, 2017
	£'000s	£'000s	£'000s
<b>Aggregate other staff costs:</b>			
Wages and salaries	540	1,027	2,136
Social security costs	42	98	182
Incremental payment for additional services	—	58	—
Share-based payment charge	137	319	1,882
Other pension costs	15	11	38
Total other staff costs	734	1,513	4,238

The Company operates a defined contribution pension scheme for U.K. employees and executive directors. The total pension cost during the year ended December 31, 2017 was £55 thousand (2016: £30 thousand and 2015: £53 thousand). There were no prepaid or accrued contributions to the scheme at December 31, 2017(2016 and 2015: £nil).

**VERONA PHARMA PLC**
**NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)**
**FOR THE YEAR ENDED DECEMBER 31, 2017**
**Finance income and expense (continued)**
**9. Finance income and expense**

	Year ended December 31, 2015	Year ended December 31, 2016	Year ended December 31, 2017
	£'000s	£'000s	£'000s
<b>Finance income:</b>			
Interest received on cash balances	45	86	345
Foreign exchange gain on translating foreign currency denominated bank balances	—	687	—
Fair value adjustment on derivative financial instruments (note 19)	—	1,068	6,650
Other Income	—	—	23
<b>Total finance income</b>	<b>45</b>	<b>1,841</b>	<b>7,018</b>
	Year ended December 31, 2015	Year ended December 31, 2016	Year ended December 31, 2017
	£'000s	£'000s	£'000s
<b>Finance expense:</b>			
Transaction costs allocated to the issue of warrants (note 19)	—	586	—
Foreign exchange loss on translating foreign currency denominated balances	—	—	2,392
Remeasurement of assumed contingent arrangement (note 18)	10	122	—
Unwinding of discount factor and foreign exchange movements related to the assumed contingent arrangement (note 18)	63	86	73
<b>Total finance expense</b>	<b>73</b>	<b>794</b>	<b>2,465</b>

**VERONA PHARMA PLC**
**NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)**
**FOR THE YEAR ENDED DECEMBER 31, 2017**
**Taxation (continued)**
**10. Taxation**

	Year ended December 31, 2015	Year ended December 31, 2016	Year ended December 31, 2017
	£'000s	£'000s	£'000s
<b>Analysis of tax credit for the year</b>			
Current tax:			
UK tax credit	(1,520)	(1,067)	(5,006)
US tax charge	—	129	306
Adjustment in respect of prior periods	11	(16)	(6)
<b>Total tax credit</b>	<b>(1,509)</b>	<b>(954)</b>	<b>(4,706)</b>
<b>Factors affecting the tax charge for the year</b>			
Loss on ordinary activities	(9,002)	(5,973)	(25,203)
Multiplied by standard rate of corporation tax of 19.25% (2016: 20% and 2015: 20.25%)	(1,823)	(1,195)	(4,852)
Effects of:			
Non-deductible expenses	114	292	675
Fair value adjustment on derivative financial instruments	—	(214)	(1,280)
Research and development incentive	(600)	(427)	(2,116)
Temporary differences not recognized	(1)	(4)	(2)
Difference in overseas tax rates	—	56	136
Tax losses carried forward not recognized	790	554	2,739
Adjustment in respect of prior periods	11	(16)	(6)
<b>Total tax credit</b>	<b>(1,509)</b>	<b>(954)</b>	<b>(4,706)</b>

UK corporation tax is charged at 19.25% (2016: 20.00% and 2015: 20.25%) and U.S. federal tax at 35% (2016 and 2015: 35%).

The following tables represent deferred tax balances recognized in the Consolidated Statement of Financial Position. There were no movements in either the deferred tax asset or the deferred tax liability.

	Year ended December 31, 2016	Year ended December 31, 2017
	£'000s	£'000s
Deferred tax assets	250	250
Deferred tax liabilities	(250)	(250)
Net balances	—	—

The deferred tax liability relates to the difference between the accounting and tax bases of the IP R&D intangible asset. A deferred tax asset relating to UK tax losses has been recognized and offset against the liability.

**Factors that may affect future tax charges**

The Company 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, 2017, the unrecognized deferred tax asset at 17% is estimated to be £5.43 million (2016: £3.15 million at 17%).

**NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)**
**FOR THE YEAR ENDED DECEMBER 31, 2017**
**11. Goodwill**

	As of December 31, 2016	As of December 31, 2017
	£'000s	£'000s
Goodwill at January 1 and December 31	441	441

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 note 2.8 to the consolidated financial statements.

**12. Intangible assets**

	IP R&D	Computer software	Patents	Total
	£'000s	£'000s	£'000s	£'000s
<b>Cost</b>				
At January 1, 2016	1,469	25	482	1,976
Additions	—	5	110	115
Disposals	—	(24)	—	(24)
At December 31, 2016	1,469	6	592	2,067
<b>Accumulated amortization</b>				
At January 1, 2016	—	24	138	162
Charge for year	—	1	51	52
Disposals	—	(24)	—	(24)
At December 31, 2016	—	1	189	190
<b>Net book value</b>				
At December 31, 2016	1,469	5	403	1,877

	IP R&D	Computer software	Patents	Total
	£'000s	£'000s	£'000s	£'000s
<b>Cost</b>				
At January 1, 2017	1,469	6	592	2,067
Additions	—	5	203	208
Disposals	—	—	(68)	(68)
At December 31, 2017	1,469	11	727	2,207
<b>Accumulated amortization</b>				
At January 1, 2017	—	1	189	190
Charge for year	—	5	111	116
Disposals	—	—	(68)	(68)
At December 31, 2017	—	6	232	238
<b>Net book value</b>				
At December 31, 2017	1,469	5	495	1,969

**VERONA PHARMA PLC**

**NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

**FOR THE YEAR ENDED DECEMBER 31, 2017**

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 2.8.

Recognizing that the Company is still in its 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, 2017, the date of testing of goodwill impairment. The market capitalization of the Company was approximately £109.7 million as of December 31, 2017, (2016: £80.0 million) compared to the Company's net assets of £79.9 million (2016: £34.5 million). Therefore, no impairment was recognized.

**VERONA PHARMA PLC**
**NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)**
**FOR THE YEAR ENDED DECEMBER 31, 2017**
**13. Property, plant and equipment**

	Computer hardware	Office equipment	Total
	£'000s	£'000s	£'000s
<b>Cost</b>			
At January 1, 2016	43	36	79
Additions	13	—	13
Disposals	(39)	(36)	(75)
At December 31, 2016	17	—	17
<b>Accumulated depreciation</b>			
At January 1, 2016	39	27	66
Charge for the year	3	7	10
Disposals	(39)	(34)	(73)
At December 31, 2016	3	—	3
<b>Net book value</b>			
At December 31, 2016	14	—	14

	Computer hardware	Office equipment	Total
	£'000s	£'000s	£'000s
<b>Cost</b>			
At January 1, 2017	17	—	17
Additions	9	—	9
At December 31, 2017	26	—	26
<b>Accumulated depreciation</b>			
At January 1, 2017	3	—	3
Charge for the year	7	—	7
At December 31, 2017	10	—	10
<b>Net book value</b>			
At December 31, 2017	16	—	16

**VERONA PHARMA PLC**
**NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)**
**FOR THE YEAR ENDED DECEMBER 31, 2017**
**14. Prepayments and other receivables**

	As of December 31, 2016	As of December 31, 2017
	£'000s	£'000s
Prepayments	1,361	1,138
Deferred IPO costs	1,527	—
Other receivables	71	672
Total prepayments and other receivables	2,959	1,810

Deferred IPO costs related to the Global Offering. These costs were offset against share premium in 2017 when the Global Offering was completed.

The prepayments balance includes prepayments for insurance and clinical activities.

There are no impaired assets within prepayments and other receivables.

**15. Share Capital**

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 movements in the Company's share capital are summarized below:

Date	Description	Number of shares	Share Capital amounts in £'000
<b>January 1, 2016</b>		<b>20,198,469</b>	<b>1,010</b>
July 29, 2016	Issuance of shares	31,115,926	1,556
September 12, 2016	Exercise of options	3,334	—
October 24, 2016	Exercise of options	3,334	—
December 28, 2016	Exercise of options	40,000	2
<b>As at December 31, 2016</b>		<b>51,361,063</b>	<b>2,568</b>
May 2, 2017	Issuance of shares	47,653,100	2,383
May 18, 2017	Issuance of shares	5,539,080	277
May 26, 2017	Issuance of shares	330,824	17
September 13, 2017	Exercise of options	133,333	6
<b>December 31, 2017</b>		<b>105,017,400</b>	<b>5,251</b>

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 105,017,400 ordinary shares at December 31, 2017 are allotted, unrestricted, called up and fully paid.

On April 26, 2017, the Company announced the closing of its Global Offering of an aggregate of 47,399,001 new ordinary shares, comprising 5,768,000 American Depositary Shares ("ADSs") at a price of \$13.50 per ADS and 1,255,001 ordinary shares at a price of £1.32 per ordinary share. During May 2017 the underwriters purchased an additional 733,738 ADSs, representing 5,869,904 ordinary shares, at a price of \$13.50 per ADS. The total gross proceeds in the Global Offering amounted to \$89.9 million (£70.0 million).



**VERONA PHARMA PLC**

**NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

**FOR THE YEAR ENDED DECEMBER 31, 2017**

**Share Capital (continued)**

In addition, the Chairman of Verona Pharma's board of directors, Dr David Ebsworth, and an existing shareholder agreed to subscribe for 254,099 new ordinary shares at a price of £1.32 per ordinary share in the Shareholder Private Placement, contingent on and concurrent with the Global Offering and generating gross proceeds of £0.3m.

Where there is a time and foreign exchange difference between proceeds from a share issue becoming due and being received, the movement is taken to Finance income or Finance expense as appropriate. In respect of the Global Offering and Shareholder Private Placement, the Company recorded a finance expense of £439 thousand arising from movements in exchange rates on funds receivable, offset by a saving on commission payable of £31 thousand, for a net finance expense of £408 thousand.

On September 13, 2017, the company issued 133,333 new shares upon exercise of share options at 110p per share, resulting in proceeds of £147 thousand to the Company.

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 (see note 19).

During 2016, the Company issued 46,666 ordinary shares upon exercise of employee share options.

As at December 31, 2017, the number of ordinary shares in issue was 105,017,400. All new ordinary shares rank pari passu with existing ordinary shares.

## NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)

## FOR THE YEAR ENDED DECEMBER 31, 2017

**16. 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 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 Income, together with a corresponding increase in equity during the vesting period. During the twelve months ended December 31, 2017, the Company recognized a share-based payment expense of £2.92 million (2016: £0.58 million ). 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"). Under the Unapproved Scheme, options are granted to employees, directors and consultants to acquire shares at a price to be determined by the Directors. In general, options granted prior to December 31, 2016 were granted at a premium to the share price at the date of grant and vested over a period of three years from the date of grant, one third vesting on the first anniversary of grant, a further third vesting on the second anniversary of grant and the remainder vesting on the third anniversary of grant.

Options granted since January 1, 2017 generally vest over three or four years from the date of the grant using two different methods. The first method is one third vesting over one year, the second third vesting over two years and the final third vesting over three years. The second method is one quarter vesting over one year, the second quarter vesting over two years, the third quarter vesting over three years and the final quarter vesting over four 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 are also issued to advisors under the Unapproved Scheme. Such options generally vest immediately and are exercisable between one and two years after grant.

In 2016 the Company issued options under its tax efficient EMI Option Scheme (the "EMI Scheme"). Under the EMI Scheme, options were 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.

The Company grants Restricted Stock Units to employees and directors. The RSUs vest over a period of three or four years from the date of the grant using 2 different methods. The first method is one third vesting over one year, the second third vesting over two years and the final third vesting over three years. The second method is one quarter vesting over one year, the second quarter vesting over two years, the third quarter vesting over three years and the final quarter vesting over four years.

In the year ended December 31, 2017, the Company granted 4,656,828 (2016: 1,670,000 ) share options, nil (2016: 32,000) share options under the EMI Scheme and 1,052,236 Restricted Stock Units ("RSUs") (2016: nil). The total fair values of the Options and RSUs were estimated using the Black-Scholes option-pricing model for equity-settled transactions and amounted to £5.33 million (2016: £1.93 million). The cost is amortized over the vesting period of the options on a straight-line basis.

Prior to the July 2016 Placement in 2016, management determined to take an option's contractual maximum life as an input into the Black-Scholes option-pricing model. Starting from the July 2016 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.

**VERONA PHARMA PLC**
**NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)**
**FOR THE YEAR ENDED DECEMBER 31, 2017**
**16. Share-based payments charge (Continued)**

The following assumptions were used for the Black-Scholes valuation of share options granted in 2016 and 2017. 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.

<b>Issued in 2016</b>	<b>EMI Scheme</b>	<b>Unapproved Scheme</b>
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%
Vesting period	3 years	3 years

<b>Issued in 2017</b>	<b>Unapproved Scheme</b>	<b>Restricted Stock Units</b>
Options granted	4,656,828	1,052,236
Risk-free interest rate	0.29% - 0.62%	0.42%-0.62%
Expected life of options	5.5 – 7.0 years	5.5 – 7.0 years
Annualized volatility	71.3% - 73.3%	71.3% - 73.3%
Dividend rate	0.00%	0.00%
Vesting period	3 and 4 years	3 and 4 years

The Company had the following share options movements in the year ended December 31, 2017:

<b>Year of issue</b>	<b>Exercise price (£)</b>	<b>At January 1, 2017</b>	<b>Options granted</b>	<b>Options exercised</b>	<b>Options forfeited</b>	<b>Options expired</b>	<b>At December 31, 2017</b>	<b>Expiry date</b>
2012	2.50 - 7.50	100,000	—	—	—	—	100,000	June 1, 2022
2013	2	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	63,333	—	—	—	(13,333)	50,000	May 15, 2024 *
2014	1.10 - 1.75	200,000	—	(133,333)	—	—	66,667	August 6, 2018 **
2015	1.25	82,000	—	—	—	—	82,000	January 29, 2025 *
2015	1.25	510,000	—	—	—	—	510,000	January 29, 2025
2016	2	260,000	—	—	—	—	260,000	February 2, 2026
2016	2.00	22,000	—	—	—	—	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
2017	1.32 - 1.525	—	4,656,828	—	—	—	4,656,828	April 26, 2027
<b>Total</b>		3,037,333	4,656,828	(133,333)	—	(33,333)	7,527,495	

\* Options granted under the EMI Scheme.

\*\* Valued based on fair value of services received.

**VERONA PHARMA PLC**
**NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)**
**FOR THE YEAR ENDED DECEMBER 31, 2017**
**16. Share-based payments charge (Continued)**

The Company had the following Restricted Share Units movements in the year ended December 31, 2017:

Year of issue	Exercise price (£)	At January 1, 2017	Units granted	Units exercised	Units forfeited	Units expired	At December 31, 2017	Expiry date
2017		—	1,052,236	—	—	—	1,052,236	April 26, 2027
<b>Total</b>		—	1,052,236	—	—	—	1,052,236	

The average fair value at grant date, by year of grant and plan, of the exercisable options as per December 31, 2017 is presented in the below table.

Year of issue	EMI Scheme (£)	Unapproved Scheme (£)	RSU (£)
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	
2017	—	0.84	1.33

Outstanding and exercisable share options by scheme as of December 31, 2017:

Plan	Outstanding	Exercisable	Weighted average exercise price in £ for Outstanding	Weighted average exercise price in £ for Exercisable
Unapproved	7,313,473	773,333	1.50	1.64
EMI	213,984	185,333	3.06	3.28
<b>Total</b>	<b>7,527,457</b>	<b>958,666</b>	<b>1.54</b>	<b>1.95</b>

As at December 31, 2017 there were no restricted share options exercisable (2016: nil) and there is no exercise price for restricted share options.

The options outstanding at December 31, 2017 had a weighted average remaining contractual life of 8.6 years (2016: 8.2 years). For 2016 and 2017, the number of options granted and expired and the weighted average

**VERONA PHARMA PLC**
**NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)**
**FOR THE YEAR ENDED DECEMBER 31, 2017**
**16. Share-based payments charge (Continued)**

exercise price of options were as follows:

	Number of options	Weighted average exercise price (£)
<b>At January 1, 2016</b>	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
<b>At December 31, 2016</b>	3,037,333	1.87
<b>Exercisable at December 31, 2016</b>	846,667	2.25

	Number of options	Weighted average exercise price (£)
<b>At January 1, 2017</b>	3,037,333	1.87
Options granted in 2017:		
Employees	3,150,846	1.32
Directors	1,505,982	1.32
Options exercised in the year	(133,333)	1.10
Options forfeited in the year	—	—
Options expired in the year	(33,333)	1.90
<b>At December 31, 2017</b>	7,527,495	1.53
<b>Exercisable at December 31, 2017</b>	797,333	2.04

The following table shows the number of RSUs issued in 2017. No RSUs were granted in 2016 and none of the RSUs granted in 2017 were forfeited, canceled or vested in the year. The fair value of each unvested RSU at grant date was £1.32.

	Number of RSUs
<b>At January 1, 2017</b>	—
Granted:	
Employees	705,841
Directors	346,395
<b>At December 31, 2017</b>	1,052,236

**NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)**
**FOR THE YEAR ENDED DECEMBER 31, 2017**
**17. Trade and other payables**

	As of December 31, 2016	As of December 31, 2017
	£'000s	£'000s
Trade payables	719	1,214
Other payables	54	74
Accruals	2,050	5,866
Total trade and other payables	<u>2,823</u>	<u>7,154</u>

As of December 31, 2016, accruals included £0.89 million related to expenses associated with the Global Offering which was fully paid during the year ended December 31, 2017.

**18. Assumed contingent obligation related to the business combination**

The value of the assumed contingent obligation as of December 31, 2017 amounts to £875 thousand (2016: £802 thousand). The increase in value of the assumed contingent obligation during 2017 amounted to £73 thousand (2016: £208 thousand ) and was recorded in finance expense as it related to the unwind of the discount on the liability and retranslation for changes in US\$ exchange rates. Periodic re-measurement is triggered by changes in the probability of success. In 2016 the remeasurement was triggered by the success of the Company's Phase 2a clinical trial, presented in March 2016. The discount percentage applied is 12%. In 2017 there were no events that triggered remeasurement.

	2016	2017
	£'000s	£'000s
January 1	594	802
Re-measurement of assumed contingent obligation	86	—
Impact of changes in foreign exchange rates	37	(23)
Unwinding of discount factor	85	96
December 31	<u>802</u>	<u>875</u>

The table below describes the reported change to the value of the liability during 2017 of £73 thousand (2016: £208 thousand) compared to what this number would be following the presented variations to the underlying assumptions (assuming the probability of success does not change):

	2016	2017
	£'000s	£'000s
Change in value of the assumed contingent obligation	208	73
10% lower revenue assumption	202	72
10% higher revenue assumption	215	73
1% lower risk assumption	205	69
1% higher risk assumption	211	76

**NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)**
**FOR THE YEAR ENDED DECEMBER 31, 2017**
**19. Warrants**

Pursuant to the July 2016 Placement, 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.

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, whereby 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 warrants. The warrants are therefore classified as a derivative financial liability, since their exercise could result in a variable number of shares to be issued.

The warrants entitled 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 (being April 26, 2017) or the first anniversary of the grant, and the exercise period shall end on the fifth anniversary of the date of grant (being July 29, 2021).

The ordinary shares and warrants were accounted for as a compound financial instrument. The warrants component of the instrument issued at the July 2016 Placement was classified as a derivative financial liability and was initially measured at fair value of £9.0 million. The residual amount of proceeds totaling £35.7 million was recognized within equity. Subsequently the financial liability was re-measured at the reporting date at fair value through profit or loss.

The total of transaction costs the Company incurred for the above transactions amounted to £2.9 million of which £0.6 million was allocated to the warrants and the remaining £2.3 million was 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.

In the year ended 31 December 2017 warrants over 45,108 shares were forfeited (2016: nil).

The table below presents the assumptions in applying the Black-Scholes model to determine the fair value of the warrants.

	As of December 31, 2016	As of December 31, 2017
Shares available to be issued under warrants	12,446,370	12,401,262
Exercise price	£ 1.7238	£ 1.7238
Risk-free interest rate	0.088%	0.420%
Expected term to exercise	2.43 years	1.79 years
Annualized volatility	73.53%	47.35%
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 1. 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 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 £1.3 million. The variance of £6.7 million is recorded as finance income in the Consolidated Statement of Comprehensive Income.

**VERONA PHARMA PLC**
**NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)**
**FOR THE YEAR ENDED DECEMBER 31, 2017**
**19. Warrants (Continued)**

	Derivative financial instrument	Derivative financial instrument
	2016	2017
	£'000s	£'000s
<b>At January 1</b>	—	7,923
On issuance of shares	8,991	—
Fair value adjustments recognized in profit or loss	(1,068)	(6,650)
<b>At December 31</b>	<b>7,923</b>	<b>1,273</b>

For the amount recognized at December 31, 2017, 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)
	£'000s	£'000s
Variable up	1,921	1,677
<b>Base case, reported fair value</b>	<b>1,273</b>	<b>1,273</b>
Variable down	694	843

**20. Financial commitments**

As of December 31, 2017, the Company was committed to making the following payments under non-cancellable operating leases related to its facilities.

	Land and Buildings	Land and Buildings
	2016	2017
	£'000s	£'000s
<b>Operating lease obligations:</b>		
Within one year	270	291
Between one and five years	—	277
<b>Total</b>	<b>270</b>	<b>568</b>



**NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

**FOR THE YEAR ENDED DECEMBER 31, 2017**

**21. Related parties transactions and other shareholder matters**

*(i) Related party transactions*

The Directors have authority and responsibility for planning, directing and controlling the activities of the Company and they therefore comprise key management personnel as defined by IAS 24, ("Related Party Disclosures").

*(ii) Other shareholder matters*

The Company has entered into the following arrangements with parties who are significant shareholders of the Company, though they are not classed as related parties.

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") and 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 2016 Placement, and the Company agreed to appoint representatives designated by Vivo Capital, OrbiMed, Abingworth, and Arix and Arthurian, to the board of directors, who are Dr. Mahendra Shah, Mr. Rishi Gupta, Dr. Andrew Sinclair and Dr. Ken Cunningham respectively.

The appointment rights within the relationship agreement with Arix and Arthurian terminated on closing of the Global Offering on April 26, 2017; Dr Cunningham has agreed to continue to serve on the Company's board of directors as an independent director. 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 entered into a management rights agreement with Novo A/S under which Novo A/S was entitled to appoint an observer to the Board; the appointment rights within the management rights agreement terminated on closing of the Global Offering on April 26, 2017.

**DEPOSIT AGREEMENT**

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by and among

**VERONA PHARMA PLC**

and

**CITIBANK, N.A.,**  
as Depositary,

and

**ALL HOLDERS AND BENEFICIAL OWNERS OF  
AMERICAN DEPOSITARY SHARES  
ISSUED HEREUNDER**

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Dated as of May 2, 2017

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## DEPOSIT AGREEMENT

**DEPOSIT AGREEMENT**, dated as of May 2, 2017, by and among (i) Verona Pharma plc, a public limited company incorporated under the laws of England and Wales and its successors (the “Company”), (ii) CITIBANK, N.A., a national banking association organized under the laws of the United States of America (“Citibank”) acting in its capacity as depositary, and any successor depositary hereunder (Citibank in such capacity, the “Depositary”), and (iii) all Holders and Beneficial Owners of American Depositary Shares issued hereunder (all such capitalized terms as hereinafter defined).

### WITNESSETH THAT:

**WHEREAS**, the Company desires to establish with the Depositary an ADR facility to provide for the deposit of the Shares (as hereinafter defined) and the creation of American Depositary Shares representing the Shares so deposited and for the execution and delivery of American Depositary Receipts (as hereinafter defined) evidencing such American Depositary Shares; and

**WHEREAS**, the Depositary is willing to act as the Depositary for such ADR facility upon the terms set forth in the Deposit Agreement (as hereinafter defined); and

**WHEREAS**, any American Depositary Receipts issued pursuant to the terms of the Deposit Agreement are to be substantially in the form of Exhibit A attached hereto, with appropriate insertions, modifications and omissions, as hereinafter provided in the Deposit Agreement.

**NOW, THEREFORE**, for good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the parties hereto agree as follows:

## ARTICLE I

### DEFINITIONS

All capitalized terms used, but not otherwise defined, herein shall have the meanings set forth below, unless otherwise clearly indicated:

**Section 1.1** “ADS Record Date” shall have the meaning given to such term in Section 4.9.

**Section 1.2** “Affiliate” shall have the meaning assigned to such term by the Commission (as hereinafter defined) under Regulation C promulgated under the Securities Act (as hereinafter defined), or under any successor regulation thereto.

**Section 1.3** “American Depositary Receipt(s)”, “ADR(s)” and “Receipt(s)” shall mean the certificate(s) issued by the Depositary to evidence the American Depositary Shares issued under the terms of the Deposit Agreement in the form of Certificated ADS(s) (as hereinafter defined), as such ADRs may be amended from time to time in accordance with the provisions of the Deposit Agreement. An ADR may evidence any number of ADSs and may, in

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the case of ADSs held through a central depository such as DTC, be in the form of a “Balance Certificate.”

**Section 1.4 “American Depositary Share(s)” and “ADS(s)”** shall mean the rights and interests in the Deposited Property (as hereinafter defined) granted to the Holders and Beneficial Owners pursuant to the terms and conditions of the Deposit Agreement and, if issued as Certificated ADS(s) (as hereinafter defined), the ADR(s) issued to evidence such ADSs. ADS(s) may be issued under the terms of the Deposit Agreement in the form of (a) Certificated ADS(s) (as hereinafter defined), in which case the ADS(s) are evidenced by ADR(s), or (b) Uncertificated ADS(s) (as hereinafter defined), in which case the ADS(s) are not evidenced by ADR(s) but are reflected on the direct registration system maintained by the Depositary for such purposes under the terms of Section 2.13. Unless otherwise specified in the Deposit Agreement or in any ADR, or unless the context otherwise requires, any reference to ADS(s) shall include Certificated ADS(s) and Uncertificated ADS(s), individually or collectively, as the context may require. Each ADS shall represent the right to receive, and to exercise the beneficial ownership interests in, the number of Shares specified in the form of ADR attached hereto as Exhibit A (as amended from time to time) that are on deposit with the Depositary and/or the Custodian, subject, in each case, to the terms and conditions of the Deposit Agreement and the applicable ADR (if issued as a Certificated ADS), until there shall occur a distribution upon Deposited Securities referred to in Section 4.2 or a change in Deposited Securities referred to in Section 4.11 with respect to which additional ADSs are not issued, and thereafter each ADS shall represent the right to receive, and to exercise the beneficial ownership interests in, the applicable Deposited Property on deposit with the Depositary and the Custodian determined in accordance with the terms of such Sections, subject, in each case, to the terms and conditions of the Deposit Agreement and the applicable ADR (if issued as a Certificated ADS). In addition, the ADS(s)-to-Share(s) ratio is subject to amendment as provided in Articles IV and VI of the Deposit Agreement (which may give rise to Depositary fees).

**Section 1.5 “Applicant”** shall have the meaning given to such term in Section 5.10.

**Section 1.6 “Articles of Association”** shall mean the Articles of Association of the Company, as amended and restated from time to time.

**Section 1.7 “Beneficial Owner”** shall mean, as to any ADS, any person or entity having a beneficial interest deriving from the ownership of such ADS. Notwithstanding anything else contained in the Deposit Agreement, any ADR(s) or any other instruments or agreements relating to the ADSs and the corresponding Deposited Property, the Depositary, the Custodian and their respective nominees are intended to be, and shall at all times during the term of the Deposit Agreement be, the record holders only of the Deposited Property represented by the ADSs for the benefit of the Holders and Beneficial Owners of the corresponding ADSs. The Depositary, on its own behalf and on behalf of the Custodian and their respective nominees, disclaims any beneficial ownership interest in the Deposited Property held on behalf of the Holders and Beneficial Owners of ADSs. The beneficial ownership interests in the Deposited Property are intended to be, and shall at all times during the term of the Deposit Agreement continue to be, vested in the Beneficial Owners of the ADSs representing the Deposited Property. The beneficial ownership interests in the Deposited Property shall, unless otherwise agreed by the Depositary, be exercisable by the Beneficial Owners of the ADSs only through the



Holders of such ADSs, by the Holders of the ADSs (on behalf of the applicable Beneficial Owners) only through the Depositary, and by the Depositary (on behalf of the Holders and Beneficial 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 and, if applicable, the terms of the ADR(s) evidencing the ADSs. A Beneficial Owner of ADSs may or may not be the Holder of such ADSs. A Beneficial Owner shall be able to exercise any right or receive any benefit hereunder solely through the person who is the Holder of the ADSs owned by such Beneficial Owner. Unless otherwise identified to the Depositary, a Holder shall be deemed to be the Beneficial Owner of all the ADSs registered in his/her/its name. The manner in which a Beneficial Owner holds ADSs (*e.g.*, in a brokerage account vs. as registered holder) may affect the rights and obligations of, the manner in which, and the extent to which, services are made available to, Beneficial Owners pursuant to the terms of the Deposit Agreement.

**Section 1.8** “Certificated ADS(s)” shall have the meaning set forth in Section 2.13.

**Section 1.9** “Citibank” shall mean Citibank, N.A., a national banking association organized under the laws of the United States of America, and its successors.

**Section 1.10** “Commission” shall mean the Securities and Exchange Commission of the United States or any successor governmental agency thereto in the United States.

**Section 1.11** “Company” shall mean Verona Pharma plc, a public limited company incorporated under the laws of England and Wales, and its successors.

**Section 1.12** “CREST” shall mean the system for the paperless settlement of trades in securities and the holding of uncertificated securities operated by Euroclear UK & Ireland Limited in accordance with the Uncertificated Securities Regulations 2001 (SI 2001 No. 3755), as amended from time to time, or any successor thereto.

**Section 1.13** “Custodian” shall mean (i) as of the date hereof, Citibank N.A., London Branch, having its principal office at 25 Canada Square, Canary Wharf, London, E14 5LB, United Kingdom, as the custodian of Deposited Property for the purposes of the Deposit Agreement, (ii) Citibank, N.A., acting as custodian of Deposited Property pursuant to the Deposit Agreement, and (iii) any other entity that may be appointed by the Depositary pursuant to the terms of Section 5.5 as successor, substitute or additional custodian hereunder. The term “Custodian” shall mean any Custodian individually or all Custodians collectively, as the context requires.

**Section 1.14** “Deliver” and “Delivery” shall mean (x) *when used in respect of Shares and other Deposited Securities*, either (i) the physical delivery of the certificate(s) representing such securities, or (ii) the book-entry transfer and recordation of such securities on the books of the Share Registrar (as hereinafter defined) or in the book-entry settlement of CREST, and (y) *when used in respect of ADSs*, either (i) the physical delivery of ADR(s) evidencing the ADSs, or (ii) the book-entry transfer and recordation of ADSs on the books of the Depositary or any book-entry settlement system in which the ADSs are settlement-eligible.



**Section 1.15 “Deposit Agreement”** shall mean this Deposit Agreement and all exhibits hereto, as the same may from time to time be amended and supplemented from time to time in accordance with the terms of the Deposit Agreement.

**Section 1.16 “Depository”** shall mean Citibank, N.A., a national banking association organized under the laws of the United States, in its capacity as depository under the terms of the Deposit Agreement, and any successor depository hereunder.

**Section 1.17 “Deposited Property”** shall mean the Deposited Securities and any cash and other property held on deposit by the Depository and the Custodian in respect of the ADSs under the terms of the Deposit Agreement, subject, in the case of cash, to the provisions of Section 4.8. All Deposited Property shall be held by the Custodian, the Depository and their respective nominees for the benefit of the Holders and Beneficial Owners of the ADSs representing the Deposited Property. The Deposited Property is not intended to, and shall not, constitute proprietary assets of the Depository, the Custodian or their nominees. Beneficial ownership in the Deposited Property is intended to be, and shall at all times during the term of the Deposit Agreement continue to be, vested in the Beneficial Owners of the ADSs representing the Deposited Property. Notwithstanding the foregoing, the collateral delivered in connection with Pre-Release Transactions described in Section 5.10 shall not constitute Deposited Property.

**Section 1.18 “Deposited Securities”** shall mean the Shares and any other securities held on deposit by the Custodian from time to time in respect of the ADSs under the Deposit Agreement and constituting Deposited Property.

**Section 1.19 “Dollars” and “\$”** shall refer to the lawful currency of the United States.

**Section 1.20 “DTC”** shall mean The Depository Trust Company, a national clearinghouse and the central book-entry settlement system for securities traded in the United States and, as such, the custodian for the securities of DTC Participants (as hereinafter defined) maintained in DTC, and any successor thereto.

**Section 1.21 “DTC Participant”** shall mean any financial institution (or any nominee of such institution) having one or more participant accounts with DTC for receiving, holding and delivering the securities and cash held in DTC. A DTC Participant may or may not be a Beneficial Owner. If a DTC Participant is not the Beneficial Owner of the ADSs credited to its account at DTC, or of the ADSs in respect of which the DTC Participant is otherwise acting, such DTC Participant shall be deemed, for all purposes hereunder, to have all requisite authority to act on behalf of the Beneficial Owner(s) of the ADSs credited to its account at DTC or in respect of which the DTC Participant is so acting. A DTC Participant, upon acceptance in any one of its DTC accounts of any ADSs (or any interest therein) issued in accordance with the terms and conditions of the Deposit Agreement, shall be deemed for all purposes to be a party to, and bound by, the terms of the Deposit Agreement and the applicable ADR(s) to the same extent as, and as if the DTC Participant were, the Holder of such ADSs.

**Section 1.22 “Exchange Act”** shall mean the United States Securities Exchange Act of 1934, as amended from time to time.

**Section 1.23 “Foreign Currency”** shall mean any currency other than Dollars.

**Section 1.24** **“Full Entitlement ADR(s)”, “Full Entitlement ADS(s)” and “Full Entitlement Share(s)”** shall have the respective meanings set forth in Section 2.12.

**Section 1.25** **“Holder(s)”** shall mean the person(s) in whose name the ADSs are registered on the books of the Depositary (or the Registrar, if any) maintained for such purpose. A Holder may or may not be a Beneficial Owner. If a Holder is not the Beneficial Owner of the ADS(s) registered in its name, such person shall be deemed, for all purposes hereunder, to have all requisite authority to act on behalf of the Beneficial Owners of the ADSs registered in its name. The manner in which a Holder holds ADSs (e.g., in certificated vs. uncertificated form) may affect the rights and obligations of, and the manner in which the services are made available to, Holders pursuant to the terms of the Deposit Agreement.

**Section 1.26** **“Partial Entitlement ADR(s)”, “Partial Entitlement ADS(s)” and “Partial Entitlement Share(s)”** shall have the respective meanings set forth in Section 2.12.

**Section 1.27** **“Pounds”, “Pence” and “£”** shall refer to the lawful currency of England. **“Pre-Release Transaction”** shall have the meaning set forth in Section 5.10.

**Section 1.29** **“Principal Office”** shall mean, when used with respect to the Depositary, the principal office of the Depositary at which at any particular time its depositary receipts business shall be administered, which, at the date of the Deposit Agreement, is located at 388 Greenwich Street, New York, New York 10013, U.S.A.

**Section 1.30** **“Registrar”** shall mean the Depositary or any bank or trust company having an office in the Borough of Manhattan, The City of New York, which shall be appointed by the Depositary to register issuances, transfers and cancellations of ADSs as herein provided, and shall include any co-registrar appointed by the Depositary for such purposes. Registrars (other than the Depositary) may be removed and substitutes appointed by the Depositary. Each Registrar (other than the Depositary) appointed pursuant to the Deposit Agreement shall be required to give notice in writing to the Depositary accepting such appointment and agreeing to be bound by the applicable terms of the Deposit Agreement.

**Section 1.31** **“Restricted Securities”** shall mean Shares, Deposited Securities or ADSs which (i) have been acquired directly or indirectly from the Company or any of its Affiliates in a transaction or chain of transactions not involving any public offering and are subject to resale limitations under the Securities Act or the rules issued thereunder, or (ii) are held by an executive officer or director (or persons performing similar functions) or other Affiliate of the Company, or (iii) are subject to other restrictions on sale or deposit under the laws of the United States, England and Wales, or under a shareholder agreement or the Articles of Association of the Company or under the regulations of an applicable securities exchange unless, in each case, such Shares, Deposited Securities or ADSs are being transferred or sold to persons other than an Affiliate of the Company in a transaction (a) covered by an effective resale registration statement, or (b) exempt from the registration requirements of the Securities Act (as hereinafter defined), and the Shares, Deposited Securities or ADSs are not, when held by such person(s), Restricted Securities.

**Section 1.32 “Restricted ADR(s)”, “Restricted ADS(s)” and “Restricted Shares”** shall have the respective meanings set forth in Section 2.14.

**Section 1.33 “Securities Act”** shall mean the United States Securities Act of 1933, as amended from time to time.

**Section 1.34 “Share Registrar”** shall mean Computershare Investor Services plc, a company registered in England and Wales under company number 3498808 and whose registered office is at The Pavilions, Bridgewater Road, Bristol BS13 8AE or any other institution organized under the laws of England and Wales appointed by the Company to carry out the duties of registrar for the Shares, and any successor thereto.

**Section 1.35 “Shares”** shall mean the Company’s ordinary shares, nominal value £0.05 per share, validly issued and outstanding and fully paid and may, if the Depositary so agrees after consultation with the Company, include evidence of the right to receive Shares; provided that in no event shall Shares include evidence of the right to receive Shares with respect to which the full purchase price has not been paid or Shares as to which preemptive rights have theretofore not been validly waived, disappplied or exercised; provided further, however, that, if there shall occur any change in nominal value, split-up, consolidation, reclassification, exchange, conversion or any other event described in Section 4.11 in respect of the Shares of the Company, the term “Shares” shall thereafter, to the maximum extent permitted by law, represent the successor securities resulting from such event.

**Section 1.36 “Uncertificated ADS(s)”** shall have the meaning set forth in Section 2.13.

**Section 1.37 “United States” and “U.S.”** shall have the meaning assigned to it in Regulation S as promulgated by the Commission under the Securities Act.

## ARTICLE II

### APPOINTMENT OF DEPOSITARY; FORM OF RECEIPTS; DEPOSIT OF SHARES; EXECUTION AND DELIVERY, TRANSFER AND SURRENDER OF RECEIPTS

**Section 2.1 Appointment of Depositary.** The Company hereby appoints the Depositary as depositary for the Deposited Property and hereby authorizes and directs the Depositary to act in accordance with the terms and conditions set forth in the Deposit Agreement and the applicable ADRs. Each Holder and each Beneficial Owner, upon acceptance of any ADSs (or any interest therein) issued in accordance with the terms and conditions of the Deposit Agreement shall be deemed for all purposes to (a) be a party to and bound by the terms of the Deposit Agreement and the applicable ADR(s), and (b) appoint the Depositary its attorney-in-fact, with full power to delegate, to act on its behalf and to take any and all actions contemplated in the Deposit Agreement and the applicable ADR(s), to adopt any and all procedures necessary to comply with applicable law and to take such action as the Depositary in its sole discretion may deem necessary or appropriate to carry out the purposes of the Deposit Agreement and the

applicable ADR(s), the taking of such actions to be the conclusive determinant of the necessity and appropriateness thereof.

## **Section 2.2 Form and Transferability of ADSs.**

(a) **Form.** Certificated ADSs shall be evidenced by definitive ADRs which shall be engraved, printed, lithographed or produced in such other manner as may be agreed upon by the Company and the Depositary. ADRs may be issued under the Deposit Agreement in denominations of any whole number of ADSs. The ADRs shall be substantially in the form set forth in Exhibit A to the Deposit Agreement, with any appropriate insertions, modifications and omissions, in each case as otherwise contemplated in the Deposit Agreement or required by law. ADRs shall be (i) dated, (ii) signed by the manual or facsimile signature of a duly authorized signatory of the Depositary, (iii) countersigned by the manual or facsimile signature of a duly authorized signatory of the Registrar, and (iv) registered in the books maintained by the Registrar for the registration of issuances and transfers of ADSs. No ADR and no Certificated ADS evidenced thereby shall be entitled to any benefits under the Deposit Agreement or be valid or enforceable for any purpose against the Depositary or the Company, unless such ADR shall have been so dated, signed, countersigned and registered. ADRs bearing the facsimile signature of a duly-authorized signatory of the Depositary or the Registrar, who at the time of signature was a duly-authorized signatory of the Depositary or the Registrar, as the case may be, shall bind the Depositary, notwithstanding the fact that such signatory has ceased to be so authorized prior to the delivery of such ADR by the Depositary. The ADRs shall bear a CUSIP number that is different from any CUSIP number that was, is or may be assigned to any depositary receipts previously or subsequently issued pursuant to any other arrangement between the Depositary (or any other depositary) and the Company and which are not ADRs outstanding hereunder.

(b) **Legends.** The ADRs may be endorsed with, or have incorporated in the text thereof, such legends or recitals not inconsistent with the provisions of the Deposit Agreement as may be (i) necessary to enable the Depositary and the Company to perform their respective obligations hereunder, (ii) required to comply with any applicable laws or regulations, or with the rules and regulations of any securities exchange or market upon which ADSs may be traded, listed or quoted, or to conform with any usage with respect thereto, (iii) necessary to indicate any special limitations or restrictions to which any particular ADRs or ADSs are subject by reason of the date of issuance of the Deposited Securities or otherwise, or (iv) required by any book-entry system in which the ADSs are held. Holders and Beneficial Owners shall be deemed, for all purposes, to have notice of, and to be bound by, the terms and conditions of the legends set forth, in the case of Holders, on the ADR registered in the name of the applicable Holders or, in the case of Beneficial Owners, on the ADR representing the ADSs owned by such Beneficial Owners.

(c) **Title.** Subject to the limitations contained herein and in the ADR, title to an ADR (and to each Certificated ADS evidenced thereby) shall be transferable upon the same terms as a certificated security under the laws of the State of New York, provided that, in the case of Certificated ADSs, such ADR has been properly endorsed or is accompanied by proper instruments of transfer. Notwithstanding any notice to the contrary, the Depositary and the Company may deem and treat the Holder of an ADS (that is, the person in whose name an ADS is registered on the books of the Depositary) as the absolute owner thereof for all purposes.

Neither the Depositary nor the Company shall have any obligation nor be subject to any liability under the Deposit Agreement or any ADR to any holder or any Beneficial Owner unless, in the case of a holder of ADSs, such holder is the Holder registered on the books of the Depositary or, in the case of a Beneficial Owner, such Beneficial Owner, or the Beneficial Owner's representative, is the Holder registered on the books of the Depositary.

(d) **Book-Entry Systems.** The Depositary shall make arrangements for the acceptance of the ADSs into DTC. All ADSs held through DTC will be registered in the name of the nominee for DTC (currently "Cede & Co."). Unless issued by the Depositary as Uncertificated ADSs, the ADSs registered in the name of Cede & Co. will be evidenced by one or more ADR(s) in the form of a "Balance Certificate," which will provide that it represents the aggregate number of ADSs from time to time indicated in the records of the Depositary as being issued hereunder and that the aggregate number of ADSs represented thereby may from time to time be increased or decreased by making adjustments on such records of the Depositary and of DTC or its nominee as hereinafter provided. Citibank, N.A. (or such other entity as is appointed by DTC or its nominee) may hold the "Balance Certificate" as custodian for DTC. Each Beneficial Owner of ADSs held through DTC must rely upon the procedures of DTC and the DTC Participants to exercise or be entitled to any rights attributable to such ADSs. The DTC Participants shall for all purposes be deemed to have all requisite power and authority to act on behalf of the Beneficial Owners of the ADSs held in the DTC Participants' respective accounts in DTC and the Depositary shall for all purposes be authorized to rely upon any instructions and information given to it by DTC Participants. So long as ADSs are held through DTC or unless otherwise required by law, ownership of beneficial interests in the ADSs registered in the name of the nominee for DTC will be shown on, and transfers of such ownership will be effected only through, records maintained by (i) DTC or its nominee (with respect to the interests of DTC Participants), or (ii) DTC Participants or their nominees (with respect to the interests of clients of DTC Participants). Any distributions made, and any notices given, by the Depositary to DTC under the terms of the Deposit Agreement shall (unless otherwise specified by the Depositary) satisfy the Depositary's obligations under the Deposit Agreement to make such distributions, and give such notices, in respect of the ADSs held in DTC (including, for avoidance of doubt, to the DTC Participants holding the ADSs in their DTC accounts and to the Beneficial Owners of such ADSs).

**Section 2.3 Deposit of Shares.** Subject to the terms and conditions of the Deposit Agreement and applicable law, Shares or evidence of rights to receive Shares (other than Restricted Securities) may be deposited by any person (including the Depositary in its individual capacity but subject, however, in the case of the Company or any Affiliate of the Company, to Section 5.7) at any time, whether or not the transfer books of the Company or the Share Registrar, if any, are closed, by Delivery of the Shares to the Custodian. Every deposit of Shares shall be accompanied by the following: (A) (i) *in the case of Shares represented by certificates issued in registered form*, appropriate instruments of transfer or endorsement, in a form satisfactory to the Custodian, (ii) *in the case of Shares represented by certificates in bearer form*, the requisite coupons and talons pertaining thereto, and (iii) *in the case of Shares delivered by book-entry transfer and recordation*, confirmation of such book-entry transfer and recordation in the books of the Share Registrar or of CREST, as applicable, to the Custodian or that irrevocable instructions have been given to cause such Shares to be so transferred and recorded, (B) such certifications and payments (including, without limitation, the Depositary's fees and related



charges) and evidence of such payments (including, without limitation, stamping or otherwise marking such Shares by way of receipt) as may be required by the Depositary or the Custodian in accordance with the provisions of the Deposit Agreement and applicable law, (C) if the Depositary so requires, a written order directing the Depositary to issue and deliver to, or upon the written order of, the person(s) stated in such order the number of ADSs representing the Shares so deposited, (D) evidence satisfactory to the Depositary (which may be an opinion of counsel) that all necessary approvals have been granted by, or there has been compliance with the rules and regulations of, any applicable governmental agency in England and Wales, and (E) if the Depositary so requires, (i) an agreement, assignment or instrument satisfactory to the Depositary or the Custodian which provides for the prompt transfer by any person in whose name the Shares are or have been recorded to the Custodian of any distribution, or right to subscribe for additional Shares or to receive other property in respect of any such deposited Shares or, in lieu thereof, such indemnity or other agreement as shall be satisfactory to the Depositary or the Custodian and (ii) if the Shares are registered in the name of the person on whose behalf they are presented for deposit, a proxy or proxies entitling the Custodian to exercise voting rights in respect of the Shares for any and all purposes until the Shares so deposited are registered in the name of the Depositary, the Custodian or any nominee.

Without limiting any other provision of the Deposit Agreement, the Depositary shall instruct the Custodian not to, and the Depositary shall not knowingly, accept for deposit (a) any Restricted Securities, except as contemplated by Section 2.14 nor (b) any fractional Shares or fractional Deposited Securities nor (c) a number of Shares or Deposited Securities which upon application of the ADS to Shares ratio would give rise to fractional ADSs. No Shares shall be accepted for deposit unless accompanied by evidence, if any is required by the Depositary, that is reasonably satisfactory to the Depositary or the Custodian that all conditions to such deposit have been satisfied by the person depositing such Shares under the laws and regulations of England and Wales and any necessary approval has been granted by any applicable governmental body in England and Wales, if any. The Depositary may issue ADSs against evidence of rights to receive Shares from the Company, any agent of the Company or any custodian, registrar, transfer agent, clearing agency or other entity involved in ownership or transaction records in respect of the Shares. Such evidence of rights shall consist of written blanket or specific guarantees of ownership of Shares furnished by the Company or any such custodian, registrar, transfer agent, clearing agency or other entity involved in ownership or transaction records in respect of the Shares.

Without limitation of the foregoing, the Depositary shall not knowingly accept for deposit under the Deposit Agreement (A) any Shares or other securities required to be registered under the provisions of the Securities Act, unless (i) a registration statement is in effect as to such Shares or other securities or (ii) the deposit is made upon terms contemplated in Section 2.14, or (B) any Shares or other securities the deposit of which would violate any provisions of the Articles of Association of the Company. For purposes of the foregoing sentence, the Depositary shall be entitled to rely upon representations and warranties made or deemed made pursuant to the Deposit Agreement and shall not be required to make any further investigation. The Depositary will comply with written instructions of the Company (received by the Depositary reasonably in advance) not to accept for deposit hereunder any Shares identified in such instructions at such times and under such circumstances as may reasonably be specified in

such instructions in order to facilitate the Company's compliance with the securities laws of the United States.

**Section 2.4 Registration and Safekeeping of Deposited Securities.** The Depositary shall instruct the Custodian upon each Delivery of registered Shares being deposited hereunder with the Custodian (or other Deposited Securities pursuant to Article IV hereof), together with the other documents above specified, to present such Shares, together with the appropriate instrument(s) of transfer or endorsement, duly stamped, to the Share Registrar for transfer and registration of the Shares (as soon as transfer and registration can be accomplished and at the expense of the person for whom the deposit is made) in the name of the Depositary, the Custodian or a nominee of either. Deposited Securities shall be held by the Depositary, or by a Custodian for the account and to the order of the Depositary or a nominee of the Depositary, in each case, on behalf of the Holders and Beneficial Owners, at such place(s) as the Depositary or the Custodian shall determine. Notwithstanding anything else contained in the Deposit Agreement, any ADR(s), or any other instruments or agreements relating to the ADSs and the corresponding Deposited Property, the registration of the Deposited Securities in the name of the Depositary, the Custodian or any of their respective nominees, shall, to the maximum extent permitted by applicable law, vest in the Depositary, the Custodian or the applicable nominee the record ownership in the applicable Deposited Securities with the beneficial ownership rights and interests in such Deposited Securities being at all times vested with the Beneficial Owners of the ADSs representing the Deposited Securities. Notwithstanding the foregoing, the Depositary, the Custodian and the applicable nominee 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, upon the terms set forth in the Deposit Agreement and, if applicable, the ADR(s) representing the ADSs. The Depositary, the Custodian and their respective nominees shall for all purposes be deemed to have all requisite power and authority to act in respect of Deposited Property on behalf of the Holders and Beneficial Owners of ADSs representing the Deposited Property, and upon making payments to, or acting upon instructions from, or information provided by, the Depositary, the Custodian or their respective nominees all persons shall be authorized to rely upon such power and authority.

**Section 2.5 Issuance of ADSs.** The Depositary has made arrangements with the Custodian for the Custodian to confirm to the Depositary upon receipt of a deposit of Shares (i) that a deposit of Shares has been made pursuant to Section 2.3, (ii) that such Deposited Securities have been recorded in the name of the Depositary, the Custodian or a nominee of either on the shareholders' register maintained by or on behalf of the Company by the Share Registrar on the books of CREST, (iii) that all required documents have been received, and (iv) the person(s) to whom or upon whose order ADSs are deliverable in respect thereof and the number of ADSs to be so delivered. Such notification may be made by letter, cable, telex, SWIFT message or, at the risk and expense of the person making the deposit, by facsimile or other means of electronic transmission. Upon receiving such notice from the Custodian, the Depositary, subject to the terms and conditions of the Deposit Agreement and applicable law, shall issue the ADSs representing the Shares so deposited to or upon the order of the person(s) named in the notice delivered to the Depositary and, if applicable, shall execute and deliver at its Principal Office Receipt(s) registered in the name(s) requested by such person(s) and evidencing the aggregate number of ADSs to which such person(s) are entitled, but, in each case, only upon payment to the Depositary of the charges of the Depositary for accepting a deposit of Shares and

issuing ADSs (as set forth in Section 5.9 and Exhibit B hereto) and all taxes and governmental charges and fees payable in connection with such deposit and the transfer of the Shares and the issuance of the ADS(s). The Depositary shall only issue ADSs in whole numbers and deliver, if applicable, ADR(s) evidencing whole numbers of ADSs. Nothing herein shall prohibit any Pre-Release Transaction upon the terms set forth in the Deposit Agreement.

#### **Section 2.6 Transfer, Combination and Split-up of ADRs.**

(a) **Transfer.** The Registrar shall register the transfer of ADRs (and of the ADSs represented thereby) on the books maintained for such purpose and the Depositary shall (x) cancel such ADRs and execute new ADRs evidencing the same aggregate number of ADSs as those evidenced by the ADRs canceled by the Depositary, (y) cause the Registrar to countersign such new ADRs and (z) Deliver such new ADRs to or upon the order of the person entitled thereto, if each of the following conditions has been satisfied: (i) the ADRs have been duly Delivered by the Holder (or by a duly authorized attorney of the Holder) to the Depositary at its Principal Office for the purpose of effecting a transfer thereof, (ii) the surrendered ADRs have been properly endorsed or are accompanied by proper instruments of transfer (including signature guarantees in accordance with standard securities industry practice), (iii) the surrendered ADRs have been duly stamped (if required by the laws of the State of New York or of the United States), and (iv) all applicable fees and charges of, and expenses incurred by, the Depositary and all applicable taxes and governmental charges (as are set forth in Section 5.9 and Exhibit B hereto) have been paid, *subject, however, in each case*, to the terms and conditions of the applicable ADRs, of the Deposit Agreement and of applicable law, in each case as in effect at the time thereof.

(b) **Combination & Split-Up.** The Registrar shall register the split-up or combination of ADRs (and of the ADSs represented thereby) on the books maintained for such purpose and the Depositary shall (x) cancel such ADRs and execute new ADRs for the number of ADSs requested, but in the aggregate not exceeding the number of ADSs evidenced by the ADRs canceled by the Depositary, (y) cause the Registrar to countersign such new ADRs and (z) Deliver such new ADRs to or upon the order of the Holder thereof, if each of the following conditions has been satisfied: (i) the ADRs have been duly Delivered by the Holder (or by a duly authorized attorney of the Holder) to the Depositary at its Principal Office for the purpose of effecting a split-up or combination thereof, and (ii) all applicable fees and charges of, and expenses incurred by, the Depositary and all applicable taxes and governmental charges (as are set forth in Section 5.9 and Exhibit B hereto) have been paid, *subject, however, in each case*, to the terms and conditions of the applicable ADRs, of the Deposit Agreement and of applicable law, in each case as in effect at the time thereof.

**Section 2.7 Surrender of ADSs and Withdrawal of Deposited Securities.** The Holder of ADSs shall be entitled to Delivery (at the Custodian's designated office) of the Deposited Securities at the time represented by the ADSs upon satisfaction of each of the following conditions: (i) the Holder (or a duly-authorized attorney of the Holder) has duly Delivered ADSs to the Depositary at its Principal Office (and if applicable, the ADRs evidencing such ADSs) for the purpose of withdrawal of the Deposited Securities represented thereby, (ii) if applicable and so required by the Depositary, the ADRs Delivered to the Depositary for such purpose have been properly endorsed in blank or are accompanied by proper instruments of



transfer in blank (including signature guarantees in accordance with standard securities industry practice), (iii) if so required by the Depositary, the Holder of the ADSs has executed and delivered to the Depositary a written order directing the Depositary to cause the Deposited Securities being withdrawn to be Delivered to or upon the written order of the person(s) designated in such order, and (iv) all applicable fees and charges of, and expenses incurred by, the Depositary and all applicable taxes and governmental charges (as are set forth in Section 5.9 and Exhibit B) have been paid, *subject, however, in each case*, to the terms and conditions of the ADRs evidencing the surrendered ADSs, of the Deposit Agreement, of the Company's Articles of Association and of any applicable laws and the rules of CREST, and to any provisions of or governing the Deposited Securities, in each case as in effect at the time thereof.

Upon satisfaction of each of the conditions specified above, the Depositary (i) shall cancel the ADSs Delivered to it (and, if applicable, the ADR(s) evidencing the ADSs so Delivered), (ii) shall direct the Registrar to record the cancellation of the ADSs so Delivered on the books maintained for such purpose, and (iii) shall direct the Custodian to Deliver, or cause the Delivery of, in each case, without unreasonable delay, the Deposited Securities represented by the ADSs so canceled together with any certificate or other document of title for the Deposited Securities, or evidence of the electronic transfer thereof (if available), as the case may be, to or upon the written order of the person(s) designated in the order delivered to the Depositary for such purpose, *subject however, in each case*, to the terms and conditions of the Deposit Agreement, of the ADRs evidencing the ADSs so canceled, of the Articles of Association of the Company, of any applicable laws and of the rules of CREST, and to the terms and conditions of or governing the Deposited Securities, in each case as in effect at the time thereof.

The Depositary shall not accept for surrender ADSs representing less than one (1) Share. In the case of Delivery to it of ADSs representing a number other than a whole number of Shares, the Depositary shall cause ownership of the appropriate whole number of Shares to be Delivered in accordance with the terms hereof, and shall, at the discretion of the Depositary, either (i) return to the person surrendering such ADSs the number of ADSs representing any remaining fractional Share, or (ii) sell or cause to be sold the fractional Share represented by the ADSs so surrendered and remit the proceeds of such sale (net of (a) applicable fees and charges of, and expenses incurred by, the Depositary and (b) applicable taxes withheld) to the person surrendering the ADSs.

Notwithstanding anything else contained in any ADR or the Deposit Agreement, the Depositary may make delivery at the Principal Office of the Depositary of Deposited Property consisting of (i) any cash dividends or cash distributions, or (ii) any proceeds from the sale of any non-cash distributions, which are at the time held by the Depositary in respect of the Deposited Securities represented by the ADSs surrendered for cancellation and withdrawal. At the request, risk and expense of any Holder so surrendering ADSs, and for the account of such Holder, the Depositary shall direct the Custodian to forward (to the extent permitted by law) any Deposited Property (other than Deposited Securities) held by the Custodian in respect of such ADSs to the Depositary for delivery at the Principal Office of the Depositary. Such direction shall be given by letter or, at the request, risk and expense of such Holder, by cable, telex or facsimile transmission.

**Section 2.8 Limitations on Execution and Delivery, Transfer, etc. of ADSs; Suspension of Delivery, Transfer, etc.**

(a) **Additional Requirements.** As a condition precedent to the execution and delivery, the registration of issuance, transfer, split-up, combination or surrender, of any ADS, the delivery of any distribution thereon, or the withdrawal of any Deposited Property, the Depositary or the Custodian may require (i) payment from the depositor of Shares or presenter of ADSs or of an ADR of a sum sufficient to reimburse it for any tax or other governmental charge and any stock transfer or registration fee with respect thereto (including any such tax or charge and fee with respect to Shares being deposited or withdrawn) and payment of any applicable fees and charges of the Depositary as provided in Section 5.9 and Exhibit B, (ii) the production of proof satisfactory to it as to the identity and genuineness of any signature or any other matter contemplated by Section 3.1, and (iii) compliance with (A) any laws or governmental regulations relating to the execution and delivery of ADRs or ADSs or to the withdrawal of Deposited Securities and (B) such reasonable regulations as the Depositary and the Company may establish consistent with the provisions of the representative ADR, if applicable, the Deposit Agreement and applicable law.

(b) **Additional Limitations.** The issuance of ADSs against deposits of Shares generally or against deposits of particular Shares may be suspended, or the deposit of particular Shares may be refused, or the registration of transfer of ADSs in particular instances may be refused, or the registration of transfers of ADSs generally may be suspended, during any period when the transfer books of the Company, the Depositary, a Registrar or the Share Registrar are closed or if any such action is deemed necessary or advisable by the Depositary or the Company, in good faith, at any time or from time to time because of any requirement of law or regulation, any government or governmental body or commission or any securities exchange on which the ADSs or Shares are listed, or under any provision of the Deposit Agreement or the representative ADR(s), if applicable, or under any provision of, or governing, the Deposited Securities, or because of a meeting of shareholders of the Company or for any other reason, subject, in all cases, to Section 7.8.

(c) **Regulatory Restrictions.** Notwithstanding any provision of the Deposit Agreement or any ADR(s) to the contrary, Holders are entitled to surrender outstanding ADSs to withdraw the Deposited Securities associated herewith at any time subject only to (i) temporary delays caused by closing the transfer books of the Depositary or the Company or the deposit of Shares in connection with voting at a shareholders' meeting or the payment of dividends, (ii) the payment of fees, taxes and similar charges, (iii) compliance with any U.S. or foreign laws or governmental regulations relating to the ADSs or to the withdrawal of the Deposited Securities, and (iv) other circumstances specifically contemplated by Instruction I.A.(I) of the General Instructions to Form F-6 (as such General Instructions may be amended from time to time).

**Section 2.9 Lost ADRs, etc.** In case any ADR shall be mutilated, destroyed, lost, or stolen, the Depositary shall execute and deliver a new ADR of like tenor at the expense of the Holder (a) *in the case of a mutilated ADR*, in exchange of and substitution for such mutilated ADR upon cancellation thereof, or (b) *in the case of a destroyed, lost or stolen ADR*, in lieu of and in substitution for such destroyed, lost, or stolen ADR, after the Holder thereof (i) has submitted to the Depositary a written request for such exchange and substitution before the

Depository has notice that the ADR has been acquired by a bona fide purchaser, (ii) has provided such security or indemnity (including an indemnity bond) as may be required by the Depository to save it and any of its agents harmless, and (iii) has satisfied any other reasonable requirements imposed by the Depository, including, without limitation, evidence satisfactory to the Depository of such destruction, loss or theft of such ADR, the authenticity thereof and the Holder's ownership thereof.

**Section 2.10 Cancellation and Destruction of Surrendered ADRs; Maintenance of Records.** All ADRs surrendered to the Depository shall be canceled by the Depository. Canceled ADRs shall not be entitled to any benefits under the Deposit Agreement or be valid or enforceable against the Depository for any purpose. The Depository is authorized to destroy ADRs so canceled, provided the Depository maintains a record of all destroyed ADRs. Any ADSs held in book-entry form (e.g., through accounts at DTC) shall be deemed canceled when the Depository causes the number of ADSs evidenced by the Balance Certificate to be reduced by the number of ADSs surrendered (without the need to physically destroy the Balance Certificate).

**Section 2.11 Escheatment.** In the event any unclaimed property relating to the ADSs, for any reason, is in the possession of Depository and has not been claimed by the Holder thereof or cannot be delivered to the Holder thereof through usual channels, the Depository shall, upon expiration of any applicable statutory period relating to abandoned property laws, escheat such unclaimed property to the relevant authorities in accordance with the laws of each of the relevant States of the United States.

**Section 2.12 Partial Entitlement ADSs.** In the event any Shares are deposited which (i) entitle the holders thereof to receive a per-share distribution or other entitlement in an amount different from the Shares then on deposit or (ii) are not fully fungible (including, without limitation, as to settlement or trading) with the Shares then on deposit (the Shares then on deposit collectively, "Full Entitlement Shares" and the Shares with different entitlement, "Partial Entitlement Shares"), the Depository shall (i) cause the Custodian to hold Partial Entitlement Shares separate and distinct from Full Entitlement Shares, and (ii) subject to the terms of the Deposit Agreement, issue ADSs representing Partial Entitlement Shares which are separate and distinct from the ADSs representing Full Entitlement Shares, by means of separate CUSIP numbering and legending (if necessary) and, if applicable, by issuing ADRs evidencing such ADSs with applicable notations thereon ("Partial Entitlement ADSs/ADRs" and "Full Entitlement ADSs/ADRs", respectively). If and when Partial Entitlement Shares become Full Entitlement Shares, the Depository shall (a) give notice thereof to Holders of Partial Entitlement ADSs and give Holders of Partial Entitlement ADRs the opportunity to exchange such Partial Entitlement ADRs for Full Entitlement ADRs, (b) cause the Custodian to transfer the Partial Entitlement Shares into the account of the Full Entitlement Shares, and (c) take such actions as are necessary to remove the distinctions between (i) the Partial Entitlement ADRs and ADSs, on the one hand, and (ii) the Full Entitlement ADRs and ADSs on the other. Holders and Beneficial Owners of Partial Entitlement ADSs shall only be entitled to the entitlements of Partial Entitlement Shares. Holders and Beneficial Owners of Full Entitlement ADSs shall be entitled only to the entitlements of Full Entitlement Shares. All provisions and conditions of the Deposit Agreement shall apply to Partial Entitlement ADRs and ADSs to the same extent as Full Entitlement ADRs and ADSs, except as contemplated by this Section 2.12. The Depository is

authorized to take any and all other actions as may be necessary (including, without limitation, making the necessary notations on ADRs) to give effect to the terms of this Section 2.12. The Company agrees to give timely written notice to the Depositary if any Shares issued or to be issued are Partial Entitlement Shares and shall assist the Depositary with the establishment of procedures enabling the identification of Partial Entitlement Shares upon Delivery to the Custodian.

**Section 2.13 Certificated/Uncertificated ADSs.** Notwithstanding any other provision of the Deposit Agreement, the Depositary may, at any time and from time to time, issue ADSs that are not evidenced by ADRs (such ADSs, the “Uncertificated ADS(s)” and the ADS(s) evidenced by ADR(s), the “Certificated ADS(s)”). When issuing and maintaining Uncertificated ADS(s) under the Deposit Agreement, the Depositary shall at all times be subject to (i) the standards applicable to registrars and transfer agents maintaining direct registration systems for equity securities in New York and issuing uncertificated securities under New York law, and (ii) the terms of New York law applicable to uncertificated equity securities. Uncertificated ADSs shall not be represented by any instruments but shall be evidenced by registration in the books of the Depositary maintained for such purpose. Holders of Uncertificated ADSs, that are not subject to any registered pledges, liens, restrictions or adverse claims of which the Depositary has notice at such time, shall at all times have the right to exchange the Uncertificated ADS(s) for Certificated ADS(s) of the same type and class, subject in each case to (x) applicable laws and any rules and regulations the Depositary may have established in respect of the Uncertificated ADSs, and (y) the continued availability of Certificated ADSs in the U.S. Holders of Certificated ADSs shall, if the Depositary maintains a direct registration system for the ADSs, have the right to exchange the Certificated ADSs for Uncertificated ADSs upon (i) the due surrender of the Certificated ADS(s) to the Depositary for such purpose and (ii) the presentation of a written request to that effect to the Depositary, subject in each case to (a) all liens and restrictions noted on the ADR evidencing the Certificated ADS(s) and all adverse claims of which the Depositary then has notice, (b) the terms of the Deposit Agreement and the rules and regulations that the Depositary may establish for such purposes hereunder, (c) applicable law, and (d) payment of the Depositary fees and expenses applicable to such exchange of Certificated ADS(s) for Uncertificated ADS(s). Uncertificated ADSs shall in all material respects be identical to Certificated ADS(s) of the same type and class, except that (i) no ADR(s) shall be, or shall need to be, issued to evidence Uncertificated ADS(s), (ii) Uncertificated ADS(s) shall, subject to the terms of the Deposit Agreement, be transferable upon the same terms and conditions as uncertificated securities under New York law, (iii) the ownership of Uncertificated ADS(s) shall be recorded on the books of the Depositary maintained for such purpose and evidence of such ownership shall be reflected in periodic statements provided by the Depositary to the Holder(s) in accordance with applicable New York law, (iv) the Depositary may from time to time, upon notice to the Holders of Uncertificated ADSs affected thereby, establish rules and regulations, and amend or supplement existing rules and regulations, as may be deemed reasonably necessary to maintain Uncertificated ADS(s) on behalf of Holders, provided that (a) such rules and regulations do not conflict with the terms of the Deposit Agreement and applicable law, and (b) the terms of such rules and regulations are readily available to Holders upon request, (v) the Uncertificated ADS(s) shall not be entitled to any benefits under the Deposit Agreement or be valid or enforceable for any purpose against the Depositary or the Company unless such Uncertificated ADS(s) is/are registered on the books of the Depositary maintained for such purpose, (vi) the Depositary may, in connection with any



deposit of Shares resulting in the issuance of Uncertificated ADSs and with any transfer, pledge, release and cancellation of Uncertificated ADSs, require the prior receipt of such documentation as the Depositary may deem reasonably appropriate, and (vii) upon termination of the Deposit Agreement, the Depositary shall not require Holders of Uncertificated ADSs to affirmatively instruct the Depositary before remitting proceeds from the sale of the Deposited Property represented by such Holders' Uncertificated ADSs under the terms of Section 6.2 of the Deposit Agreement. When issuing ADSs under the terms of the Deposit Agreement, including, without limitation, issuances pursuant to Sections 2.5, 4.2, 4.3, 4.4, 4.5 and 4.11, the Depositary may in its discretion determine to issue Uncertificated ADSs rather than Certificated ADSs, unless otherwise specifically instructed by the applicable Holder to issue Certificated ADSs. All provisions and conditions of the Deposit Agreement shall apply to Uncertificated ADSs to the same extent as to Certificated ADSs, except as contemplated by this Section 2.13. The Depositary is authorized and directed to take any and all actions and establish any and all procedures deemed reasonably necessary to give effect to the terms of this Section 2.13. Any references in the Deposit Agreement or any ADR(s) to the terms "American Depositary Share(s)" or "ADS(s)" shall, unless the context otherwise requires, include Certificated ADS(s) and Uncertificated ADS(s). Except as set forth in this Section 2.13 and except as required by applicable law, the Uncertificated ADSs shall be treated as ADSs issued and outstanding under the terms of the Deposit Agreement. In the event that, in determining the rights and obligations of parties hereto with respect to any Uncertificated ADSs, any conflict arises between (a) the terms of the Deposit Agreement (other than this Section 2.13) and (b) the terms of this Section 2.13, the terms and conditions set forth in this Section 2.13 shall be controlling and shall govern the rights and obligations of the parties to the Deposit Agreement pertaining to the Uncertificated ADSs.

**Section 2.14 Restricted ADSs.** The Depositary shall, at the request and expense of the Company, establish procedures enabling the deposit hereunder of Shares that are Restricted Securities in order to enable the holder of such Shares to hold its ownership interests in such Restricted Securities in the form of ADSs issued under the terms hereof (such Shares, "Restricted Shares"). Upon receipt of a written request from the Company to accept Restricted Shares for deposit hereunder, the Depositary agrees to establish procedures permitting the deposit of such Restricted Shares and the issuance of ADSs representing the right to receive, subject to the terms of the Deposit Agreement and the applicable ADR (if issued as a Certificated ADS), such deposited Restricted Shares (such ADSs, the "Restricted ADSs," and the ADRs evidencing such Restricted ADSs, the "Restricted ADRs"). Notwithstanding anything contained in this Section 2.14, the Depositary and the Company may, to the extent not prohibited by law, agree to issue the Restricted ADSs in uncertificated form ("Uncertificated Restricted ADSs") upon such terms and conditions as the Company and the Depositary may deem necessary and appropriate. The Company shall assist the Depositary in the establishment of such procedures and agrees that it shall take all steps necessary and satisfactory to the Depositary to ensure that the establishment of such procedures does not violate the provisions of the Securities Act or any other applicable laws. The depositors of such Restricted Shares and the Holders of the Restricted ADSs may be required prior to the deposit of such Restricted Shares, the transfer of the Restricted ADRs and Restricted ADSs or the withdrawal of the Restricted Shares represented by Restricted ADSs to provide such written certifications or agreements as the Depositary or the Company may require. The Company shall provide to the Depositary in writing the legend(s) to be affixed to the Restricted ADRs (if the Restricted ADSs are to be issued as Certificated ADSs),

or to be included in the statements issued from time to time to Holders of Uncertificated ADSs (if issued as Uncertificated Restricted ADSs), which legends shall (i) be in a form reasonably satisfactory to the Depositary and (ii) contain the specific circumstances under which the Restricted ADSs, and, if applicable, the Restricted ADRs evidencing the Restricted ADSs, may be transferred or the Restricted Shares withdrawn. The Restricted ADSs issued upon the deposit of Restricted Shares shall be separately identified on the books of the Depositary and the Restricted Shares so deposited shall, to the extent required by law, be held separate and distinct from the other Deposited Securities held hereunder. The Restricted Shares and the Restricted ADSs shall not be eligible for Pre-Release Transactions. The Restricted ADSs shall not be eligible for inclusion in any book-entry settlement system, including, without limitation, DTC, and shall not in any way be fungible with the ADSs issued under the terms hereof that are not Restricted ADSs. The Restricted ADSs, and, if applicable, the Restricted ADRs evidencing the Restricted ADSs, shall be transferable only by the Holder thereof upon delivery to the Depositary of (i) all documentation otherwise contemplated by the Deposit Agreement and (ii) an opinion of counsel satisfactory to the Depositary setting forth, *inter alia*, the conditions upon which the Restricted ADSs presented, and, if applicable, the Restricted ADRs evidencing the Restricted ADSs, are transferable by the Holder thereof under applicable securities laws and the transfer restrictions contained in the legend applicable to the Restricted ADSs presented for transfer. Except as set forth in this Section 2.14 and except as required by applicable law, the Restricted ADSs and the Restricted ADRs evidencing Restricted ADSs shall be treated as ADSs and ADRs issued and outstanding under the terms of the Deposit Agreement. In the event that, in determining the rights and obligations of parties hereto with respect to any Restricted ADSs, any conflict arises between (a) the terms of the Deposit Agreement (other than this Section 2.14) and (b) the terms of (i) this Section 2.14 or (ii) the applicable Restricted ADR, the terms and conditions set forth in this Section 2.14 and of the Restricted ADR shall be controlling and shall govern the rights and obligations of the parties to the Deposit Agreement pertaining to the deposited Restricted Shares, the Restricted ADSs and Restricted ADRs.

If the Restricted ADRs, the Restricted ADSs and the Restricted Shares cease to be Restricted Securities, the Depositary, upon receipt of (x) an opinion of counsel satisfactory to the Depositary setting forth, *inter alia*, that the Restricted ADRs, the Restricted ADSs and the Restricted Shares are not as of such time Restricted Securities, and (y) instructions from the Company to remove the restrictions applicable to the Restricted ADRs, the Restricted ADSs and the Restricted Shares, shall (i) eliminate the distinctions and separations that may have been established between the applicable Restricted Shares held on deposit under this Section 2.14 and the other Shares held on deposit under the terms of the Deposit Agreement that are not Restricted Shares, (ii) treat the newly unrestricted ADRs and ADSs on the same terms as, and fully fungible with, the other ADRs and ADSs issued and outstanding under the terms of the Deposit Agreement that are not Restricted ADRs or Restricted ADSs, and (iii) take all actions necessary to remove any distinctions, limitations and restrictions previously existing under this Section 2.14 between the applicable Restricted ADRs and Restricted ADSs, respectively, on the one hand, and the other ADRs and ADSs that are not Restricted ADRs or Restricted ADSs, respectively, on the other hand, including, without limitation, by making the newly-unrestricted ADSs eligible for Pre-Release Transactions and for inclusion in the applicable book-entry settlement systems.

## ARTICLE III

### CERTAIN OBLIGATIONS OF HOLDERS AND BENEFICIAL OWNERS OF ADSs

**Section 3.1 Proofs, Certificates and Other Information.** Any person presenting Shares for deposit, any Holder and any Beneficial Owner may be required, and every Holder and Beneficial Owner agrees, from time to time to provide to the Depositary and the Custodian such proof of citizenship or residence, taxpayer status, payment of all applicable taxes or other governmental charges, exchange control approval, legal or beneficial ownership of ADSs and Deposited Property, compliance with applicable laws, the terms of the Deposit Agreement or the ADR(s) evidencing the ADSs and the provisions of, or governing, the Deposited Property, to execute such certifications and to make such representations and warranties, and to provide such other information and documentation (or, in the case of Shares in registered form presented for deposit, such information relating to the registration on the books of the Company or of the Share Registrar) as the Depositary or the Custodian may deem necessary or proper or as the Company may reasonably require by written request to the Depositary consistent with its obligations under the Deposit Agreement and the applicable ADR(s). The Depositary and the Registrar, as applicable, may withhold the execution or delivery or registration of transfer of any ADR or ADS or the distribution or sale of any dividend or distribution of rights or of the proceeds thereof or, to the extent not limited by the terms of Section 7.8, the delivery of any Deposited Property until such proof or other information is filed or such certifications are executed, or such representations and warranties are made, or such other documentation or information provided, in each case to the Depositary's, the Registrar's and the Company's satisfaction. The Depositary shall provide the Company, in a timely manner, with copies or originals if necessary and appropriate of (i) any such proofs of citizenship or residence, taxpayer status, or exchange control approval or copies of written representations and warranties which it receives from Holders and Beneficial Owners, and (ii) any other information or documents which the Company may reasonably request and which the Depositary shall request and receive from any Holder or Beneficial Owner or any person presenting Shares for deposit or ADSs for cancellation, transfer or withdrawal. Nothing herein shall obligate the Depositary to (i) obtain any information for the Company if not provided by the Holders or Beneficial Owners, or (ii) verify or vouch for the accuracy of the information so provided by the Holders or Beneficial Owners.

**Section 3.2 Liability for Taxes and Other Charges.** Any tax or other governmental charge payable by the Custodian or by the Depositary with respect to any Deposited Property, ADSs or ADRs shall be payable by the Holders and Beneficial Owners to the Depositary. The Company, the Custodian and/or the Depositary may withhold or deduct from any distributions made in respect of Deposited Property, and may sell for the account of a Holder and/or Beneficial Owner any or all of the Deposited Property and apply such distributions and sale proceeds in payment of, any taxes (including applicable interest and penalties) or charges that are or may be payable by Holders or Beneficial Owners in respect of the ADSs, Deposited Property and ADRs, the Holder and the Beneficial Owner remaining liable for any deficiency. The Custodian may refuse the deposit of Shares and the Depositary may refuse to issue ADSs, to deliver ADRs, register the transfer of ADSs, register the split-up or combination of ADRs and (subject to Section 7.8) the withdrawal of Deposited Property until payment in full of such tax,

charge, penalty or interest is received. Every Holder and Beneficial Owner agrees to indemnify the Depositary, the Company, the Custodian, and any of their agents, officers, employees and Affiliates for, and to hold each of them harmless from, any claims with respect to taxes (including applicable interest and penalties thereon) arising from any tax benefit obtained for such Holder and/or Beneficial Owner. The obligations of Holders and Beneficial Owners under this Section 3.2 shall survive any transfer of ADSs, any cancellation of ADSs and withdrawal of Deposited Securities, and the termination of the Deposit Agreement.

**Section 3.3 Representations and Warranties on Deposit of Shares.** Each person depositing Shares under the Deposit Agreement shall be deemed thereby to represent and warrant that (i) such Shares and the certificates therefor are duly authorized, validly allotted and issued, fully paid, not subject to any call for the payment of further capital and legally obtained by such person, (ii) all preemptive (and similar) rights, if any, with respect to such Shares have been validly waived, disappplied or exercised, (iii) the person making such deposit is duly authorized so to do, (iv) the Shares presented for deposit are free and clear of any lien, encumbrance, security interest, charge, mortgage or adverse claim, (v) the Shares presented for deposit are not, and the ADSs issuable upon such deposit will not be, Restricted Securities (except as contemplated in Section 2.14), and (vi) the Shares presented for deposit have not been stripped of any rights or entitlements. Such representations and warranties shall survive the deposit and withdrawal of Shares, the issuance and cancellation of ADSs in respect thereof and the transfer of such ADSs. If any such representations or warranties are false in any way, the Company and the Depositary shall be authorized, at the cost and expense of the person depositing Shares, to take any and all actions necessary to correct the consequences thereof.

**Section 3.4 Compliance with Information Requests.** Notwithstanding any other provision of the Deposit Agreement or any ADR(s), each Holder and Beneficial Owner agrees to comply with requests from the Company pursuant to applicable law, the rules and requirements of The NASDAQ Global Market and any other stock exchange on which the Shares or ADSs are, or will be, registered, traded or listed or the Articles of Association of the Company, which are made to provide information, *inter alia*, as to the capacity in which such Holder or Beneficial Owner owns ADSs (and Shares as the case may be) and regarding the identity of any other person(s) interested in such ADSs and the nature of such interest and various other matters, whether or not they are Holders and/or Beneficial Owners at the time of such request. The Depositary agrees to use its reasonable efforts to forward, upon the request of the Company and at the Company's expense, any such request from the Company to the Holders and to forward to the Company any such responses to such requests received by the Depositary.

**Section 3.5 Ownership Restrictions.** Notwithstanding any other provision in the Deposit Agreement or any ADR, the Company may restrict transfers of the Shares where such transfer might result in ownership of Shares exceeding limits imposed by applicable law or the Articles of Association of the Company. The Company may also restrict, in such manner as it deems appropriate, transfers of the ADSs where such transfer may result in the total number of Shares represented by the ADSs owned by a single Holder or Beneficial Owner to exceed any such limits. The Company may, in its sole discretion but subject to applicable law, instruct the Depositary to take action with respect to the ownership interest of any Holder or Beneficial Owner in excess of the limits set forth in the preceding sentence, including, but not limited to, the imposition of restrictions on the transfer of ADSs, the removal or limitation of voting rights



or mandatory sale or disposition on behalf of a Holder or Beneficial Owner of the Shares represented by the ADSs held by such Holder or Beneficial Owner in excess of such limitations, if and to the extent such disposition is permitted by applicable law and the Articles of Association of the Company. Nothing herein shall be interpreted as obligating the Depositary or the Company to ensure compliance with the ownership restrictions described in this Section 3.5.

**Section 3.6 Reporting Obligations and Regulatory Approvals.** Applicable laws and regulations may require holders and beneficial owners of Shares, including the Holders and Beneficial Owners of ADSs, to satisfy reporting requirements and obtain regulatory approvals in certain circumstances. Holders and Beneficial Owners of ADSs are solely responsible for determining and complying with such reporting requirements and obtaining such approvals. Each Holder and each Beneficial Owner hereby agrees to make such determination, file such reports, and obtain such approvals to the extent and in the form required by applicable laws and regulations as in effect from time to time. Neither the Depositary, the Custodian, the Company or any of their respective agents or affiliates shall be required to take any actions whatsoever on behalf of Holders or Beneficial Owners to determine or satisfy such reporting requirements or obtain such regulatory approvals under applicable laws and regulations.

## ARTICLE IV

### THE DEPOSITED SECURITIES

**Section 4.1 Cash Distributions.** Whenever the Company intends to make a distribution of a cash dividend or other cash distribution in respect of any Deposited Securities, the Company shall give notice thereof to the Depositary at least twenty (20) days (or such other number of days as mutually agreed to in writing by the Depositary and the Company) prior to the proposed distribution specifying, *inter alia*, the record date applicable for determining the holders of Deposited Securities entitled to receive such distribution. Upon the timely receipt of such notice, the Depositary shall establish the ADS Record Date upon the terms described in Section 4.9. Upon receipt of confirmation of the receipt of (x) any cash dividend or other cash distribution on any Deposited Securities, or (y) proceeds from the sale of any Deposited Property held in respect of the ADSs under the terms hereof, the Depositary will (i) if at the time of receipt thereof any amounts received in a Foreign Currency can, in the judgment of the Depositary (pursuant to Section 4.8), be converted on a practicable basis into Dollars transferable to the United States, promptly convert or cause to be converted such cash dividend, distribution or proceeds into Dollars (on the terms described in Section 4.8), (ii) if applicable and unless previously established, establish the ADS Record Date upon the terms described in Section 4.9, and (iii) distribute promptly the amount thus received (net of (a) the applicable fees and charges of, and expenses incurred by, the Depositary and (b) applicable taxes withheld) to the Holders entitled thereto as of the ADS Record Date in proportion to the number of ADSs held as of the ADS Record Date. The Depositary shall distribute only such amount, however, as can be distributed without attributing to any Holder a fraction of one cent, and any balance not so distributed shall be held by the Depositary (without liability for interest thereon) and shall be added to and become part of the next sum received by the Depositary for distribution to Holders of ADSs outstanding at the time of the next distribution. If the Company, the Custodian or the Depositary is required to withhold and does withhold from any cash dividend or other cash distribution in respect of any Deposited Securities, or from any cash proceeds from the sales of

Deposited Property, an amount on account of taxes, duties or other governmental charges, the amount distributed to Holders on the ADSs shall be reduced accordingly. Such withheld amounts shall be forwarded by the Company, the Custodian or the Depositary to the relevant governmental authority. Evidence of payment thereof by the Company shall be forwarded by the Company to the Depositary upon request. 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. Notwithstanding anything contained in the Deposit Agreement to the contrary, in the event the Company fails to give the Depositary timely notice of the proposed distribution provided for in this Section 4.1, the Depositary agrees to use commercially reasonable efforts to perform the actions contemplated in this Section 4.1, and the Company, the Holders and the Beneficial Owners acknowledge that the Depositary shall have no liability for the Depositary's failure to perform the actions contemplated in this Section 4.1 where such notice has not been so timely given, other than its failure to use commercially reasonable efforts, as provided herein.

**Section 4.2 Distribution in Shares.** Whenever the Company intends to make a distribution that consists of a dividend in, or free distribution of, Shares, the Company shall give notice thereof to the Depositary at least twenty (20) days (or such other number of days as mutually agreed to in writing by the Depositary and the Company) prior to the proposed distribution, specifying, *inter alia*, the record date applicable to holders of Deposited Securities entitled to receive such distribution. Upon the timely receipt of such notice from the Company, the Depositary shall establish the ADS Record Date upon the terms described in Section 4.9. Upon receipt of confirmation from the Custodian of the receipt of the Shares so distributed by the Company, the Depositary shall either (i) subject to Section 5.9, distribute to the Holders as of the ADS Record Date in proportion to the number of ADSs held as of the ADS Record Date, additional ADSs, which represent in the aggregate the number of Shares received as such dividend, or free distribution, subject to the other terms of the Deposit Agreement (including, without limitation, (a) the applicable fees and charges of, and expenses incurred by, the Depositary and (b) applicable taxes), or (ii) if additional ADSs are not so distributed, take all actions necessary so that each ADS issued and outstanding after the ADS Record Date shall, to the extent permissible by law, thenceforth also represent rights and interests in the additional integral number of Shares distributed upon the Deposited Securities represented thereby (net of (a) the applicable fees and charges of, and expenses incurred by, the Depositary and (b) applicable taxes). In lieu of delivering fractional ADSs, the Depositary shall sell the number of Shares or ADSs, as the case may be, represented by the aggregate of such fractions and distribute the net proceeds upon the terms described in Section 4.1. In the event that the Depositary determines that any distribution in property (including Shares) is subject to any tax or other governmental charges which the Depositary is obligated to withhold, or, if the Company in the fulfillment of its obligation under Section 5.7, has furnished an opinion of U.S. counsel determining that Shares must be registered under the Securities Act or other laws in order to be distributed to Holders (and no such registration statement has been declared effective), the Depositary may dispose of all or a portion of such property (including Shares and rights to subscribe therefor) in such amounts and in such manner, including by public or private sale, as the Depositary deems necessary and practicable, and the Depositary shall distribute the net proceeds of any such sale (after deduction of (a) applicable taxes and (b) fees and charges of, and

expenses incurred by, the Depositary) to Holders entitled thereto upon the terms described in Section 4.1. The Depositary shall hold and/or distribute any unsold balance of such property in accordance with the provisions of the Deposit Agreement. Notwithstanding anything contained in the Deposit Agreement to the contrary, in the event the Company fails to give the Depositary timely notice of the proposed distribution provided for in this Section 4.2, the Depositary agrees to use commercially reasonable efforts to perform the actions contemplated in this Section 4.2, and the Company, the Holders and the Beneficial Owners acknowledge that the Depositary shall have no liability for the Depositary's failure to perform the actions contemplated in this Section 4.2 where such notice has not been so timely given, other than its failure to use commercially reasonable efforts, as provided herein.

**Section 4.3 Elective Distributions in Cash or Shares.** Whenever the Company intends to make a distribution payable at the election of the holders of Deposited Securities in cash or in additional Shares, the Company shall give notice thereof to the Depositary at least sixty (60) days (or such other number of days as mutually agreed to in writing by the Depositary and the Company) prior to the proposed distribution specifying, *inter alia*, the record date applicable to holders of Deposited Securities entitled to receive such elective distribution and whether or not it wishes such elective distribution to be made available to Holders of ADSs. Upon the timely receipt of a notice indicating that the Company wishes such elective distribution to be made available to Holders of ADSs, the Depositary shall consult with the Company to determine, and the Company shall assist the Depositary in its determination, whether it is lawful and reasonably practicable to make such elective distribution available to the Holders of ADSs. The Depositary shall make such elective distribution available to Holders only if (i) the Company shall have timely requested that the elective distribution be made available to Holders, (ii) the Depositary shall have determined that such distribution is reasonably practicable and (iii) the Depositary shall have received satisfactory documentation within the terms of Section 5.7. If the above conditions are not satisfied or if the Company requests such elective distribution not to be made available to Holders of ADSs, the Depositary shall establish the ADS Record Date on the terms described in Section 4.9 and, to the extent permitted by law, distribute to the Holders, on the basis of the same determination as is made in England and Wales in respect of the Shares for which no election is made, either (X) cash upon the terms described in Section 4.1 or (Y) additional ADSs representing such additional Shares upon the terms described in Section 4.2. If the above conditions are satisfied, the Depositary shall establish an ADS Record Date on the terms described in Section 4.9 and establish procedures to enable Holders to elect the receipt of the proposed distribution in cash or in additional ADSs. The Company shall assist the Depositary in establishing such procedures to the extent necessary. If a Holder elects to receive the proposed distribution (X) in cash, the distribution shall be made upon the terms described in Section 4.1, or (Y) in ADSs, the distribution shall be made upon the terms described in Section 4.2. Nothing herein shall obligate the Depositary to make available to Holders a method to receive the elective distribution in Shares (rather than ADSs). There can be no assurance that Holders generally, or any Holder in particular, will be given the opportunity to receive elective distributions on the same terms and conditions as the holders of Shares. Notwithstanding anything contained in the Deposit Agreement to the contrary, in the event the Company fails to give the Depositary timely notice of the proposed distribution provided for in this Section 4.3, the Depositary agrees to use commercially reasonable efforts to perform the actions contemplated in this Section 4.3, and the Company, the Holders and the Beneficial Owners acknowledge that the Depositary shall have no liability for the Depositary's failure to perform

the actions contemplated in this Section 4.3 where such notice has not been so timely given, other than its failure to use commercially reasonable efforts, as provided herein.

#### **Section 4.4 Distribution of Rights to Purchase Additional ADSs.**

(a) **Distribution to ADS Holders.** Whenever the Company intends to distribute to the holders of the Deposited Securities rights to subscribe for additional Shares, the Company shall give notice thereof to the Depositary at least sixty (60) days (or such other number of days as mutually agreed to in writing by the Depositary and the Company) prior to the proposed distribution specifying, *inter alia*, the record date applicable to holders of Deposited Securities entitled to receive such distribution and whether or not it wishes such rights to be made available to Holders of ADSs. Upon the timely receipt of a notice indicating that the Company wishes such rights to be made available to Holders of ADSs, the Depositary shall consult with the Company to determine, and the Company shall assist the Depositary in its determination, whether it is lawful and reasonably practicable to make such rights available to the Holders. The Depositary shall make such rights available to Holders only if (i) the Company shall have timely requested that such rights be made available to Holders, (ii) the Depositary shall have received satisfactory documentation within the terms of Section 5.7, and (iii) the Depositary shall have determined that such distribution of rights is reasonably practicable. In the event any of the conditions set forth above are not satisfied or if the Company requests that the rights not be made available to Holders of ADSs, the Depositary shall proceed with the sale of the rights as contemplated in Section 4.4(b) below. In the event all conditions set forth above are satisfied, the Depositary shall establish the ADS Record Date (upon the terms described in Section 4.9) and establish procedures to (x) distribute rights to purchase additional ADSs (by means of warrants or otherwise), (y) enable the Holders to exercise such rights (upon payment of the subscription price and of the applicable (a) fees and charges of, and expenses incurred by, the Depositary and (b) taxes), and (z) deliver ADSs upon the valid exercise of such rights. The Company shall assist the Depositary to the extent necessary in establishing such procedures. Nothing herein shall obligate the Depositary to make available to the Holders a method to exercise rights to subscribe for Shares (rather than ADSs).

(b) **Sale of Rights.** If (i) the Company does not timely request the Depositary to make the rights available to Holders or requests that the rights not be made available to Holders, (ii) the Depositary fails to receive satisfactory documentation within the terms of Section 5.7, or determines it is not reasonably practicable to make the rights available to Holders, or (iii) any rights made available are not exercised and appear to be about to lapse, the Depositary shall determine whether it is lawful and reasonably practicable to sell such rights, in a riskless principal capacity, at such place and upon such terms (including public or private sale) as it may deem practicable. The Company shall assist the Depositary to the extent necessary to determine such legality and practicability. The Depositary shall, upon such sale, convert and distribute proceeds of such sale (net of applicable (a) fees and charges of, and expenses incurred by, the Depositary and (b) taxes) upon the terms set forth in Section 4.1.

(c) **Lapse of Rights.** If the Depositary is unable to make any rights available to Holders upon the terms described in Section 4.4(a) or to arrange for the sale of the rights upon the terms described in Section 4.4(b), the Depositary shall allow such rights to lapse.



The Depositary shall not be liable for (i) any failure to accurately determine whether it may be lawful or practicable to make such rights available to Holders in general or any Holders in particular, (ii) any foreign exchange exposure or loss incurred in connection with such sale, or exercise, or (iii) the content of any materials forwarded to the Holders on behalf of the Company in connection with the rights distribution.

Notwithstanding anything to the contrary in this Section 4.4, if registration (under the Securities Act or any other applicable law) of the rights or the securities to which any rights relate may be required in order for the Company to offer such rights or such securities to Holders and to sell the securities represented by such rights, the Depositary will not distribute such rights to the Holders (i) unless and until a registration statement under the Securities Act (or other applicable law) covering such offering is in effect or (ii) unless the Company furnishes the Depositary opinion(s) of counsel for the Company in the United States and counsel to the Company in any other applicable country in which rights would be distributed, in each case satisfactory to the Depositary, to the effect that the offering and sale of such securities to Holders and Beneficial Owners are exempt from, or do not require registration under, the provisions of the Securities Act or any other applicable laws.

In the event that the Company, the Depositary or the Custodian shall be required to withhold and does withhold from any distribution of Deposited Property (including rights) an amount on account of taxes or other governmental charges, the amount distributed to the Holders of ADSs shall be reduced accordingly. In the event that the Depositary determines that any distribution of Deposited Property (including Shares and rights to subscribe therefor) is subject to any tax or other governmental charges which the Depositary is obligated to withhold, the Depositary may dispose of all or a portion of such Deposited Property (including Shares and rights to subscribe therefor) in such amounts and in such manner, including by public or private sale, as the Depositary deems necessary and practicable to pay any such taxes or charges.

There can be no assurance that Holders generally, or any Holder in particular, will be given the opportunity to receive or exercise rights on the same terms and conditions as the holders of Shares or be able to exercise such rights. Nothing herein shall obligate the Company to file any registration statement in respect of any rights or Shares or other securities to be acquired upon the exercise of such rights.

#### **Section 4.5 Distributions Other Than Cash, Shares or Rights to Purchase Shares.**

(a) Whenever the Company intends to distribute to the holders of Deposited Securities property other than cash, Shares or rights to purchase additional Shares, the Company shall give timely notice thereof to the Depositary and shall indicate whether or not it wishes such distribution to be made to Holders of ADSs. Upon receipt of a notice indicating that the Company wishes such distribution to be made to Holders of ADSs, the Depositary shall consult with the Company, and the Company shall assist the Depositary, to determine whether such distribution to Holders is lawful and reasonably practicable. The Depositary shall not make such distribution unless (i) the Company shall have requested the Depositary to make such distribution to Holders, (ii) the Depositary shall have received satisfactory documentation within the terms of Section 5.7, and (iii) the Depositary shall have determined that such distribution is reasonably practicable.

(b) Upon receipt of satisfactory documentation and the request of the Company to distribute property to Holders of ADSs and after making the requisite determinations set forth in (a) above, the Depositary shall distribute the property so received to the Holders of record, as of the ADS Record Date, in proportion to the number of ADSs held by them respectively and in such manner as the Depositary may deem practicable for accomplishing such distribution (i) upon receipt of payment or net of the applicable fees and charges of, and expenses incurred by, the Depositary, and (ii) net of any applicable taxes withheld. The Depositary may dispose of all or a portion of the property so distributed and deposited, in such amounts and in such manner (including public or private sale) as the Depositary may deem practicable or necessary to satisfy any taxes (including applicable interest and penalties) or other governmental charges applicable to the distribution.

(c) If (i) the Company does not request the Depositary to make such distribution to Holders or requests the Depositary not to make such distribution to Holders, (ii) the Depositary does not receive satisfactory documentation within the terms of Section 5.7, or (iii) the Depositary determines that all or a portion of such distribution is not reasonably practicable, the Depositary shall sell or cause such property to be sold in a public or private sale, at such place or places and upon such terms as it may deem practicable and shall (i) cause the proceeds of such sale, if any, to be converted into Dollars and (ii) distribute the proceeds of such conversion received by the Depositary (net of applicable (a) fees and charges of, and expenses incurred by, the Depositary and (b) taxes) to the Holders as of the ADS Record Date upon the terms of Section 4.1. If the Depositary is unable to sell such property, the Depositary may dispose of such property for the account of the Holders in any way it deems reasonably practicable under the circumstances.

(d) Neither the Depositary nor the Company shall be liable for (i) any failure to accurately determine whether it is lawful or practicable to make the property described in this Section 4.5 available to Holders in general or any Holders in particular, nor (ii) any loss incurred in connection with the sale or disposal of such property.

**Section 4.6 Distributions with Respect to Deposited Securities in Bearer Form.**

Subject to the terms of this Article IV, distributions in respect of Deposited Securities that are held by the Depositary or the Custodian in bearer form shall be made to the Depositary for the account of the respective Holders of ADS(s) with respect to which any such distribution is made upon due presentation by the Depositary or the Custodian to the Company of any relevant coupons, talons, or certificates. The Company shall promptly notify the Depositary of such distributions. The Depositary or the Custodian shall promptly present such coupons, talons or certificates, as the case may be, in connection with any such distribution.

**Section 4.7 Redemption.** If the Company intends to exercise any right of redemption in respect of any of the Deposited Securities, the Company shall give notice thereof to the Depositary at least sixty (60) days (or such other number of days as mutually agreed to in writing by the Depositary and the Company) prior to the intended date of redemption which notice shall set forth the particulars of the proposed redemption. Upon timely receipt of (i) such notice and (ii) satisfactory documentation given by the Company to the Depositary within the terms of Section 5.7, and only if the Depositary shall have determined that such proposed redemption is practicable, the Depositary shall provide to each Holder a notice setting forth the intended

exercise by the Company of the redemption rights and any other particulars set forth in the Company's notice to the Depositary. The Depositary shall instruct the Custodian to present to the Company the Deposited Securities in respect of which redemption rights are being exercised against payment of the applicable redemption price. Upon receipt of confirmation from the Custodian that the redemption has taken place and that funds representing the redemption price have been received, the Depositary shall convert, transfer, and distribute the proceeds (net of applicable (a) fees and charges of, and the expenses incurred by, the Depositary, and (b) taxes), retire ADSs and cancel ADRs, if applicable, upon delivery of such ADSs by Holders thereof and the terms set forth in Sections 4.1 and 6.2. If less than all outstanding Deposited Securities are redeemed, the ADSs to be retired will be selected by lot or on a pro rata basis, as may be determined by the Depositary. The redemption price per ADS shall be the dollar equivalent of the per share amount received by the Depositary (adjusted to reflect the ADS(s)-to-Share(s) ratio) upon the redemption of the Deposited Securities represented by ADSs (subject to the terms of Section 4.8 and the applicable fees and charges of, and expenses incurred by, the Depositary, and applicable taxes) multiplied by the number of Deposited Securities represented by each ADS redeemed.

Notwithstanding anything contained in the Deposit Agreement to the contrary, in the event the Company fails to give the Depositary timely notice of the proposed redemption provided for in this Section 4.7, the Depositary agrees to use commercially reasonable efforts to perform the actions contemplated in this Section 4.7, and the Company, the Holders and the Beneficial Owners acknowledge that the Depositary shall have no liability for the Depositary's failure to perform the actions contemplated in this Section 4.7 where such notice has not been so timely given, other than its failure to use commercially reasonable efforts, as provided herein.

**Section 4.8 Conversion of Foreign Currency.** Whenever the Depositary or the Custodian shall receive Foreign Currency, by way of dividends or other distributions or the net proceeds from the sale of Deposited Property, which in the judgment of the Depositary can at such time be converted on a practicable basis, by sale or in any other manner that it may determine in accordance with applicable law, into Dollars transferable to the United States and distributable to the Holders entitled thereto, the Depositary shall convert or cause to be converted, by sale or in any other manner that it may determine, such Foreign Currency into Dollars, and shall distribute such Dollars (net of any applicable fees, any reasonable and customary expenses incurred in such conversion and any expenses incurred on behalf of the Holders in complying with currency exchange control or other governmental requirements) in accordance with the terms of the applicable sections of the Deposit Agreement. If the Depositary shall have distributed warrants or other instruments that entitle the holders thereof to such Dollars, the Depositary shall distribute such Dollars to the holders of such warrants and/or instruments upon surrender thereof for cancellation, in either case without liability for interest thereon. Such distribution may be made upon an averaged or other practicable basis without regard to any distinctions among Holders on account of any application of exchange restrictions or otherwise.

If such conversion or distribution generally or with regard to a particular Holder can be effected only with the approval or license of any government or agency thereof, the Depositary shall have authority to file such application for approval or license, if any, as it may deem desirable. In no event, however, shall the Depositary be obligated to make such a filing.

If at any time the Depositary shall determine that in its judgment the conversion of any Foreign Currency and the transfer and distribution of proceeds of such conversion received by the Depositary is not practicable or lawful, or if any approval or license of any governmental authority or agency thereof that is required for such conversion, transfer and distribution is denied or, in the opinion of the Depositary, not obtainable at a reasonable cost or within a reasonable period, the Depositary may, in its discretion, (i) make such conversion and distribution in Dollars to the Holders for whom such conversion, transfer and distribution is lawful and practicable, (ii) distribute the Foreign Currency (or an appropriate document evidencing the right to receive such Foreign Currency) to Holders for whom this is lawful and practicable, or (iii) hold (or cause the Custodian to hold) such Foreign Currency (without liability for interest thereon) for the respective accounts of the Holders entitled to receive the same.

**Section 4.9 Fixing of ADS Record Date.** Whenever the Depositary shall receive notice of the fixing of a record date by the Company for the determination of holders of Deposited Securities entitled to receive any distribution (whether in cash, Shares, rights, or other distribution), or whenever for any reason the Depositary causes a change in the number of Shares that are represented by each ADS, or whenever the Depositary shall receive notice of any meeting of, or solicitation of consents or proxies of, holders of Shares or other Deposited Securities, or whenever the Depositary shall find it necessary or convenient in connection with the giving of any notice, solicitation of any consent or any other matter, the Depositary shall fix the record date (the “ADS Record Date”) for the determination of the Holders of ADS(s) who shall be entitled to receive such distribution, to give instructions for the exercise of voting rights at any such meeting, to give or withhold such consent, to receive such notice or solicitation or to otherwise take action, or to exercise the rights of Holders with respect to such changed number of Shares represented by each ADS. The Depositary shall make reasonable efforts to establish the ADS Record Date as closely as practicable to the applicable record date for the Deposited Securities (if any) set by the Company in England and Wales and shall not announce the establishment of any ADS Record Date prior to the relevant corporate action having been made public by the Company (if such corporate action affects the Deposited Securities). Subject to applicable law and the provisions of Section 4.1 through 4.8 and to the other terms and conditions of the Deposit Agreement, only the Holders of ADSs at the close of business in New York on such ADS Record Date shall be entitled to receive such distribution, to give such voting instructions, to receive such notice or solicitation, or otherwise take action.

**Section 4.10 Voting of Deposited Securities.** As soon as practicable after receipt of notice of any meeting at which the holders of Deposited Securities are entitled to vote, or of solicitation of consents or proxies from holders of Deposited Securities, the Depositary shall fix the ADS Record Date in respect of such meeting or solicitation of consent or proxy in accordance with Section 4.9. The Depositary shall, if requested by the Company in writing in a timely manner (the Depositary having no obligation to take any further action if the request shall not have been received by the Depositary at least thirty (30) days prior to the date of such vote or meeting), at the Company’s expense and provided no U.S. legal prohibitions exist, distribute to Holders as of the ADS Record Date: (a) such notice of meeting or solicitation of consent or proxy, (b) a statement that the Holders at the close of business on the ADS Record Date will be entitled, subject to any applicable law, the provisions of the Deposit Agreement, the Articles of Association of the Company and the provisions of or governing the Deposited Securities (which provisions, if any, shall be summarized in pertinent part by the Company), to instruct the



Depository as to the exercise of the voting rights, if any, pertaining to the Deposited Securities represented by such Holder's ADSs, and (c) a brief statement as to the manner in which such voting instructions may be given to the Depository or in which voting instructions may be deemed to have been given in accordance with this Section 4.10 if no instructions are received prior to the deadline set for such purposes to the Depository to give a discretionary proxy to a person designated by the Company.

Notwithstanding anything contained in the Deposit Agreement or any ADR, with the Company's prior consent, the Depository may, to the extent not prohibited by law or regulations, or by the requirements of the stock exchange on which the ADSs are listed, in lieu of distribution of the materials provided to the Depository in connection with any meeting of, or solicitation of consents or proxies from, holders of Deposited Securities, distribute to the Holders a notice that provides Holders with, or otherwise publicizes to Holders, instructions on how to retrieve such materials or receive such materials upon request (*e.g.*, by reference to a website containing the materials for retrieval or a contact for requesting copies of the materials).

The Depository has been advised by the Company that under the Articles of Association of the Company as in effect on the date of the Deposit Agreement, voting at any meeting of shareholders of the Company is by show of hands unless (before or upon the declaration of the result of the show of hands) a poll is demanded. The Depository will not join in demanding a poll, whether or not requested to do so by Holders of ADSs. Under the Articles of Association of the Company as in effect on the date of the Deposit Agreement, a poll may be demanded by (a) the chairman of the Company's board of directors, (b) not fewer than five shareholders present in person or by proxy and having the right to vote at the meeting, (c) any shareholder(s) present in person or by proxy and representing not less than 10% of the total voting rights of all the shareholders having the right to vote on the resolution (excluding any shares held in treasury), or (d) any shareholder(s) present in person or by proxy and holding shares in the Company conferring a right to vote on the resolution 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 (excluding any shares held in treasury).

Voting instructions may be given only in respect of a number of ADSs representing an integral number of Deposited Securities. Upon the timely receipt from a Holder of ADSs as of the ADS Record Date of voting instructions in the manner specified by the Depository, the Depository shall endeavor, insofar as practicable and permitted under applicable law, the provisions of the Deposit Agreement, Articles of Association of the Company and the provisions of the Deposited Securities, to vote, or cause the Custodian to vote, the Deposited Securities (in person or by proxy) represented by such Holder's ADSs as follows: (a) in the event voting takes place at a shareholders' meeting by a show of hands, the Depository will instruct the Custodian to vote all Deposited Securities in accordance with the voting instructions received from a majority of Holders of ADSs who provided voting instructions, and (b) in the event voting takes place at a shareholders' meeting by poll, the Depository will instruct the Custodian to vote the Deposited Securities in accordance with the voting instructions received from the Holders of ADSs. If voting is by poll and the Depository does not receive voting instructions from a Holder as of the ADS Record Date on or before the date established by the Depository for such purpose, such Holder shall be deemed, and the Depository shall deem such Holder, to have instructed the Depository to give a discretionary proxy to a person designated by the Company to vote the

Deposited Securities; provided, however, that no such discretionary proxy shall be given by the Depositary with respect to any matter to be voted upon as to which the Company informs the Depositary that (a) the Company does not wish such proxy to be given, (b) substantial opposition exists, or (c) the rights of holders of Deposited Securities may be adversely affected.

Neither the Depositary nor the Custodian shall under any circumstances exercise any discretion as to voting and neither the Depositary nor the Custodian shall vote, attempt to exercise the right to vote, or in any way make use of, for purposes of establishing a quorum or otherwise, the Deposited Securities represented by ADSs, except pursuant to and in accordance with the voting instructions timely received from Holders or as otherwise contemplated herein. If the Depositary timely receives voting instructions from a Holder which fail to specify the manner in which the Depositary is to vote the Deposited Securities represented by such Holder's ADSs, the Depositary will deem such Holder (unless otherwise specified in the notice distributed to Holders) to have instructed the Depositary to vote in favor of the items set forth in such voting instructions. Deposited Securities represented by ADSs for which no timely voting instructions are received by the Depositary from the Holder shall not be voted (except (a) in the case voting is by show of hands, in which case the Depositary will instruct the Custodian to vote all Deposited Securities in accordance with the voting instructions received from a majority of Holders of ADSs who provided voting instructions, and (b) as contemplated in this Section 4.10). Notwithstanding anything else contained herein, the Depositary shall, if so requested in writing by the Company, represent all Deposited Securities (whether or not voting instructions have been received in respect of such Deposited Securities from Holders as of the ADS Record Date) for the sole purpose of establishing quorum at a meeting of shareholders.

Notwithstanding anything else contained in the Deposit Agreement or any ADR, the Depositary shall not have any obligation to take any action with respect to any meeting, or solicitation of consents or proxies, of holders of Deposited Securities if the taking of such action would violate U.S. laws. The Company agrees to take any and all actions reasonably necessary and as permitted by the laws of England and Wales to enable Holders and Beneficial Owners to exercise the voting rights accruing to the Deposited Securities and to deliver to the Depositary an opinion of U.S. counsel addressing any actions requested to be taken if so requested by the Depositary.

There can be no assurance that Holders generally or any Holder in particular will receive the notice described above with sufficient time to enable the Holder to return voting instructions to the Depositary in a timely manner.

**Section 4.11 Changes Affecting Deposited Securities.** Upon any change in nominal or par value, split-up, cancellation, consolidation or any other reclassification of Deposited Securities, or upon any recapitalization, reorganization, merger, consolidation or sale of assets affecting the Company or to which it is a party, any property which shall be received by the Depositary or the Custodian in exchange for, or in conversion of, or replacement of, or otherwise in respect of, such Deposited Securities shall, to the extent permitted by law, be treated as new Deposited Property under the Deposit Agreement, and the ADSs shall, subject to the provisions of the Deposit Agreement, any ADR(s) evidencing such ADSs and applicable law, represent the right to receive such additional or replacement Deposited Property. In giving effect to such change, split-up, cancellation, consolidation or other reclassification of Deposited Securities,

recapitalization, reorganization, merger, consolidation or sale of assets, the Depositary may, with the Company's approval, and shall, if the Company shall so request, subject to the terms of the Deposit Agreement (including, without limitation, (a) the applicable fees and charges of, and expenses incurred by, the Depositary, and (b) applicable taxes) and receipt of an opinion of counsel to the Company satisfactory to the Depositary that such actions are not in violation of any applicable laws or regulations, (i) issue and deliver additional ADSs as in the case of a stock dividend on the Shares, (ii) amend the Deposit Agreement and the applicable ADRs, (iii) amend the applicable Registration Statement(s) on Form F-6 as filed with the Commission in respect of the ADSs, (iv) call for the surrender of outstanding ADRs to be exchanged for new ADRs, and (v) take such other actions as are appropriate to reflect the transaction with respect to the ADSs. The Company agrees to, jointly with the Depositary, amend the Registration Statement on Form F-6 as filed with the Commission to permit the issuance of such new form of ADRs. Notwithstanding the foregoing, in the event that any Deposited Property so received may not be lawfully distributed to some or all Holders, the Depositary may, with the Company's approval, and shall, if the Company requests, subject to receipt of an opinion of Company's counsel satisfactory to the Depositary that such action is not in violation of any applicable laws or regulations, sell such Deposited Property at public or private sale, at such place or places and upon such terms as it may deem proper and may allocate the net proceeds of such sales (net of applicable (a) fees and charges of, and expenses incurred by, the Depositary and (b) taxes) for the account of the Holders otherwise entitled to such Deposited Property upon an averaged or other practicable basis without regard to any distinctions among such Holders and distribute the net proceeds so allocated to the extent practicable as in the case of a distribution received in cash pursuant to Section 4.1. The Depositary shall not be responsible for (i) any failure to determine that it may be lawful or practicable to make such Deposited Property available to Holders in general or to any Holder in particular, (ii) any foreign exchange exposure or loss incurred in connection with such sale, or (iii) any liability to the purchaser of such Deposited Property.

#### **Section 4.12 Available Information.**

The Company is subject to the periodic reporting requirements of the Exchange Act and, accordingly, is required to file or furnish certain reports with the Commission. These reports can be retrieved from the Commission's website ([www.sec.gov](http://www.sec.gov)) and can be inspected and copied at the public reference facilities maintained by the Commission located (as of the date of the Deposit Agreement) at 100 F Street, N.E., Washington D.C. 20549.

**Section 4.13 Reports.** The Depositary shall make available for inspection by Holders at its Principal Office any reports and communications, including any proxy soliciting materials, received from the Company which are both (a) received by the Depositary, the Custodian, or the nominee of either of them as the holder of the Deposited Property and (b) made generally available to the holders of such Deposited Property by the Company. The Depositary shall also provide or make available to Holders copies of such reports when furnished by the Company pursuant to Section 5.6.

**Section 4.14 List of Holders.** Promptly upon written request by the Company, the Depositary shall furnish to it a list, as of a recent date, of the names, addresses and holdings of ADSs of all Holders.



**Section 4.15 Taxation.** The Depositary will, and will instruct the Custodian to, forward to the Company or its agents such information from its records as the Company may reasonably request to enable the Company or its agents to file the necessary tax reports with governmental authorities or agencies. The Depositary, the Custodian or the Company and its agents may file such reports as are necessary to reduce or eliminate applicable taxes on dividends and on other distributions in respect of Deposited Property under applicable tax treaties or laws for the Holders and Beneficial Owners. In accordance with instructions from the Company and to the extent practicable, the Depositary or the Custodian will take reasonable administrative actions to obtain tax refunds, reduced withholding of tax at source on dividends and other benefits under applicable tax treaties or laws with respect to dividends and other distributions on the Deposited Property. As a condition to receiving such benefits, Holders and Beneficial Owners of ADSs may be required from time to time, and in a timely manner, to file such proof of taxpayer status, residence and beneficial ownership (as applicable), to execute such certificates and to make such representations and warranties, or to provide any other information or documents, as the Depositary or the Custodian may deem necessary or proper to fulfill the Depositary's or the Custodian's obligations under applicable law. The Depositary and the Company shall have no obligation or liability to any person if any Holder or Beneficial Owner fails to provide such information or if such information does not reach the relevant tax authorities in time for any Holder or Beneficial Owner to obtain the benefits of any tax treatment. The Holders and Beneficial Owners shall indemnify the Depositary, the Company, the Custodian and any of their respective directors, employees, agents and Affiliates against, and hold each of them harmless from, any claims by any governmental authority with respect to taxes, additions to tax, penalties or interest arising out of any refund of taxes, reduced rate of withholding at source or other tax benefit obtained.

If the Company (or any of its agents) withholds from any distribution any amount on account of taxes or governmental charges, or pays any other tax in respect of such distribution (e.g., stamp duty tax, capital gains or other similar tax), the Company shall (and shall cause such agent to) remit promptly to the Depositary information about such taxes or governmental charges withheld or paid, and, if so requested, the tax receipt (or other proof of payment to the applicable governmental authority) therefor, in each case, in a form satisfactory to the Depositary. The Depositary shall, to the extent required by U.S. law, report to Holders any taxes withheld by it or the Custodian, and, if such information is provided to it by the Company, any taxes withheld by the Company. The Depositary and the Custodian shall not be required to provide the Holders with any evidence of the remittance by the Company (or its agents) of any taxes withheld, or of the payment of taxes by the Company, except to the extent the evidence is provided by the Company to the Depositary or the Custodian, as applicable. Neither the Depositary nor the Custodian shall be liable for the failure by any Holder or Beneficial Owner to obtain the benefits of credits on the basis of non-U.S. tax paid against such Holder's or Beneficial Owner's income tax liability.

The Depositary is under no obligation to provide the Holders and Beneficial Owners with any information about the tax status of the Company. The Depositary shall not incur any liability for any tax consequences that may be incurred by Holders and Beneficial Owners on account of their ownership of the ADSs, including without limitation, tax consequences resulting from the Company (or any of its subsidiaries) being treated as a "Passive Foreign Investment

Company” (in each case as defined in the U.S. Internal Revenue Code and the regulations issued thereunder) or otherwise.

## ARTICLE V

### THE DEPOSITARY, THE CUSTODIAN AND THE COMPANY

**Section 5.1 Maintenance of Office and Transfer Books by the Registrar.** Until termination of the Deposit Agreement in accordance with its terms, the Registrar shall maintain in the Borough of Manhattan, the City of New York, an office and facilities for the issuance and delivery of ADSs, the acceptance for surrender of ADS(s) for the purpose of withdrawal of Deposited Securities, the registration of issuances, cancellations, transfers, combinations and split-ups of ADS(s) and, if applicable, to countersign ADRs evidencing the ADSs so issued, transferred, combined or split-up, in each case in accordance with the provisions of the Deposit Agreement.

The Registrar shall keep books for the registration of ADSs which at all reasonable times shall be open for inspection by the Company and by the Holders of such ADSs, provided that such inspection shall not be, to the Registrar’s knowledge, for the purpose of communicating with Holders of such ADSs in the interest of a business or object other than the business of the Company or other than a matter related to the Deposit Agreement or the ADSs.

The Registrar may close the transfer books with respect to the ADSs, at any time or from time to time, when deemed necessary or advisable by it in good faith in connection with the performance of its duties hereunder, or at the reasonable written request of the Company subject, in all cases, to Section 7.8.

If any ADSs are listed on one or more stock exchanges or automated quotation systems in the United States, the Depositary shall act as Registrar or appoint a Registrar or one or more co-registrars for registration of issuances, cancellations, transfers, combinations and split-ups of ADSs and, if applicable, to countersign ADRs evidencing the ADSs so issued, transferred, combined or split-up, in accordance with any requirements of such exchanges or systems. Such Registrar or co-registrars may be removed and a substitute or substitutes appointed by the Depositary.

**Section 5.2 Exoneration.** Notwithstanding anything contained in the Deposit Agreement or any ADR, neither the Depositary nor the Company shall be obligated to do or perform any act which is inconsistent with the provisions of the Deposit Agreement or incur any liability (i) if the Depositary or the Company shall be prevented or forbidden from, or delayed in, doing or performing any act or thing required by the terms of the Deposit Agreement, by reason of any provision of any present or future law or regulation of the United States, England and Wales or any other country, or of any other governmental authority or regulatory authority or stock exchange, or on account of potential criminal or civil penalties or restraint, or by reason of any provision, present or future, of the Articles of Association of the Company or any provision of or governing any Deposited Securities, or by reason of any act of God or war or other circumstances beyond its control (including, without limitation, nationalization, expropriation, currency restrictions, work stoppage, strikes, civil unrest, acts of terrorism, revolutions,

rebellions, explosions and computer failure), (ii) by reason of any exercise of, or failure to exercise, any discretion provided for in the Deposit Agreement or in the Articles of Association of the Company or provisions of or governing Deposited Securities, (iii) for any action or inaction in reliance upon the advice of or information from legal counsel, accountants, any person presenting Shares for deposit, any Holder, any Beneficial Owner or authorized representative thereof, or any other person believed by it in good faith to be competent to give such advice or information, (iv) for the inability by a Holder or Beneficial Owner to benefit from any distribution, offering, right or other benefit which is made available to holders of Deposited Securities but is not, under the terms of the Deposit Agreement, made available to Holders of ADSs, or (v) for any consequential or punitive damages (including lost profits) for any breach of the terms of the Deposit Agreement.

The Depositary, its controlling persons, its agents, any Custodian and the Company, its controlling persons and its agents may rely and shall be protected in acting upon any written notice, request or other document believed by it to be genuine and to have been signed or presented by the proper party or parties.

No disclaimer of liability under the Securities Act is intended by any provision of the Deposit Agreement.

**Section 5.3 Standard of Care.** The Company and the Depositary assume no obligation and shall not be subject to any liability under the Deposit Agreement or any ADRs to any Holder(s) or Beneficial Owner(s), except that the Company and the Depositary agree to perform their respective obligations specifically set forth in the Deposit Agreement or the applicable ADRs without negligence or bad faith.

Without limitation of the foregoing, neither the Depositary, nor the Company, nor any of their respective controlling persons, or agents, shall be under any obligation to appear in, prosecute or defend any action, suit or other proceeding in respect of any Deposited Property or in respect of the ADSs, which in its opinion may involve it in expense or liability, unless indemnity satisfactory to it against all expense (including fees and disbursements of counsel) and liability be furnished as often as may be required (and no Custodian shall be under any obligation whatsoever with respect to such proceedings, the responsibility of the Custodian being solely to the Depositary).

The Depositary and its agents shall not be liable for any failure to carry out any instructions to vote any of the Deposited Securities, or for the manner in which any vote is cast or the effect of any vote, provided that any such action or omission is in good faith and without negligence and in accordance with the terms of the Deposit Agreement. The Depositary shall not incur any liability for any failure to accurately determine that any distribution or action may be lawful or reasonably practicable, for the content of any information submitted to it by the Company for distribution to the Holders or for any inaccuracy of any translation thereof, for any investment risk associated with acquiring an interest in the Deposited Property, for the validity or worth of the Deposited Property or for any tax consequences that may result from the ownership of ADSs, Shares or other Deposited Property, for the credit-worthiness of any third party, for allowing any rights to lapse upon the terms of the Deposit Agreement, for the failure or

timeliness of any notice from the Company, or for any action of or failure to act by, or any information provided or not provided by, DTC or any DTC Participant.

The Depositary shall not be liable for any acts or omissions made by a successor depositary whether in connection with a previous act or omission of the Depositary or in connection with any matter arising wholly after the removal or resignation of the Depositary, provided that in connection with the issue out of which such potential liability arises the Depositary performed its obligations without negligence or bad faith while it acted as Depositary.

The Depositary shall not be liable for any acts or omissions made by a predecessor depositary whether in connection with an act or omission of the Depositary or in connection with any matter arising wholly prior to the appointment of the Depositary or after the removal or resignation of the Depositary, provided that in connection with the issue out of which such potential liability arises the Depositary performed its obligations without negligence or bad faith while it acted as Depositary.

**Section 5.4 Resignation and Removal of the Depositary: Appointment of Successor Depositary.** The Depositary may at any time resign as Depositary hereunder by written notice of resignation delivered to the Company, such resignation to be effective on the earlier of (i) the 90th day after delivery thereof to the Company (whereupon the Depositary shall be entitled to take the actions contemplated in Section 6.2), or (ii) the appointment by the Company of a successor depositary and its acceptance of such appointment as hereinafter provided.

The Depositary may at any time be removed by the Company by written notice of such removal, which removal shall be effective on the later of (i) the 90th day after delivery thereof to the Depositary (whereupon the Depositary shall be entitled to take the actions contemplated in Section 6.2), or (ii) upon the appointment by the Company of a successor depositary and its acceptance of such appointment as hereinafter provided.

In case at any time the Depositary acting hereunder shall resign or be removed, the Company shall use its best efforts to appoint a successor depositary, which shall be a bank or trust company having an office in the Borough of Manhattan, the City of New York. Every successor depositary shall be required by the Company to execute and deliver to its predecessor and to the Company an instrument in writing accepting its appointment hereunder, and thereupon such successor depositary, without any further act or deed (except as required by applicable law), shall become fully vested with all the rights, powers, duties and obligations of its predecessor (other than as contemplated in Sections 5.8 and 5.9). The predecessor depositary, upon payment of all sums due it and on the written request of the Company, shall, (i) execute and deliver an instrument transferring to such successor all rights and powers of such predecessor hereunder (other than as contemplated in Sections 5.8 and 5.9), (ii) duly assign, transfer and deliver all of the Depositary's right, title and interest to the Deposited Property to such successor, and (iii) deliver to such successor a list of the Holders of all outstanding ADSs and such other information relating to ADSs and Holders thereof as the successor may reasonably request. Any such successor depositary shall promptly provide notice of its appointment to such Holders.

Any entity into or with which the Depositary may be merged or consolidated shall be the successor of the Depositary without the execution or filing of any document or any further act.

**Section 5.5    The Custodian.** The Depositary has initially appointed Citibank N.A., London Branch, as Custodian for the purpose of the Deposit Agreement. The Custodian or its successors in acting hereunder shall be subject at all times and in all respects to the direction of the Depositary for the Deposited Property for which the Custodian acts as custodian and shall be responsible solely to it. If any Custodian resigns or is discharged from its duties hereunder with respect to any Deposited Property and no other Custodian has previously been appointed hereunder, the Depositary shall promptly appoint a substitute custodian. The Depositary shall require such resigning or discharged Custodian to Deliver, or cause the Delivery of, the Deposited Property held by it, together with all such records maintained by it as Custodian with respect to such Deposited Property as the Depositary may request, to the Custodian designated by the Depositary. Whenever the Depositary determines, in its discretion, that it is appropriate to do so, it may appoint an additional custodian with respect to any Deposited Property, or discharge the Custodian with respect to any Deposited Property and appoint a substitute custodian, which shall thereafter be Custodian hereunder with respect to the Deposited Property. Immediately upon any such change, the Depositary shall give notice thereof in writing to all Holders of ADSs, each other Custodian and the Company.

Citibank, N.A. may at any time act as Custodian of the Deposited Property pursuant to the Deposit Agreement, in which case any reference to Custodian shall mean Citibank, N.A. solely in its capacity as Custodian pursuant to the Deposit Agreement. Notwithstanding anything contained in the Deposit Agreement or any ADR, the Depositary shall not be obligated to give notice to the Company, any Holders of ADSs or any other Custodian of its acting as Custodian pursuant to the Deposit Agreement.

Upon the appointment of any successor depositary, any Custodian then acting hereunder shall, unless otherwise instructed by the Depositary, continue to be the Custodian of the Deposited Property without any further act or writing, and shall be subject to the direction of the successor depositary. The successor depositary so appointed shall, nevertheless, on the written request of any Custodian, execute and deliver to such Custodian all such instruments as may be proper to give to such Custodian full and complete power and authority to act on the direction of such successor depositary.

**Section 5.6    Notices and Reports.** On or before the first date on which the Company gives notice, by publication or otherwise, of any meeting of holders of Shares or other Deposited Securities, or of any adjourned meeting of such holders, or of the taking of any action by such holders other than at a meeting, or of the taking of any action in respect of any cash or other distributions or the offering of any rights in respect of Deposited Securities, the Company shall transmit to the Depositary and the Custodian a copy of the notice thereof in the English language but otherwise in the form given or to be given to holders of Shares or other Deposited Securities. The Company shall also furnish to the Custodian and the Depositary a summary, in English, of any applicable provisions or proposed provisions of the Articles of Association of the Company that may be relevant or pertain to such notice of meeting or be the subject of a vote thereat.



The Company will also transmit to the Depositary (a) an English language version of the other notices, reports and communications which are made generally available by the Company to holders of its Shares or other Deposited Securities and (b) the English-language versions of the Company's annual and semi-annual reports prepared in accordance with the applicable requirements of the Commission. The Depositary shall arrange, at the request of the Company and at the Company's expense, to provide copies thereof to all Holders or make such notices, reports and other communications available to all Holders on a basis similar to that for holders of Shares or other Deposited Securities or on such other basis as the Company may advise the Depositary or as may be required by any applicable law, regulation or stock exchange requirement. The Company has delivered to the Depositary and the Custodian a copy of the Company's Articles of Association along with the provisions of or governing the Shares and any other Deposited Securities issued by the Company in connection with such Shares, and promptly upon any amendment thereto or change therein, the Company shall deliver to the Depositary and the Custodian a copy of such amendment thereto or change therein. The Depositary may rely upon such copy for all purposes of the Deposit Agreement.

The Depositary will, at the expense of the Company, make available a copy of any such notices, reports or communications issued by the Company and delivered to the Depositary for inspection by the Holders of the ADSs at the Depositary's Principal Office, at the office of the Custodian and at any other designated transfer office.

**Section 5.7 Issuance of Additional Shares, ADSs etc.** The Company agrees that in the event it or any of its Affiliates proposes (i) an issuance, sale or distribution of additional Shares, (ii) an offering of rights to subscribe for Shares or other Deposited Securities, (iii) an issuance or assumption of securities convertible into or exchangeable for Shares, (iv) an issuance of rights to subscribe for securities convertible into or exchangeable for Shares, (v) an elective dividend of cash or Shares, (vi) a redemption of Deposited Securities, (vii) a meeting of holders of Deposited Securities, or solicitation of consents or proxies, relating to any reclassification of securities, merger or consolidation or transfer of assets, (viii) any assumption, reclassification, recapitalization, reorganization, merger, consolidation or sale of assets which affects the Deposited Securities, or (ix) a distribution of securities other than Shares, it will obtain U.S. legal advice and take all steps necessary to ensure that the application of the proposed transaction to Holders and Beneficial Owners does not violate the registration provisions of the Securities Act, or any other applicable laws (including, without limitation, the Investment Company Act of 1940, as amended, the Exchange Act and the securities laws of the states of the U.S.). In support of the foregoing, the Company will furnish to the Depositary (a) a written opinion of U.S. counsel (reasonably satisfactory to the Depositary) stating whether such transaction (1) requires a registration statement under the Securities Act to be in effect or (2) is exempt from the registration requirements of the Securities Act and (b) an opinion of English counsel stating that (1) making the transaction available to Holders and Beneficial Owners does not violate the laws or regulations of England and Wales and (2) all requisite regulatory consents and approvals have been obtained in England and Wales. If the filing of a registration statement is required, the Depositary shall not have any obligation to proceed with the transaction unless it shall have received evidence reasonably satisfactory to it that such registration statement has been declared effective. If, being advised by counsel, the Company determines that a transaction is required to be registered under the Securities Act, the Company will either (i) register such transaction to the extent necessary, (ii) alter the terms of the transaction to avoid the registration requirements of

the Securities Act or (iii) direct the Depositary to take specific measures, in each case as contemplated in the Deposit Agreement, to prevent such transaction from violating the registration requirements of the Securities Act. The Company agrees with the Depositary that neither the Company nor any of its Affiliates will at any time (i) deposit any Shares or other Deposited Securities, either upon original issuance or upon a sale of Shares or other Deposited Securities previously issued and reacquired by the Company or by any such Affiliate, or (ii) issue additional Shares, rights to subscribe for such Shares, securities convertible into or exchangeable for Shares or rights to subscribe for such securities or distribute securities other than Shares, unless such transaction and the securities issuable in such transaction do not violate the registration provisions of the Securities Act, or any other applicable laws (including, without limitation, the Investment Company Act of 1940, as amended, the Exchange Act and the securities laws of the states of the U.S.).

Notwithstanding anything else contained in the Deposit Agreement, nothing in the Deposit Agreement shall be deemed to obligate the Company to file any registration statement in respect of any proposed transaction.

**Section 5.8 Indemnification.** The Depositary agrees to indemnify the Company and its directors, officers, employees, agents and Affiliates against, and hold each of them harmless from, any direct loss, liability, tax, charge or expense of any kind whatsoever (including, but not limited to, the reasonable fees and expenses of counsel) which may arise out of acts performed or omitted by the Depositary under the terms hereof due to the negligence or bad faith of the Depositary.

The Company agrees to indemnify the Depositary, the Custodian and any of their respective directors, officers, employees, agents and Affiliates against, and hold each of them harmless from, any direct loss, liability, tax, charge or expense of any kind whatsoever (including, but not limited to, the reasonable fees and expenses of counsel) that may arise (a) out of, or in connection with, any offer, issuance, sale, resale, transfer, deposit or withdrawal of ADRs, ADSs, the Shares, or other Deposited Securities, as the case may be, (b) out of, or as a result of, any offering documents in respect thereof or (c) out of acts performed or omitted, including, but not limited to, any delivery by the Depositary on behalf of the Company of information regarding the Company, in connection with the Deposit Agreement, any ancillary or supplemental agreement entered into between the Company and the Depositary, the ADRs, the ADSs, the Shares, or any Deposited Property, in any such case (i) by the Depositary, the Custodian or any of their respective directors, officers, employees, agents and Affiliates, except to the extent such loss, liability, tax, charge or expense is due to the negligence or bad faith of any of them, or (ii) by the Company or any of its directors, officers, employees, agents and Affiliates. The Company shall not indemnify the Depositary or the Custodian (for so long as the Custodian is a branch of Citibank, N.A.) against any liability or expense arising out of information relating to the Depositary or such Custodian, as the case may be, furnished in a signed writing to the Company, executed by the Depositary expressly for use in any registration statement, prospectus or preliminary prospectus relating to any Deposited Securities represented by the ADSs.

The obligations set forth in this Section shall survive the termination of the Deposit Agreement and the succession or substitution of any party hereto.

Any person seeking indemnification hereunder (an “indemnified person”) shall notify the person from whom it is seeking indemnification (the “indemnifying person”) of the commencement of any indemnifiable action or claim promptly after such indemnified person becomes aware of such commencement (provided that the failure to make such notification shall not affect such indemnified person’s rights to seek indemnification except to the extent the indemnifying person is materially prejudiced by such failure) and shall consult in good faith with the indemnifying person as to the conduct of the defense of such action or claim that may give rise to an indemnity hereunder, which defense shall be reasonable in the circumstances. No indemnified person shall compromise or settle any action or claim that may give rise to an indemnity hereunder without the consent of the indemnifying person, which consent shall not be unreasonably withheld.

**Section 5.9 ADS Fees and Charges.** The Company, the Holders, the Beneficial Owners, and persons receiving ADSs upon issuance or whose ADSs are being cancelled shall be required to pay the ADS fees and charges identified as payable by them respectively in the ADS fee schedule attached hereto as Exhibit B. All ADS fees and charges so payable may be deducted from distributions or must be remitted to the Depositary, or its designee, may be waived by the Depositary in full or in part with respect to some or all ADSs upon such terms, and subject to such conditions, as the Depositary may determine and may, at any time and from time to time, be changed by agreement between the Depositary and the Company, but, in the case of ADS fees and charges payable by Holders and Beneficial Owners, only in the manner contemplated in Section 6.1. The Depositary shall provide, without charge, a copy of its latest ADS fee schedule to anyone upon request.

ADS fees and charges payable upon (i) the issuance of ADSs and (ii) the cancellation of ADSs will be payable by the person to whom the ADSs are so issued by the Depositary (in the case of ADS issuances) and by the person whose ADSs are being cancelled (in the case of ADS cancellations). In the case of ADSs issued by the Depositary into DTC or presented to the Depositary via DTC, the ADS issuance and cancellation fees and charges will be payable by the DTC Participant(s) receiving the ADSs from the Depositary 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(s) of the applicable Beneficial Owner(s) in accordance with the procedures and practices of the DTC participant(s) as in effect at the time. ADS fees and charges in respect of distributions and the ADS service fee are payable by Holders as of the applicable ADS Record Date established by the Depositary. 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, the applicable Holders as of the ADS Record Date established by the Depositary will be invoiced for the amount of the ADS fees and charges and such ADS fees may be deducted from distributions made to Holders. 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 from time to time and the DTC Participants in turn charge the amount of such ADS fees and charges to the Beneficial Owners for whom they hold ADSs.

The Depositary may reimburse the Company for certain expenses incurred by the Company in respect of the ADR program established pursuant to the Deposit Agreement, by

making available a portion of the ADS fees charged in respect of the ADR program or otherwise, upon such terms and conditions as the Company and the Depositary agree from time to time. The Company shall pay to the Depositary such fees and charges, and reimburse the Depositary for such out-of-pocket expenses, as the Depositary and the Company may agree from time to time. Responsibility for payment of such fees, charges and reimbursements may from time to time be changed by agreement between the Company and the Depositary. Unless otherwise agreed, the Depositary shall present its statement for such fees, charges and reimbursements to the Company once every three months. The charges and expenses of the Custodian are for the sole account of the Depositary.

The obligations of Holders and Beneficial Owners to pay ADS fees and charges shall survive the termination of the Deposit Agreement. As to any Depositary, upon the resignation or removal of such Depositary as described in Section 5.4, the right to collect ADS fees and charges shall extend for those ADS fees and charges incurred prior to the effectiveness of such resignation or removal.

**Section 5.10 Pre-Release Transactions.** Subject to the further terms and provisions of this Section 5.10, the Depositary, its Affiliates and their agents, on their own behalf, may own and deal in any class of securities of the Company and its Affiliates and in ADSs. In its capacity as Depositary, the Depositary shall not lend Shares or ADSs; provided, however, that the Depositary may (i) issue ADSs prior to the receipt of Shares pursuant to Section 2.3 and (ii) deliver Shares prior to the receipt of ADSs for withdrawal of Deposited Securities pursuant to Section 2.7, including ADSs which were issued under (i) above but for which Shares may not have been received (each such transaction a “Pre-Release Transaction”). The Depositary may receive ADSs in lieu of Shares under (i) above and receive Shares in lieu of ADSs under (ii) above. Each such Pre-Release Transaction will be (a) subject to a written agreement whereby the person or entity (the “Applicant”) to whom ADSs or Shares are to be delivered (w) represents that at the time of the Pre-Release Transaction the Applicant or its customer owns the Shares or ADSs that are to be delivered by the Applicant under such Pre-Release Transaction, (x) agrees to indicate the Depositary as owner of such Shares or ADSs in its records and to hold such Shares or ADSs in trust for the Depositary until such Shares or ADSs are delivered to the Depositary or the Custodian, (y) unconditionally guarantees to deliver to the Depositary or the Custodian, as applicable, such Shares or ADSs, and (z) agrees to any additional restrictions or requirements that the Depositary deems appropriate, (b) at all times fully collateralized with cash, U.S. government securities or such other collateral as the Depositary deems appropriate, (c) terminable by the Depositary on not more than five (5) business days’ notice and (d) subject to such further indemnities and credit regulations as the Depositary deems appropriate. The Depositary will normally limit the number of ADSs and Shares involved in such Pre-Release Transactions at any one time to thirty percent (30%) of the ADSs outstanding (without giving effect to ADSs outstanding under (i) above), provided, however, that the Depositary reserves the right to change or disregard such limit from time to time as it deems appropriate.

The Depositary may also set limits with respect to the number of ADSs and Shares involved in Pre-Release Transactions with any one person on a case-by-case basis as it deems appropriate. The Depositary may retain for its own account any compensation received by it in conjunction with the foregoing. Collateral provided pursuant to (b) above, but not the earnings thereon, shall be held for the benefit of the Holders (other than the Applicant).



**Section 5.11 Restricted Securities Owners.** The Company agrees to advise in writing each of the persons or entities who, to the knowledge of the Company, holds Restricted Securities that such Restricted Securities are ineligible for deposit hereunder (except under the circumstances contemplated in Section 2.14) and, to the extent practicable, shall require each of such persons to represent in writing that such person will not deposit Restricted Securities hereunder (except under the circumstances contemplated in Section 2.14).

## ARTICLE VI

### AMENDMENT AND TERMINATION

**Section 6.1 Amendment/Supplement.** Subject to the terms and conditions of this Section 6.1 and applicable law, the ADRs outstanding at any time, the provisions of the Deposit Agreement and the form of ADR attached hereto and to be issued under the terms hereof may at any time and from time to time be amended or supplemented by written agreement between the Company and the Depositary in any respect which they may deem necessary or desirable without the prior written consent of the Holders or Beneficial Owners. Any amendment or supplement which shall impose or increase any fees or charges (other than charges in connection with foreign exchange control regulations, and taxes and other governmental charges, delivery and other such expenses), or which shall otherwise materially prejudice any substantial existing right of Holders or Beneficial Owners, shall not, however, become effective as to outstanding ADSs until the expiration of thirty (30) days after notice of such amendment or supplement shall have been given to the Holders of outstanding ADSs. Notice of any amendment to the Deposit Agreement or any ADR shall not need to describe in detail the specific amendments effectuated thereby, and failure to describe the specific amendments in any such notice shall not render such notice invalid, provided, however, that, in each such case, the notice given to the Holders identifies a means for Holders and Beneficial Owners to retrieve or receive the text of such amendment (*e.g.*, upon retrieval from the Commission's, the Depositary's or the Company's website or upon request from the Depositary). The parties hereto agree that any amendments or supplements which (i) are reasonably necessary (as agreed by the Company and the Depositary) in order for (a) the ADSs to be registered on Form F-6 under the Securities Act or (b) the ADSs to be settled solely in electronic book-entry form and (ii) do not in either such case impose or increase any fees or charges to be borne by Holders, shall be deemed not to materially prejudice any substantial rights of Holders or Beneficial Owners. Every Holder and Beneficial Owner at the time any amendment or supplement so becomes effective shall be deemed, by continuing to hold such ADSs, to consent and agree to such amendment or supplement and to be bound by the Deposit Agreement and the ADR, if applicable, as amended or supplemented thereby. In no event shall any amendment or supplement impair the right of the Holder to surrender such ADS and receive therefor the Deposited Securities represented thereby, except in order to comply with mandatory provisions of applicable law. Notwithstanding the foregoing, if any governmental body should adopt new laws, rules or regulations which would require an amendment of, or supplement to, the Deposit Agreement to ensure compliance therewith, the Company and the Depositary may amend or supplement the Deposit Agreement and any ADRs at any time in accordance with such changed laws, rules or regulations. Such amendment or supplement to the Deposit Agreement and any ADRs in such circumstances may become effective before a notice of such amendment or supplement is given to Holders or within any other period of time as required for compliance with such laws, rules or regulations.

**Section 6.2 Termination.** The Depositary shall, at any time at the written direction of the Company, terminate the Deposit Agreement by distributing notice of such termination to the Holders of all ADSs then outstanding at least thirty (30) days prior to the date fixed in such notice for such termination. If ninety (90) days shall have expired after (i) the Depositary shall have delivered to the Company a written notice of its election to resign, or (ii) the Company shall have delivered to the Depositary a written notice of the removal of the Depositary, and, in either case, a successor depositary shall not have been appointed and accepted its appointment as provided in Section 5.4 of the Deposit Agreement, the Depositary may terminate the Deposit Agreement by distributing notice of such termination to the Holders of all ADSs then outstanding at least thirty (30) days prior to the date fixed in such notice for such termination. The date so fixed for termination of the Deposit Agreement in any termination notice so distributed by the Depositary to the Holders of ADSs is referred to as the “Termination Date”. Until the Termination Date, the Depositary shall continue to perform all of its obligations under the Deposit Agreement, and the Holders and Beneficial Owners will be entitled to all of their rights under the Deposit Agreement.

If any ADSs shall remain outstanding after the Termination Date, the Registrar and the Depositary shall not, after the Termination Date, have any obligation to perform any further acts under the Deposit Agreement, except that the Depositary shall, subject, in each case, to the terms and conditions of the Deposit Agreement, continue to (i) collect dividends and other distributions pertaining to Deposited Securities, (ii) sell Deposited Property received in respect of Deposited Securities, (iii) deliver Deposited Securities, together with any dividends or other distributions received with respect thereto and the net proceeds of the sale of any other Deposited Property, in exchange for ADSs surrendered to the Depositary (after deducting, or charging, as the case may be, in each case, the fees and charges of, and expenses incurred by, the Depositary, and all applicable taxes or governmental charges for the account of the Holders and Beneficial Owners, in each case upon the terms set forth in Section 5.9 of the Deposit Agreement), and (iv) take such actions as may be required under applicable law in connection with its role as Depositary under the Deposit Agreement.

At any time after the Termination Date, the Depositary may sell the Deposited Property then held under the Deposit Agreement and shall after such sale hold un-invested the net proceeds of such sale, together with any other cash then held by it under the Deposit Agreement, in an un-segregated account and without liability for interest, for the pro rata benefit of the Holders whose ADSs have not theretofore been surrendered. After making such sale, the Depositary shall be discharged from all obligations under the Deposit Agreement except (i) to account for such net proceeds and other cash (after deducting, or charging, as the case may be, in each case, the fees and charges of, and expenses incurred by, the Depositary, and all applicable taxes or governmental charges for the account of the Holders and Beneficial Owners, in each case upon the terms set forth in Section 5.9 of the Deposit Agreement), and (ii) as may be required at law in connection with the termination of the Deposit Agreement. After the Termination Date, the Company shall be discharged from all obligations under the Deposit Agreement, except for its obligations to the Depositary under Sections 5.8, 5.9 and 7.6 of the Deposit Agreement. The obligations under the terms of the Deposit Agreement of Holders and Beneficial Owners of ADSs outstanding as of the Termination Date shall survive the Termination Date and shall be discharged only when the applicable ADSs are presented by their

Holders to the Depositary for cancellation under the terms of the Deposit Agreement (except as specifically provided in the Deposit Agreement).

## ARTICLE VII

### MISCELLANEOUS

**Section 7.1 Counterparts.** The Deposit Agreement may be executed in any number of counterparts, each of which shall be deemed an original and all of such counterparts together shall constitute one and the same agreement. Copies of the Deposit Agreement shall be maintained with the Depositary and shall be open to inspection by any Holder during business hours.

**Section 7.2 No Third-Party Beneficiaries.** The Deposit Agreement is for the exclusive benefit of the parties hereto (and their successors) and shall not be deemed to give any legal or equitable right, remedy or claim whatsoever to any other person, except to the extent specifically set forth in the Deposit Agreement. Nothing in the Deposit Agreement shall be deemed to give rise to a partnership or joint venture among the parties nor establish a fiduciary or similar relationship among the parties. The parties hereto acknowledge and agree that (i) Citibank and its Affiliates may at any time have multiple banking relationships with the Company, the Holders, the Beneficial Owners, and their respective Affiliates, (ii) Citibank and its Affiliates may be engaged at any time in transactions in which parties adverse to the Company, the Holders, the Beneficial Owners or their respective Affiliates may have interests, (iii) the Depositary and its Affiliates may from time to time have on their possession non-public information about the Company, the Holders, the Beneficial Owners, and their respective Affiliates, (iv) nothing contained in the Deposit Agreement shall (a) preclude Citibank or any of its Affiliates from engaging in such transactions or establishing or maintaining such relationships, (b) obligate Citibank or any of its Affiliates to disclose such information, transactions or relationships, or to account for any profit made or payment received in such transactions or relationships, and (v) the Depositary shall not be deemed to have knowledge of any information any other division of Citibank or any of its Affiliates may have about the Company, the Holders, the Beneficial Owners, or any of their respective Affiliates.

**Section 7.3 Severability.** In case any one or more of the provisions contained in the Deposit Agreement or in the ADRs should be or become invalid, illegal or unenforceable in any respect, the validity, legality and enforceability of the remaining provisions contained herein or therein shall in no way be affected, prejudiced or disturbed thereby.

**Section 7.4 Holders and Beneficial Owners as Parties; Binding Effect.** The Holders and Beneficial Owners from time to time of ADSs issued hereunder shall be parties to the Deposit Agreement and shall be bound by all of the terms and conditions hereof and of any ADR evidencing their ADSs by acceptance thereof or any beneficial interest therein.

**Section 7.5 Notices.** Any and all notices to be given to the Company shall be deemed to have been duly given if personally delivered or sent by mail, air courier or cable, telex or facsimile transmission, confirmed by letter personally delivered or sent by mail or air courier, addressed to Verona Pharma plc, 3 More London Riverside, London SE1 2RE UK, Attention:

Legal Counsel, or to any other address which the Company may specify in writing to the Depositary.

Any and all notices to be given to the Depositary shall be deemed to have been duly given if personally delivered or sent by mail, air courier or cable, telex or facsimile transmission, confirmed by letter personally delivered or sent by mail or air courier, addressed to Citibank, N.A., 388 Greenwich Street, New York, New York 10013, U.S.A., Attention: Depositary Receipts Department, or to any other address which the Depositary may specify in writing to the Company.

Any and all notices to be given to any Holder shall be deemed to have been duly given (a) if personally delivered or sent by mail or cable, telex or facsimile transmission, confirmed by letter, addressed to such Holder at the address of such Holder as it appears on the books of the Depositary or, if such Holder shall have filed with the Depositary a request that notices intended for such Holder be mailed to some other address, at the address specified in such request, or (b) if a Holder shall have designated such means of notification as an acceptable means of notification under the terms of the Deposit Agreement, by means of electronic messaging addressed for delivery to the e-mail address designated by the Holder for such purpose. Notice to Holders shall be deemed to be notice to Beneficial Owners for all purposes of the Deposit Agreement. Failure to notify a Holder or any defect in the notification to a Holder shall not affect the sufficiency of notification to other Holders or to the Beneficial Owners of ADSs held by such other Holders. Any notices given to DTC under the terms of the Deposit Agreement shall (unless otherwise specified by the Depositary) constitute notice to the DTC Participants who hold as the ADSs in their DTC accounts and to the Beneficial Owners of such ADSs.

Delivery of a notice sent by mail, air courier or cable, telex or facsimile transmission shall be deemed to be effective at the time when a duly addressed letter containing the same (or a confirmation thereof in the case of a cable, telex or facsimile transmission) is deposited, postage prepaid, in a post-office letter box or delivered to an air courier service, without regard for the actual receipt or time of actual receipt thereof by a Holder. The Depositary or the Company may, however, act upon any cable, telex or facsimile transmission received by it from any Holder, the Custodian, the Depositary, or the Company, notwithstanding that such cable, telex or facsimile transmission shall not be subsequently confirmed by letter.

Delivery of a notice by means of electronic messaging shall be deemed to be effective at the time of the initiation of the transmission by the sender (as shown on the sender's records), notwithstanding that the intended recipient retrieves the message at a later date, fails to retrieve such message, or fails to receive such notice on account of its failure to maintain the designated e-mail address, its failure to designate a substitute e-mail address or for any other reason.

**Section 7.6 Governing Law and Jurisdiction.** The Deposit Agreement and the ADRs shall be interpreted in accordance with, and all rights hereunder and thereunder and provisions hereof and thereof shall be governed by, the laws of the State of New York applicable to contracts made and to be wholly performed in that State. Notwithstanding anything contained in the Deposit Agreement, any ADR or any present or future provisions of the laws of the State of New York, the rights of holders of Shares and of any other Deposited Securities and the obligations and duties of the Company in respect of the holders of Shares and other Deposited



Securities, as such, shall be governed by the laws of England and Wales (or, if applicable, such other laws as may govern the Deposited Securities).

Except as set forth in the following paragraph of this Section 7.6, the Company and the Depositary agree that the federal or state courts in the City of New York shall have jurisdiction to hear and determine any suit, action or proceeding and to settle any dispute between them that may arise out of or in connection with the Deposit Agreement and, for such purposes, each irrevocably submits to the non-exclusive jurisdiction of such courts. The Company hereby irrevocably designates, appoints and empowers National Corporate Research, Ltd. (the "Agent") now at 10 East 40th Street, 10th Floor, New York, New York 10016, as its authorized agent to receive and accept for and on its behalf, and on behalf of its properties, assets and revenues, service by mail of any and all legal process, summons, notices and documents that may be served in any suit, action or proceeding brought against the Company in any federal or state court as described in the preceding sentence or in the next paragraph of this Section 7.6. If for any reason the Agent shall cease to be available to act as such, the Company agrees to designate a new agent in New York on the terms and for the purposes of this Section 7.6 reasonably satisfactory to the Depositary. The Company further hereby irrevocably consents and agrees to the service of any and all legal process, summons, notices and documents in any suit, action or proceeding against the Company, by service by mail of a copy thereof upon the Agent (whether or not the appointment of such Agent shall for any reason prove to be ineffective or such Agent shall fail to accept or acknowledge such service), with a copy mailed to the Company by registered or certified air mail, postage prepaid, to its address provided in Section 7.5. The Company agrees that the failure of the Agent to give any notice of such service to it shall not impair or affect in any way the validity of such service or any judgment rendered in any action or proceeding based thereon.

Notwithstanding the foregoing, the Depositary and the Company unconditionally agree that in the event that a Holder or Beneficial Owner brings a suit, action or proceeding against (a) the Company, (b) the Depositary in its capacity as Depositary under the Deposit Agreement or (c) against both the Company and the Depositary, in any such case, in any state or federal court of the United States, and the Depositary or the Company have any claim, for indemnification or otherwise, against each other arising out of the subject matter of such suit, action or proceeding, then the Company and the Depositary may pursue such claim against each other in the state or federal court in the United States in which such suit, action, or proceeding is pending and, for such purposes, the Company and the Depositary irrevocably submit to the non-exclusive jurisdiction of such courts. The Company agrees that service of process upon the Agent in the manner set forth in the preceding paragraph shall be effective service upon it for any suit, action or proceeding brought against it as described in this paragraph.

The Company irrevocably and unconditionally waives, to the fullest extent permitted by law, any objection that it may now or hereafter have to the laying of venue of any actions, suits or proceedings brought in any court as provided in this Section 7.6, and hereby further irrevocably and unconditionally waives and agrees not to plead or claim in any such court that any such action, suit or proceeding brought in any such court has been brought in an inconvenient forum.

The Company irrevocably and unconditionally waives, to the fullest extent permitted by law, and agrees not to plead or claim, any right of immunity from legal action, suit or proceeding, from setoff or counterclaim, from the jurisdiction of any court, from service of process, from attachment upon or prior to judgment, from attachment in aid of execution or judgment, from execution of judgment, or from any other legal process or proceeding for the giving of any relief or for the enforcement of any judgment, and consents to such relief and enforcement against it, its assets and its revenues in any jurisdiction, in each case with respect to any matter arising out of, or in connection with, the Deposit Agreement, any ADR or the Deposited Property.

**EACH OF THE PARTIES TO THE DEPOSIT AGREEMENT (INCLUDING, WITHOUT LIMITATION, EACH HOLDER AND BENEFICIAL OWNER) IRREVOCABLY WAIVES, TO THE FULLEST EXTENT PERMITTED BY APPLICABLE LAW, ANY AND ALL RIGHT TO TRIAL BY JURY IN ANY LEGAL PROCEEDING AGAINST THE COMPANY AND/OR THE DEPOSITARY ARISING OUT OF, OR RELATING TO, THE DEPOSIT AGREEMENT, ANY ADR AND ANY TRANSACTIONS CONTEMPLATED THEREIN (WHETHER BASED ON CONTRACT, TORT, COMMON LAW OR OTHERWISE).**

No disclaimer of liability under the Securities Act is intended by any provision of the Deposit Agreement. The provisions of this Section 7.6 shall survive any termination of the Deposit Agreement, in whole or in part.

**Section 7.7 Assignment.** Subject to the provisions of Section 5.4, the Deposit Agreement may not be assigned by either the Company or the Depositary.

**Section 7.8 Compliance with U.S. Securities Laws.** Notwithstanding anything in the Deposit Agreement to the contrary, the withdrawal or delivery of Deposited Securities will not be suspended by the Company or the Depositary except as would be permitted by Instruction I.A.(1) of the General Instructions to Form F-6 Registration Statement, as amended from time to time, under the Securities Act.

**Section 7.9 England and Wales Law References.** Any summary of laws and regulations of England and Wales and of the terms of the Company's Articles of Association set forth in the Deposit Agreement have been provided by the Company solely for the convenience of Holders, Beneficial Owners and the Depositary. While such summaries are believed by the Company to be accurate as of the date of the Deposit Agreement, (i) they are summaries and as such may not include all aspects of the materials summarized applicable to a Holder or Beneficial Owner, and (ii) these laws and regulations and the Company's Articles of Association may change after the date of the Deposit Agreement. Neither the Depositary nor the Company has any obligation under the terms of the Deposit Agreement to update any such summaries.

**Section 7.10 Titles and References.**

(a) **Deposit Agreement.** All references in the Deposit Agreement to exhibits, articles, sections, subsections, and other subdivisions refer to the exhibits, articles, sections, subsections and other subdivisions of the Deposit Agreement unless expressly provided

otherwise. The words “the Deposit Agreement”, “herein”, “hereof”, “hereby”, “hereunder”, and words of similar import refer to the Deposit Agreement as a whole as in effect at the relevant time between the Company, the Depositary and the Holders and Beneficial Owners of ADSs and not to any particular subdivision unless expressly so limited. Pronouns in masculine, feminine and neuter gender shall be construed to include any other gender, and words in the singular form shall be construed to include the plural and *vice versa* unless the context otherwise requires. Titles to sections of the Deposit Agreement are included for convenience only and shall be disregarded in construing the language contained in the Deposit Agreement. References to “applicable laws and regulations” shall refer to laws and regulations applicable to ADRs, ADSs or Deposited Property as in effect at the relevant time of determination, unless otherwise required by law or regulation.

(b) **ADRs.** All references in any ADR(s) to paragraphs, exhibits, articles, sections, subsections, and other subdivisions refer to the paragraphs, exhibits, articles, sections, subsections and other subdivisions of the ADR(s) in question unless expressly provided otherwise. The words “the Receipt”, “the ADR”, “herein”, “hereof”, “hereby”, “hereunder”, and words of similar import used in any ADR refer to the ADR as a whole and as in effect at the relevant time, and not to any particular subdivision unless expressly so limited. Pronouns in masculine, feminine and neuter gender in any ADR shall be construed to include any other gender, and words in the singular form shall be construed to include the plural and *vice versa* unless the context otherwise requires. Titles to paragraphs of any ADR are included for convenience only and shall be disregarded in construing the language contained in the ADR. References to “applicable laws and regulations” shall refer to laws and regulations applicable to ADRs, ADSs or Deposited Property as in effect at the relevant time of determination, unless otherwise required by law or regulation.

IN WITNESS WHEREOF, VERONA PHARMA PLC and CITIBANK, N.A. have duly executed the Deposit Agreement as of the day and year first above set forth and all Holders and Beneficial Owners shall become parties hereto upon acceptance by them of ADSs issued in accordance with the terms hereof, or upon acquisition of any beneficial interest therein.

VERONA PHARMA PLC

By: /s/ Jan-Anders Karlsson, Ph.D.  
Name: Jan-Anders Karlsson, Ph.D.  
Title: Chief Executive Officer

CITIBANK, N.A.

By: /s/ Keith Galfo  
Name: Keith Galfo  
Title: Vice President

**EXHIBIT A**  
**[FORM OF ADR]**

Number \_\_\_\_\_

CUSIP NUMBER: \_\_\_\_\_

American Depositary Shares (each  
American Depositary Share  
representing the right to receive eight  
(8) fully paid ordinary shares)

AMERICAN DEPOSITARY RECEIPT  
for  
AMERICAN DEPOSITARY SHARES  
representing  
DEPOSITED ORDINARY SHARES  
of  
VERONA PHARMA PLC

(Incorporated under the laws of England and Wales)

CITIBANK, N.A., a national banking association organized and existing under the laws of the United States of America, as depositary (the "Depositary"), hereby certifies that \_\_\_\_\_ is the owner of \_\_\_\_\_ American Depositary Shares (hereinafter "ADS") representing deposited ordinary shares, including evidence of rights to receive such ordinary shares (the "Shares"), of Verona Pharma plc, a public limited company incorporated under the laws of England and Wales (the "Company"). As of the date of issuance of this ADR, each ADS represents the right to receive eight (8) Shares deposited under the Deposit Agreement (as hereinafter defined) with the Custodian, which at the date of execution of the Deposit Agreement is Citibank, N.A. London Branch (the "Custodian"). The ADS(s)-to-Share(s) ratio is subject to amendment as provided in Articles IV and VI of the Deposit Agreement. The Depositary's Principal Office is located at 388 Greenwich Street, New York, New York 10013, U.S.A.

(1) **The Deposit Agreement.** This American Depositary Receipt is one of an issue of American Depositary Receipts ("ADRs"), all issued and to be issued upon the terms and conditions set forth in the Deposit Agreement, dated as of May 2, 2017 (as amended and supplemented from time to time, the "Deposit Agreement"), by and among the Company, the Depositary, and all Holders and Beneficial Owners from time to time of ADSs issued thereunder. The Deposit Agreement sets forth the rights and obligations of Holders and Beneficial Owners of ADSs and the rights and duties of the Depositary in respect of the Shares deposited thereunder and any and all other Deposited Property (as defined in the Deposit Agreement) from time to time received and held on deposit in respect of the ADSs. Copies of the Deposit Agreement are on file at the Principal Office of the Depositary and with the Custodian. Each Holder and each

Beneficial Owner, upon acceptance of any ADSs (or any interest therein) issued in accordance with the terms and conditions of the Deposit Agreement, shall be deemed for all purposes to (a) be a party to and bound by the terms of the Deposit Agreement and the applicable ADR(s), and (b) appoint the Depositary its attorney-in-fact, with full power to delegate, to act on its behalf and to take any and all actions contemplated in the Deposit Agreement and the applicable ADR(s), to adopt any and all procedures necessary to comply with applicable law and to take such action as the Depositary in its sole discretion may deem necessary or appropriate to carry out the purposes of the Deposit Agreement and the applicable ADR(s), the taking of such actions to be the conclusive determinant of the necessity and appropriateness thereof.

The statements made on the face and reverse of this ADR are summaries of certain provisions of the Deposit Agreement and the Articles of Association of the Company (as in effect on the date of the signing of the Deposit Agreement) and are qualified by and subject to the detailed provisions of the Deposit Agreement and the Articles of Association, to which reference is hereby made.

All capitalized terms not defined herein shall have the meanings ascribed thereto in the Deposit Agreement.

The Depositary makes no representation or warranty as to the validity or worth of the Deposited Property. The Depositary has made arrangements for the acceptance of the ADSs into DTC. Each Beneficial Owner of ADSs held through DTC must rely on the procedures of DTC and the DTC Participants to exercise and be entitled to any rights attributable to such ADSs. The Depositary may issue Uncertificated ADSs subject, however, to the terms and conditions of Section 2.13 of the Deposit Agreement.

(2) **Surrender of ADSs and Withdrawal of Deposited Securities.** The Holder of this ADR (and of the ADSs evidenced hereby) shall be entitled to Delivery (at the Custodian's designated office) of the Deposited Securities at the time represented by the ADSs evidenced hereby upon satisfaction of each of the following conditions: (i) the Holder (or a duly-authorized attorney of the Holder) has duly Delivered ADSs to the Depositary at its Principal Office the ADSs evidenced hereby (and if applicable, this ADR evidencing such ADSs) for the purpose of withdrawal of the Deposited Securities represented thereby, (ii) if applicable and so required by the Depositary, this ADR Delivered to the Depositary for such purpose has been properly endorsed in blank or is accompanied by proper instruments of transfer in blank (including signature guarantees in accordance with standard securities industry practice), (iii) if so required by the Depositary, the Holder of the ADSs has executed and delivered to the Depositary a written order directing the Depositary to cause the Deposited Securities being withdrawn to be Delivered to or upon the written order of the person(s) designated in such order, and (iv) all applicable fees and charges of, and expenses incurred by, the Depositary and all applicable taxes and governmental charges (as are set forth in Section 5.9 of, and Exhibit B to, the Deposit Agreement) have been paid, *subject, however, in each case*, to the terms and conditions of this ADR evidencing the surrendered ADSs, of the Deposit Agreement, of the Company's Articles of Association and of any applicable laws and the rules of CREST, and to any provisions of or governing the Deposited Securities, in each case as in effect at the time thereof.



Upon satisfaction of each of the conditions specified above, the Depositary (i) shall cancel the ADSs Delivered to it (and, if applicable, the ADR(s) evidencing the ADSs so Delivered), (ii) shall direct the Registrar to record the cancellation of the ADSs so Delivered on the books maintained for such purpose, and (iii) shall direct the Custodian to Deliver, or cause the Delivery of, in each case, without unreasonable delay, the Deposited Securities represented by the ADSs so canceled together with any certificate or other document of title for the Deposited Securities, or evidence of the electronic transfer thereof (if available), as the case may be, to or upon the written order of the person(s) designated in the order delivered to the Depositary for such purpose, *subject however, in each case*, to the terms and conditions of the Deposit Agreement, of this ADR evidencing the ADSs so canceled, of the Articles of Association of the Company, of any applicable laws and of the rules of CREST, and to the terms and conditions of or governing the Deposited Securities, in each case as in effect at the time thereof.

The Depositary shall not accept for surrender ADSs representing less than one (1) Share. In the case of Delivery to it of ADSs representing a number other than a whole number of Shares, the Depositary shall cause ownership of the appropriate whole number of Shares to be Delivered in accordance with the terms hereof, and shall, at the discretion of the Depositary, either (i) return to the person surrendering such ADSs the number of ADSs representing any remaining fractional Share, or (ii) sell or cause to be sold the fractional Share represented by the ADSs so surrendered and remit the proceeds of such sale (net of (a) applicable fees and charges of, and expenses incurred by, the Depositary and (b) applicable taxes withheld) to the person surrendering the ADSs.

Notwithstanding anything else contained in this ADR or the Deposit Agreement, the Depositary may make delivery at the Principal Office of the Depositary of Deposited Property consisting of (i) any cash dividends or cash distributions, or (ii) any proceeds from the sale of any non-cash distributions, which are at the time held by the Depositary in respect of the Deposited Securities represented by the ADSs surrendered for cancellation and withdrawal. At the request, risk and expense of any Holder so surrendering ADSs represented by this ADR, and for the account of such Holder, the Depositary shall direct the Custodian to forward (to the extent permitted by law) any Deposited Property (other than Deposited Securities) held by the Custodian in respect of such ADSs to the Depositary for delivery at the Principal Office of the Depositary. Such direction shall be given by letter or, at the request, risk and expense of such Holder, by cable, telex or facsimile transmission.

(3) **Transfer, Combination and Split-up of ADRs.** The Registrar shall register the transfer of this ADR (and of the ADSs represented hereby) on the books maintained for such purpose and the Depositary shall (x) cancel this ADR and execute new ADRs evidencing the same aggregate number of ADSs as those evidenced by this ADR when canceled by the Depositary, (y) cause the Registrar to countersign such new ADRs and (z) Deliver such new ADRs to or upon the order of the person entitled thereto, if each of the following conditions has been satisfied: (i) this ADR has been duly Delivered by the Holder (or by a duly authorized attorney of the Holder) to the Depositary at its Principal Office for the purpose of effecting a transfer thereof, (ii) this surrendered ADR has been properly endorsed or is accompanied by proper instruments of transfer (including signature guarantees in accordance with standard

securities industry practice), (iii) this surrendered ADR has been duly stamped (if required by the laws of the State of New York or of the United States), and (iv) all applicable fees and charges of, and expenses incurred by, the Depositary and all applicable taxes and governmental charges (as are set forth in Section 5.9 of, and Exhibit B to, the Deposit Agreement) have been paid, *subject, however, in each case, to the terms and conditions of this ADR, of the Deposit Agreement and of applicable law, in each case as in effect at the time thereof.*

The Registrar shall register the split-up or combination of this ADR (and of the ADSs represented hereby) on the books maintained for such purpose and the Depositary shall (x) cancel this ADR and execute new ADRs for the number of ADSs requested, but in the aggregate not exceeding the number of ADSs evidenced by this ADR canceled by the Depositary, (y) cause the Registrar to countersign such new ADRs and (z) Deliver such new ADRs to or upon the order of the Holder thereof, if each of the following conditions has been satisfied: (i) this ADR has been duly Delivered by the Holder (or by a duly authorized attorney of the Holder) to the Depositary at its Principal Office for the purpose of effecting a split-up or combination thereof, and (ii) all applicable fees and charges of, and expenses incurred by, the Depositary and all applicable taxes and governmental charges (as are set forth in Section 5.9 of, and Exhibit B to, the Deposit Agreement) have been paid, *subject, however, in each case, to the terms and conditions of this ADR, of the Deposit Agreement and of applicable law, in each case as in effect at the time thereof.*

**(4) Pre-Conditions to Registration, Transfer, Etc.** As a condition precedent to the execution and delivery, the registration of issuance, transfer, split-up, combination or surrender, of any ADS, the delivery of any distribution thereon, or the withdrawal of any Deposited Property, the Depositary or the Custodian may require (i) payment from the depositor of Shares or presenter of ADSs or of this ADR of a sum sufficient to reimburse it for any tax or other governmental charge and any stock transfer or registration fee with respect thereto (including any such tax or charge and fee with respect to Shares being deposited or withdrawn) and payment of any applicable fees and charges of the Depositary as provided in Section 5.9 and Exhibit B to the Deposit Agreement and in this ADR, (ii) the production of proof satisfactory to it as to the identity and genuineness of any signature or any other matter contemplated by Section 3.1 of the Deposit Agreement, and (iii) compliance with (A) any laws or governmental regulations relating to the execution and delivery of this ADR or ADSs or to the withdrawal of Deposited Securities and (B) such reasonable regulations as the Depositary and the Company may establish consistent with the provisions of this ADR, if applicable, the Deposit Agreement and applicable law.

The issuance of ADSs against deposits of Shares generally or against deposits of particular Shares may be suspended, or the deposit of particular Shares may be refused, or the registration of transfer of ADSs in particular instances may be refused, or the registration of transfers of ADSs generally may be suspended, during any period when the transfer books of the Company, the Depositary, a Registrar or the Share Registrar are closed or if any such action is deemed necessary or advisable by the Depositary or the Company, in good faith, at any time or from time to time because of any requirement of law or regulation, any government or governmental body or commission or any securities exchange on which the ADSs or Shares are listed, or under any provision of the Deposit Agreement or this ADR, if applicable, or under any provision of, or governing, the Deposited Securities, or because of a meeting of shareholders of



the Company or for any other reason, subject, in all cases, to paragraph (25) of this ADR and Section 7.8 of the Deposit Agreement. Notwithstanding any provision of the Deposit Agreement or this ADR to the contrary, Holders are entitled to surrender outstanding ADSs to withdraw the Deposited Securities associated herewith at any time subject only to (i) temporary delays caused by closing the transfer books of the Depositary or the Company or the deposit of Shares in connection with voting at a shareholders' meeting or the payment of dividends, (ii) the payment of fees, taxes and similar charges, (iii) compliance with any U.S. or foreign laws or governmental regulations relating to the ADSs or to the withdrawal of the Deposited Securities, and (iv) other circumstances specifically contemplated by Instruction I.A.(I) of the General Instructions to Form F-6 (as such General Instructions may be amended from time to time).

(5) **Compliance with Information Requests.** Notwithstanding any other provision of the Deposit Agreement or this ADR, each Holder and Beneficial Owner of the ADSs represented hereby agrees to comply with requests from the Company pursuant to applicable law, the rules and requirements of The NASDAQ Global Market and any other stock exchange on which the Shares or ADSs are, or will be, registered, traded or listed or the Articles of Association of the Company, which are made to provide information, *inter alia*, as to the capacity in which such Holder or Beneficial Owner owns ADSs (and the Shares represented by such ADSs, as the case may be) and regarding the identity of any other person(s) interested in such ADSs (and the Shares represented by such ADSs, as the case may be) and the nature of such interest and various other matters, whether or not they are Holders and/or Beneficial Owners at the time of such request. The Depositary agrees to use its reasonable efforts to forward, upon the request of the Company and at the Company's expense, any such request from the Company to the Holders and to forward to the Company any such responses to such requests received by the Depositary.

(6) **Ownership Restrictions.** Notwithstanding any other provision of this ADR or of the Deposit Agreement or any ADR, the Company may restrict transfers of the Shares where such transfer might result in ownership of Shares exceeding limits imposed by applicable law or the Articles of Association of the Company. The Company may also restrict, in such manner as it deems appropriate, transfers of the ADSs where such transfer may result in the total number of Shares represented by the ADSs owned by a single Holder or Beneficial Owner to exceed any such limits. The Company may, in its sole discretion but subject to applicable law, instruct the Depositary to take action with respect to the ownership interest of any Holder or Beneficial Owner in excess of the limits set forth in the preceding sentence, including, but not limited to, the imposition of restrictions on the transfer of ADSs, the removal or limitation of voting rights or mandatory sale or disposition on behalf of a Holder or Beneficial Owner of the Shares represented by the ADSs held by such Holder or Beneficial Owner in excess of such limitations, if and to the extent such disposition is permitted by applicable law and the Articles of Association of the Company. Nothing herein or in the Deposit Agreement shall be interpreted as obligating the Depositary or the Company to ensure compliance with the ownership restrictions described herein or in Section 3.5 of the Deposit Agreement.

(7) **Reporting Obligations and Regulatory Approvals.** Applicable laws and regulations may require holders and beneficial owners of Shares, including the Holders and Beneficial Owners of ADSs, to satisfy reporting requirements and obtain regulatory approvals in certain circumstances. Holders and Beneficial Owners of ADSs are solely responsible for

determining and complying with such reporting requirements and obtaining such approvals. Each Holder and each Beneficial Owner hereby agrees to make such determination, file such reports, and obtain such approvals to the extent and in the form required by applicable laws and regulations as in effect from time to time. Neither the Depositary, the Custodian, the Company or any of their respective agents or affiliates shall be required to take any actions whatsoever on behalf of Holders or Beneficial Owners to determine or satisfy such reporting requirements or obtain such regulatory approvals under applicable laws and regulations.

(8) **Liability for Taxes and Other Charges.** Any tax or other governmental charge payable by the Custodian or by the Depositary with respect to any Deposited Property, ADSs or this ADR shall be payable by the Holders and Beneficial Owners to the Depositary. The Company, the Custodian and/or the Depositary may withhold or deduct from any distributions made in respect of Deposited Property, and may sell for the account of a Holder and/or Beneficial Owner any or all of the Deposited Property and apply such distributions and sale proceeds in payment of, any taxes (including applicable interest and penalties) or charges that are or may be payable by Holders or Beneficial Owners in respect of the ADSs, Deposited Property and this ADR, the Holder and the Beneficial Owner hereof remaining liable for any deficiency. The Custodian may refuse the deposit of Shares and the Depositary may refuse to issue ADSs, to deliver ADRs, register the transfer of ADSs, register the split-up or combination of ADRs and (subject to paragraph (25) of this ADR and Section 7.8 of the Deposit Agreement) the withdrawal of Deposited Property until payment in full of such tax, charge, penalty or interest is received. Every Holder and Beneficial Owner agrees to indemnify the Depositary, the Company, the Custodian, and any of their agents, officers, employees and Affiliates for, and to hold each of them harmless from, any claims with respect to taxes (including applicable interest and penalties thereon) arising from any tax benefit obtained for such Holder and/or Beneficial Owner. The obligations of Holders and Beneficial Owners under Section 3.2 of the Deposit Agreement shall survive any transfer of ADSs, any cancellation of ADSs and withdrawal of Deposited Securities, and the termination of the Deposit Agreement.

(9) **Representations and Warranties on Deposit of Shares.** Each person depositing Shares under the Deposit Agreement shall be deemed thereby to represent and warrant that (i) such Shares and the certificates therefor are duly authorized, validly allotted and issued, fully paid, not subject to any call for the payment of further capital and legally obtained by such person, (ii) all preemptive (and similar) rights, if any, with respect to such Shares have been validly waived, disappplied or exercised, (iii) the person making such deposit is duly authorized so to do, (iv) the Shares presented for deposit are free and clear of any lien, encumbrance, security interest, charge, mortgage or adverse claim, (v) the Shares presented for deposit are not, and the ADSs issuable upon such deposit will not be, Restricted Securities (except as contemplated in Section 2.14 of the Deposit Agreement), and (vi) the Shares presented for deposit have not been stripped of any rights or entitlements. Such representations and warranties shall survive the deposit and withdrawal of Shares, the issuance and cancellation of ADSs in respect thereof and the transfer of such ADSs. If any such representations or warranties are false in any way, the Company and the Depositary shall be authorized, at the cost and expense of the person depositing Shares, to take any and all actions necessary to correct the consequences thereof.

**(10) Proofs, Certificates and Other Information.** Any person presenting Shares for deposit, any Holder and any Beneficial Owner may be required, and every Holder and Beneficial Owner agrees, from time to time to provide to the Depositary and the Custodian such proof of citizenship or residence, taxpayer status, payment of all applicable taxes or other governmental charges, exchange control approval, legal or beneficial ownership of ADSs and Deposited Property, compliance with applicable laws, the terms of the Deposit Agreement or this ADR evidencing the ADSs and the provisions of, or governing, the Deposited Property, to execute such certifications and to make such representations and warranties, and to provide such other information and documentation (or, in the case of Shares in registered form presented for deposit, such information relating to the registration on the books of the Company or of the Share Registrar) as the Depositary or the Custodian may deem necessary or proper or as the Company may reasonably require by written request to the Depositary consistent with its obligations under the Deposit Agreement and this ADR. The Depositary and the Registrar, as applicable, may withhold the execution or delivery or registration of transfer of any ADR or ADS or the distribution or sale of any dividend or distribution of rights or of the proceeds thereof or, to the extent not limited by paragraph (25) and the terms of Section 7.8 of the Deposit Agreement, the delivery of any Deposited Property until such proof or other information is filed or such certifications are executed, or such representations and warranties are made, or such other documentation or information provided, in each case to the Depositary's, the Registrar's and the Company's satisfaction. The Depositary shall provide the Company, in a timely manner, with copies or originals if necessary and appropriate of (i) any such proofs of citizenship or residence, taxpayer status, or exchange control approval or copies of written representations and warranties which it receives from Holders and Beneficial Owners, and (ii) any other information or documents which the Company may reasonably request and which the Depositary shall request and receive from any Holder or Beneficial Owner or any person presenting Shares for deposit or ADSs for cancellation, transfer or withdrawal. Nothing herein shall obligate the Depositary to (i) obtain any information for the Company if not provided by the Holders or Beneficial Owners, or (ii) verify or vouch for the accuracy of the information so provided by the Holders or Beneficial Owners.

**(11) ADS Fees and Charges.** The following ADS fees are payable under the terms of the Deposit Agreement:

- (i) **ADS Issuance Fee:** by any person to whom the ADSs are issued (*e.g.*, an issuance of ADSs upon a deposit of Shares, upon a change in the ADS(s)-to-Share(s) ratio, or for any other reason), excluding ADS issuances as a result of distributions described in paragraph (iv) below, a fee not in excess of U.S. \$5.00 per 100 ADSs (or fraction thereof) issued under the terms of the Deposit Agreement;
- (ii) **ADS Cancellation Fee:** by any person whose ADSs are being cancelled (*e.g.*, a cancellation of ADSs for delivery of Deposited Shares, upon a change in the ADS(s)-to-Share(s) ratio, or for any other reason), a fee not in excess of U.S. \$5.00 per 100 ADSs (or fraction thereof) cancelled;

- (iii) Cash Distribution Fee: by any Holder of ADSs, a fee not in excess of U.S. \$5.00 per 100 ADSs (or fraction thereof) held for the distribution of cash dividends or other cash distributions (*e.g.*, upon sale of rights and other entitlements);
- (iv) Stock Distribution /Rights Exercise Fee: by any Holder of ADS(s), a fee not in excess of U.S. \$5.00 per 100 ADSs (or fraction thereof) held for
  - (a) the distribution of stock dividends or other free stock distributions or
  - (b) the exercise of rights to purchase additional ADSs;
- (v) Other Distribution Fee: by any Holder of ADS(s), a fee not in excess of U.S. \$5.00 per 100 ADSs (or fraction thereof) held for the distribution of securities other than ADSs or rights to purchase additional ADSs (*e.g.*, spin-off shares); and
- (vi) Depository Services Fee: by any Holder of ADS(s), a fee not in excess of U.S. \$5.00 per 100 ADSs (or fraction thereof) held on the applicable record date(s) established by the Depositary.

The Company, Holders, Beneficial Owners, persons receiving ADSs upon issuance, and persons whose ADSs are being cancelled shall be responsible for the following ADS charges under the terms of the Deposit Agreement:

- (a) taxes (including applicable interest and penalties) and other governmental charges;
- (b) such registration fees as may from time to time be in effect for the registration of Shares or other Deposited Securities on the share register and applicable to transfers of Shares or other Deposited Securities to or from the name of the Custodian, the Depositary or any nominees upon the making of deposits and withdrawals, respectively;
- (c) such cable, telex and facsimile transmission and delivery expenses as are expressly provided in the Deposit Agreement to be at the expense of the person depositing Shares or withdrawing Deposited Securities or of the Holders and Beneficial Owners of ADSs;
- (d) the expenses and charges incurred by the Depositary in the conversion of foreign currency;
- (e) such fees and expenses as are incurred by the Depositary in connection with compliance with exchange control regulations and other regulatory requirements applicable to Shares, Deposited Securities, ADSs and ADRs; and

- (f) the fees and expenses incurred by the Depositary, the Custodian, or any nominee in connection with the delivery or servicing of Deposited Property.

All ADS fees and charges so payable may be deducted from distributions or must be remitted to the Depositary, or its designee, may be waived by the Depositary in full or in part with respect to some or all ADSs upon such terms, and subject to such conditions, as the Depositary may determine and may, at any time and from time to time, be changed by agreement between the Depositary and the Company, but, in the case of ADS fees and charges payable by Holders and Beneficial Owners, only in the manner contemplated by paragraph (23) of this ADR and as contemplated in Section 6.1 of the Deposit Agreement. The Depositary shall provide, without charge, a copy of its latest ADS fee schedule to anyone upon request.

ADS fees and charges payable upon (i) the issuance of ADSs and (ii) the cancellation of ADSs will be payable by the person to whom the ADSs are so issued by the Depositary (in the case of ADS issuances) and by the person whose ADSs are being cancelled (in the case of ADS cancellations). In the case of ADSs issued by the Depositary into DTC or presented to the Depositary via DTC, the ADS issuance and cancellation fees and charges will be payable by the DTC Participant(s) receiving the ADSs from the Depositary 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(s) of the applicable Beneficial Owner(s) in accordance with the procedures and practices of the DTC participant(s) as in effect at the time. ADS fees and charges in respect of distributions and the ADS service fee are payable by Holders as of the applicable ADS Record Date established by the Depositary. 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, the applicable Holders as of the ADS Record Date established by the Depositary will be invoiced for the amount of the ADS fees and charges and such ADS fees may be deducted from distributions made to Holders. 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 from time to time and the DTC Participants in turn charge the amount of such ADS fees and charges to the Beneficial Owners for whom they hold ADSs.

The Depositary may reimburse the Company for certain expenses incurred by the Company in respect of the ADR program established pursuant to the Deposit Agreement, by making available a portion of the ADS fees charged in respect of the ADR program or otherwise, upon such terms and conditions as the Company and the Depositary agree from time to time. The Company shall pay to the Depositary such fees and charges, and reimburse the Depositary for such out-of-pocket expenses, as the Depositary and the Company may agree from time to time. Responsibility for payment of such fees, charges and reimbursements may from time to time be changed by agreement between the Company and the Depositary. Unless otherwise agreed, the Depositary shall present its statement for such fees, charges and reimbursements to the Company once every three months. The charges and expenses of the Custodian are for the sole account of the Depositary.



The obligations of Holders and Beneficial Owners to pay ADS fees and charges shall survive the termination of the Deposit Agreement. As to any Depositary, upon the resignation or removal of such Depositary as described in Section 5.4 of the Deposit Agreement, the right to collect ADS fees and charges shall extend for those ADS fees and charges incurred prior to the effectiveness of such resignation or removal.

(12) **Title to ADRs.** Subject to the limitations contained in the Deposit Agreement and in this ADR, it is a condition of this ADR, and every successive Holder of this ADR by accepting or holding the same consents and agrees, that title to this ADR (and to each Certificated ADS evidenced hereby) shall be transferable upon the same terms as a certificated security under the laws of the State of New York, provided that, in the case of Certificated ADSs, this ADR has been properly endorsed or is accompanied by proper instruments of transfer. Notwithstanding any notice to the contrary, the Depositary and the Company may deem and treat the Holder of this ADR (that is, the person in whose name this ADR is registered on the books of the Depositary) as the absolute owner thereof for all purposes. Neither the Depositary nor the Company shall have any obligation nor be subject to any liability under the Deposit Agreement or this ADR to any holder of this ADR or any Beneficial Owner unless, in the case of a holder of ADSs, such holder is the Holder of this ADR registered on the books of the Depositary or, in the case of a Beneficial Owner, such Beneficial Owner, or the Beneficial Owner's representative, is the Holder registered on the books of the Depositary.

(13) **Validity of ADR.** The Holder(s) of this ADR (and the ADSs represented hereby) shall not be entitled to any benefits under the Deposit Agreement or be valid or enforceable for any purpose against the Depositary or the Company unless this ADR has been (i) dated, (ii) signed by the manual or facsimile signature of a duly-authorized signatory of the Depositary, (iii) countersigned by the manual or facsimile signature of a duly-authorized signatory of the Registrar, and (iv) registered in the books maintained by the Registrar for the registration of issuances and transfers of ADRs. An ADR bearing the facsimile signature of a duly-authorized signatory of the Depositary or the Registrar, who at the time of signature was a duly authorized signatory of the Depositary or the Registrar, as the case may be, shall bind the Depositary, notwithstanding the fact that such signatory has ceased to be so authorized prior to the delivery of such ADR by the Depositary.

(14) **Available Information; Reports; Inspection of Transfer Books.** The Company is subject to the periodic reporting requirements of the Exchange Act and, accordingly, is required to file or furnish certain reports with the Commission. These reports can be retrieved from the Commission's website ([www.sec.gov](http://www.sec.gov)) and can be inspected and copied at the public reference facilities maintained by the Commission located (as of the date of the Deposit Agreement) at 100 F Street, N.E., Washington D.C. 20549.

The Depositary shall make available for inspection by Holders at its Principal Office any reports and communications, including any proxy soliciting materials, received from the Company which are both (a) received by the Depositary, the Custodian, or the nominee of either of them as the holder of the Deposited Property and (b) made generally available to the holders of such Deposited Property by the Company. The Depositary shall also provide or make available to Holders copies of such reports when furnished by the Company pursuant to Section 5.6 of the Deposit Agreement.

Until termination of the Deposit Agreement in accordance with its terms, the Registrar shall maintain in the Borough of Manhattan, the City of New York, an office and facilities for the issuance and delivery of ADSs, the acceptance for surrender of ADS(s) for the purpose of withdrawal of Deposited Securities, the registration of issuances, cancellations, transfers, combinations and split-ups of ADS(s) and, if applicable, to countersign ADRs evidencing the ADSs so issued, transferred, combined or split-up, in each case in accordance with the provisions of the Deposit Agreement.

The Registrar shall keep books for the registration of ADSs which at all reasonable times shall be open for inspection by the Company and by the Holders of such ADSs, provided that such inspection shall not be, to the Registrar's knowledge, for the purpose of communicating with Holders of such ADSs in the interest of a business or object other than the business of the Company or other than a matter related to the Deposit Agreement or the ADSs.

The Registrar may close the transfer books with respect to the ADSs, at any time or from time to time, when deemed necessary or advisable by it in good faith in connection with the performance of its duties hereunder, or at the reasonable written request of the Company subject, in all cases, to Section 7.8 of the Deposit Agreement.

Dated:

CITIBANK, N.A.  
Transfer Agent and Registrar

CITIBANK, N.A.  
as Depositary

By: \_\_\_\_\_  
Authorized Signatory

By: \_\_\_\_\_  
Authorized Signatory

The address of the Principal Office of the Depositary is 388 Greenwich Street, New York, New York 10013, U.S.A.

**[FORM OF REVERSE OF ADR]**  
**SUMMARY OF CERTAIN ADDITIONAL PROVISIONS**  
**OF THE DEPOSIT AGREEMENT**

**(15) Dividends and Distributions in Cash, Shares, etc. (a) *Cash Distributions:***

Whenever the Company intends to make a distribution of a cash dividend or other cash distribution in respect of any Deposited Securities, the Company shall give notice thereof to the Depositary at least twenty (20) days (or such other number of days as mutually agreed to in writing by the Depositary and the Company) prior to the proposed distribution specifying, *inter alia*, the record date applicable for determining the holders of Deposited Securities entitled to receive such distribution. Upon the timely receipt of such notice, the Depositary shall establish the ADS Record Date upon the terms described in Section 4.9 of the Deposit Agreement. Upon receipt of confirmation of the receipt of (x) any cash dividend or other cash distribution on any Deposited Securities, or (y) proceeds from the sale of any Deposited Property held in respect of the ADSs under the terms of the Deposit Agreement, the Depositary will (i) if at the time of receipt thereof any amounts received in a Foreign Currency can, in the judgment of the Depositary (pursuant to Section 4.8 of the Deposit Agreement), be converted on a practicable basis into Dollars transferable to the United States, promptly convert or cause to be converted such cash dividend, distribution or proceeds into Dollars (on the terms described in Section 4.8 of the Deposit Agreement), (ii) if applicable and unless previously established, establish the ADS Record Date upon the terms described in Section 4.9 of the Deposit Agreement, and (iii) distribute promptly the amount thus received (net of (a) the applicable fees and charges of, and expenses incurred by, the Depositary and (b) applicable taxes withheld) to the Holders entitled thereto as of the ADS Record Date in proportion to the number of ADSs held as of the ADS Record Date. The Depositary shall distribute only such amount, however, as can be distributed without attributing to any Holder a fraction of one cent, and any balance not so distributed shall be held by the Depositary (without liability for interest thereon) and shall be added to and become part of the next sum received by the Depositary for distribution to Holders of ADSs outstanding at the time of the next distribution. If the Company, the Custodian or the Depositary is required to withhold and does withhold from any cash dividend or other cash distribution in respect of any Deposited Securities, or from any cash proceeds from the sales of Deposited Property, an amount on account of taxes, duties or other governmental charges, the amount distributed to Holders on the ADSs shall be reduced accordingly. Such withheld amounts shall be forwarded by the Company, the Custodian or the Depositary to the relevant governmental authority. Evidence of payment thereof by the Company shall be forwarded by the Company to the Depositary upon request. 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. Notwithstanding anything contained in the Deposit Agreement to the contrary, in the event the Company fails to give the Depositary timely notice of the proposed distribution provided for in Section 4.1 of the Deposit Agreement, the Depositary agrees to use commercially reasonable efforts to perform the actions contemplated in Section 4.1 of the Deposit Agreement, and the Company, the Holders and the Beneficial Owners acknowledge that the Depositary shall have no liability for the Depositary's failure to perform



the actions contemplated in Section 4.1 of the Deposit Agreement where such notice has not been so timely given, other than its failure to use commercially reasonable efforts, as provided herein.

(b) **Share Distributions:** Whenever the Company intends to make a distribution that consists of a dividend in, or free distribution of, Shares, the Company shall give notice thereof to the Depositary at least twenty (20) days (or such other number of days as mutually agreed to in writing by the Depositary and the Company) prior to the proposed distribution, specifying, *inter alia*, the record date applicable to holders of Deposited Securities entitled to receive such distribution. Upon the timely receipt of such notice from the Company, the Depositary shall establish the ADS Record Date upon the terms described in Section 4.9 of the Deposit Agreement. Upon receipt of confirmation from the Custodian of the receipt of the Shares so distributed by the Company, the Depositary shall either (i) subject to Section 5.9 of the Deposit Agreement, distribute to the Holders as of the ADS Record Date in proportion to the number of ADSs held as of the ADS Record Date, additional ADSs, which represent in the aggregate the number of Shares received as such dividend, or free distribution, subject to the other terms of the Deposit Agreement (including, without limitation, (a) the applicable fees and charges of, and expenses incurred by, the Depositary and (b) applicable taxes), or (ii) if additional ADSs are not so distributed, take all actions necessary so that each ADS issued and outstanding after the ADS Record Date shall, to the extent permissible by law, thenceforth also represent rights and interests in the additional integral number of Shares distributed upon the Deposited Securities represented thereby (net of (a) the applicable fees and charges of, and expenses incurred by, the Depositary and (b) applicable taxes). In lieu of delivering fractional ADSs, the Depositary shall sell the number of Shares or ADSs, as the case may be, represented by the aggregate of such fractions and distribute the net proceeds upon the terms described in Section 4.1 of the Deposit Agreement. In the event that the Depositary determines that any distribution in property (including Shares) is subject to any tax or other governmental charges which the Depositary is obligated to withhold, or, if the Company in the fulfillment of its obligation under Section 5.7 of the Deposit Agreement, has furnished an opinion of U.S. counsel determining that Shares must be registered under the Securities Act or other laws in order to be distributed to Holders (and no such registration statement has been declared effective), the Depositary may dispose of all or a portion of such property (including Shares and rights to subscribe therefor) in such amounts and in such manner, including by public or private sale, as the Depositary deems necessary and practicable, and the Depositary shall distribute the net proceeds of any such sale (after deduction of (a) applicable taxes and (b) fees and charges of, and expenses incurred by, the Depositary) to Holders entitled thereto upon the terms described in Section 4.1 of the Deposit Agreement. The Depositary shall hold and/or distribute any unsold balance of such property in accordance with the provisions of the Deposit Agreement. Notwithstanding anything contained in the Deposit Agreement to the contrary, in the event the Company fails to give the Depositary timely notice of the proposed distribution provided for above, the Depositary agrees to use commercially reasonable efforts to perform the actions contemplated in Section 4.2 of the Deposit Agreement, and the Company, the Holders and the Beneficial Owners acknowledge that the Depositary shall have no liability for the Depositary's failure to perform the actions contemplated in Section 4.2 of the Deposit Agreement where such notice has not been so timely given, other than its failure to use commercially reasonable efforts, as provided herein.

(c) ***Elective Distributions in Cash or Shares:*** Whenever the Company intends to make a distribution payable at the election of the holders of Deposited Securities in cash or in additional Shares, the Company shall give notice thereof to the Depositary at least sixty (60) days (or such other number of days as mutually agreed to in writing by the Depositary and the Company) prior to the proposed distribution specifying, *inter alia*, the record date applicable to holders of Deposited Securities entitled to receive such elective distribution and whether or not it wishes such elective distribution to be made available to Holders of ADSs. Upon the timely receipt of a notice indicating that the Company wishes such elective distribution to be made available to Holders of ADSs, the Depositary shall consult with the Company to determine, and the Company shall assist the Depositary in its determination, whether it is lawful and reasonably practicable to make such elective distribution available to the Holders of ADSs. The Depositary shall make such elective distribution available to Holders only if (i) the Company shall have timely requested that the elective distribution be made available to Holders, (ii) the Depositary shall have determined that such distribution is reasonably practicable and (iii) the Depositary shall have received satisfactory documentation within the terms of Section 5.7 of the Deposit Agreement. If the above conditions are not satisfied or if the Company requests such elective distribution not to be made available to Holders of ADSs, the Depositary shall establish the ADS Record Date on the terms described in Section 4.9 of the Deposit Agreement and, to the extent permitted by law, distribute to the Holders, on the basis of the same determination as is made in England and Wales in respect of the Shares for which no election is made, either (X) cash upon the terms described in Section 4.1 of the Deposit Agreement or (Y) additional ADSs representing such additional Shares upon the terms described in Section 4.2 of the Deposit Agreement. If the above conditions are satisfied, the Depositary shall establish an ADS Record Date on the terms described in Section 4.9 of the Deposit Agreement and establish procedures to enable Holders to elect the receipt of the proposed distribution in cash or in additional ADSs. The Company shall assist the Depositary in establishing such procedures to the extent necessary. If a Holder elects to receive the proposed distribution (X) in cash, the distribution shall be made upon the terms described in Section 4.1 of the Deposit Agreement, or (Y) in ADSs, the distribution shall be made upon the terms described in Section 4.2 of the Deposit Agreement. Nothing herein shall obligate the Depositary to make available to Holders a method to receive the elective distribution in Shares (rather than ADSs). There can be no assurance that Holders generally, or any Holder in particular, will be given the opportunity to receive elective distributions on the same terms and conditions as the holders of Shares. Notwithstanding anything contained in the Deposit Agreement to the contrary, in the event the Company fails to give the Depositary timely notice of the proposed distribution provided for in Section 4.3 of the Deposit Agreement, the Depositary agrees to use commercially reasonable efforts to perform the actions contemplated in Section 4.3 of the Deposit Agreement, and the Company, the Holders and the Beneficial Owners acknowledge that the Depositary shall have no liability for the Depositary's failure to perform the actions contemplated in Section 4.3 of the Deposit Agreement where such notice has not been so timely given, other than its failure to use commercially reasonable efforts, as provided herein.

(d) ***Distribution of Rights to Purchase Additional ADSs:*** Whenever the Company intends to distribute to the holders of the Deposited Securities rights to subscribe for additional Shares, the Company shall give notice thereof to the Depositary at least sixty (60) days (or such other number of days as mutually agreed to in writing by the Depositary and the Company) prior to the proposed distribution specifying, *inter alia*, the record date applicable to holders of

Deposited Securities entitled to receive such distribution and whether or not it wishes such rights to be made available to Holders of ADSs. Upon the timely receipt of a notice indicating that the Company wishes such rights to be made available to Holders of ADSs, the Depositary shall consult with the Company to determine, and the Company shall assist the Depositary in its determination, whether it is lawful and reasonably practicable to make such rights available to the Holders. The Depositary shall make such rights available to Holders only if (i) the Company shall have timely requested that such rights be made available to Holders, (ii) the Depositary shall have received satisfactory documentation within the terms of Section 5.7 of the Deposit Agreement, and (iii) the Depositary shall have determined that such distribution of rights is reasonably practicable. In the event any of the conditions set forth above are not satisfied or if the Company requests that the rights not be made available to Holders of ADSs, the Depositary shall proceed with the sale of the rights as contemplated in Section 4.4(b) of the Deposit Agreement. In the event all conditions set forth above are satisfied, the Depositary shall establish the ADS Record Date (upon the terms described in Section 4.9 of the Deposit Agreement) and establish procedures to (x) distribute rights to purchase additional ADSs (by means of warrants or otherwise), (y) enable the Holders to exercise such rights (upon payment of the subscription price and of the applicable (a) fees and charges of, and expenses incurred by, the Depositary and (b) taxes), and (z) deliver ADSs upon the valid exercise of such rights. The Company shall assist the Depositary to the extent necessary in establishing such procedures. Nothing herein shall obligate the Depositary to make available to the Holders a method to exercise rights to subscribe for Shares (rather than ADSs).

If (i) the Company does not timely request the Depositary to make the rights available to Holders or requests that the rights not be made available to Holders, (ii) the Depositary fails to receive satisfactory documentation within the terms of Section 5.7 of the Deposit Agreement, or determines it is not reasonably practicable to make the rights available to Holders, or (iii) any rights made available are not exercised and appear to be about to lapse, the Depositary shall determine whether it is lawful and reasonably practicable to sell such rights, in a riskless principal capacity, at such place and upon such terms (including public or private sale) as it may deem practicable. The Company shall assist the Depositary to the extent necessary to determine such legality and practicability. The Depositary shall, upon such sale, convert and distribute proceeds of such sale (net of applicable (a) fees and charges of, and expenses incurred by, the Depositary and (b) taxes) upon the terms set forth in Section 4.1 of the Deposit Agreement.

If the Depositary is unable to make any rights available to Holders upon the terms described in Section 4.4(a) of the Deposit Agreement or to arrange for the sale of the rights upon the terms described in Section 4.4(b) of the Deposit Agreement, the Depositary shall allow such rights to lapse.

The Depositary shall not be liable for (i) any failure to accurately determine whether it may be lawful or practicable to make such rights available to Holders in general or any Holders in particular, (ii) any foreign exchange exposure or loss incurred in connection with such sale, or exercise, or (iii) the content of any materials forwarded to the Holders on behalf of the Company in connection with the rights distribution.

Notwithstanding anything to the contrary in Section 4.4 of the Deposit Agreement, if registration (under the Securities Act or any other applicable law) of the rights or the securities to

which any rights relate may be required in order for the Company to offer such rights or such securities to Holders and to sell the securities represented by such rights, the Depositary will not distribute such rights to the Holders (i) unless and until a registration statement under the Securities Act (or other applicable law) covering such offering is in effect or (ii) unless the Company furnishes the Depositary opinion(s) of counsel for the Company in the United States and counsel to the Company in any other applicable country in which rights would be distributed, in each case satisfactory to the Depositary, to the effect that the offering and sale of such securities to Holders and Beneficial Owners are exempt from, or do not require registration under, the provisions of the Securities Act or any other applicable laws.

In the event that the Company, the Depositary or the Custodian shall be required to withhold and does withhold from any distribution of Deposited Property (including rights) an amount on account of taxes or other governmental charges, the amount distributed to the Holders of ADSs shall be reduced accordingly. In the event that the Depositary determines that any distribution of Deposited Property (including Shares and rights to subscribe therefor) is subject to any tax or other governmental charges which the Depositary is obligated to withhold, the Depositary may dispose of all or a portion of such Deposited Property (including Shares and rights to subscribe therefor) in such amounts and in such manner, including by public or private sale, as the Depositary deems necessary and practicable to pay any such taxes or charges.

There can be no assurance that Holders generally, or any Holder in particular, will be given the opportunity to receive or exercise rights on the same terms and conditions as the holders of Shares or be able to exercise such rights. Nothing herein shall obligate the Company to file any registration statement in respect of any rights or Shares or other securities to be acquired upon the exercise of such rights.

(e) ***Distributions Other Than Cash, Shares or Rights to Purchase Shares:***

Whenever the Company intends to distribute to the holders of Deposited Securities property other than cash, Shares or rights to purchase additional Shares, the Company shall give timely notice thereof to the Depositary and shall indicate whether or not it wishes such distribution to be made to Holders of ADSs. Upon receipt of a notice indicating that the Company wishes such distribution to be made to Holders of ADSs, the Depositary shall consult with the Company, and the Company shall assist the Depositary, to determine whether such distribution to Holders is lawful and reasonably practicable. The Depositary shall not make such distribution unless (i) the Company shall have requested the Depositary to make such distribution to Holders, (ii) the Depositary shall have received satisfactory documentation within the terms of Section 5.7 of the Deposit Agreement, and (iii) the Depositary shall have determined that such distribution is reasonably practicable.

Upon receipt of satisfactory documentation and the request of the Company to distribute property to Holders of ADSs and after making the requisite determinations set forth in (a) above, the Depositary shall distribute the property so received to the Holders of record, as of the ADS Record Date, in proportion to the number of ADSs held by them respectively and in such manner as the Depositary may deem practicable for accomplishing such distribution (i) upon receipt of payment or net of the applicable fees and charges of, and expenses incurred by, the Depositary, and (ii) net of any applicable taxes withheld. The Depositary may dispose of all or a portion of



the property so distributed and deposited, in such amounts and in such manner (including public or private sale) as the Depositary may deem practicable or necessary to satisfy any taxes (including applicable interest and penalties) or other governmental charges applicable to the distribution.

If (i) the Company does not request the Depositary to make such distribution to Holders or requests the Depositary not to make such distribution to Holders, (ii) the Depositary does not receive satisfactory documentation within the terms of Section 5.7 of the Deposit Agreement, or (iii) the Depositary determines that all or a portion of such distribution is not reasonably practicable, the Depositary shall sell or cause such property to be sold in a public or private sale, at such place or places and upon such terms as it may deem practicable and shall (i) cause the proceeds of such sale, if any, to be converted into Dollars and (ii) distribute the proceeds of such conversion received by the Depositary (net of applicable (a) fees and charges of, and expenses incurred by, the Depositary and (b) taxes) to the Holders as of the ADS Record Date upon the terms of Section 4.1 of the Deposit Agreement. If the Depositary is unable to sell such property, the Depositary may dispose of such property for the account of the Holders in any way it deems reasonably practicable under the circumstances.

Neither the Depositary nor the Company shall be liable for (i) any failure to accurately determine whether it is lawful or practicable to make the property described in Section 4.5 of the Deposit Agreement available to Holders in general or any Holders in particular, nor (ii) any loss incurred in connection with the sale or disposal of such property.

**(16) Redemption.** If the Company intends to exercise any right of redemption in respect of any of the Deposited Securities, the Company shall give **notice** thereof to the Depositary at least sixty (60) days (or such other number of days as mutually agreed to in writing by the Depositary and the Company) prior to the intended date of redemption which notice shall set forth the particulars of the proposed redemption. Upon timely receipt of (i) such notice and (ii) satisfactory documentation given by the Company to the Depositary within the terms of Section 5.7 of the Deposit Agreement, and only if the Depositary shall have determined that such proposed redemption is practicable, the Depositary shall provide to each Holder a notice setting forth the intended exercise by the Company of the redemption rights and any other particulars set forth in the Company's notice to the Depositary. The Depositary shall instruct the Custodian to present to the Company the Deposited Securities in respect of which redemption rights are being exercised against payment of the applicable redemption price. Upon receipt of confirmation from the Custodian that the redemption has taken place and that funds representing the redemption price have been received, the Depositary shall convert, transfer, and distribute the proceeds (net of applicable (a) fees and charges of, and the expenses incurred by, the Depositary, and (b) taxes), retire ADSs and cancel ADRs, if applicable, upon delivery of such ADSs by Holders thereof and the terms set forth in Sections 4.1 and 6.2 of the Deposit Agreement. If less than all outstanding Deposited Securities are redeemed, the ADSs to be retired will be selected by lot or on a pro rata basis, as may be determined by the Depositary. The redemption price per ADS shall be the dollar equivalent of the per share amount received by the Depositary (adjusted to reflect the ADS(s)-to-Share(s) ratio) upon the redemption of the Deposited Securities represented by ADSs (subject to the terms of Section 4.8 of the Deposit Agreement and the applicable fees and charges of, and expenses incurred by, the Depositary, and applicable taxes) multiplied by the number of Deposited Securities represented by each ADS redeemed.

Notwithstanding anything contained in the Deposit Agreement to the contrary, in the event the Company fails to give the Depositary timely notice of the proposed redemption provided for in Section 4.7 of the Deposit Agreement, the Depositary agrees to use commercially reasonable efforts to perform the actions contemplated in Section 4.7 of the Deposit Agreement, and the Company, the Holders and the Beneficial Owners acknowledge that the Depositary shall have no liability for the Depositary's failure to perform the actions contemplated in Section 4.7 of the Deposit Agreement where such notice has not been so timely given, other than its failure to use commercially reasonable efforts, as provided herein.

(17) **Fixing of ADS Record Date.** Whenever the Depositary shall receive notice of the fixing of a record date by the Company for the determination of holders of Deposited Securities entitled to receive any distribution (whether in cash, Shares, rights, or other distribution), or whenever for any reason the Depositary causes a change in the number of Shares that are represented by each ADS, or whenever the Depositary shall receive notice of any meeting of, or solicitation of consents or proxies of, holders of Shares or other Deposited Securities, or whenever the Depositary shall find it necessary or convenient in connection with the giving of any notice, solicitation of any consent or any other matter, the Depositary shall fix the record date (the "ADS Record Date") for the determination of the Holders of ADS(s) who shall be entitled to receive such distribution, to give instructions for the exercise of voting rights at any such meeting, to give or withhold such consent, to receive such notice or solicitation or to otherwise take action, or to exercise the rights of Holders with respect to such changed number of Shares represented by each ADS. The Depositary shall make reasonable efforts to establish the ADS Record Date as closely as practicable to the applicable record date for the Deposited Securities (if any) set by the Company in England and Wales and shall not announce the establishment of any ADS Record Date prior to the relevant corporate action having been made public by the Company (if such corporate action affects the Deposited Securities). Subject to applicable law and the provisions of Section 4.1 through 4.8 of the Deposit Agreement and to the other terms and conditions of the Deposit Agreement, only the Holders of ADSs at the close of business in New York on such ADS Record Date shall be entitled to receive such distribution, to give such voting instructions, to receive such notice or solicitation, or otherwise take action.

(18) **Voting of Deposited Securities.** As soon as practicable after receipt of notice of any meeting at which the holders of Deposited Securities are entitled to vote, or of solicitation of consents or proxies from holders of Deposited Securities, the Depositary shall fix the ADS Record Date in respect of such meeting or solicitation of consent or proxy in accordance with Section 4.9 of the Deposit Agreement. The Depositary shall, if requested by the Company in writing in a timely manner (the Depositary having no obligation to take any further action if the request shall not have been received by the Depositary at least thirty (30) days prior to the date of such vote or meeting), at the Company's expense and provided no U.S. legal prohibitions exist, distribute to Holders as of the ADS Record Date: (a) such notice of meeting or solicitation of consent or proxy, (b) a statement that the Holders at the close of business on the ADS Record Date will be entitled, subject to any applicable law, the provisions of the Deposit Agreement, the Articles of Association of the Company and the provisions of or governing the Deposited Securities (which provisions, if any, shall be summarized in pertinent part by the Company), to instruct the Depositary as to the exercise of the voting rights, if any, pertaining to the Deposited Securities represented by such Holder's ADSs, and (c) a brief statement as to the manner in which such voting instructions may be given to the Depositary or in which voting instructions

may be deemed to have been given in accordance with this Section 4.10 if no instructions are received prior to the deadline set for such purposes to the Depositary to give a discretionary proxy to a person designated by the Company.

Notwithstanding anything contained in the Deposit Agreement or any ADR, with the Company's prior written consent, the Depositary may, to the extent not prohibited by law or regulations, or by the requirements of the stock exchange on which the ADSs are listed, in lieu of distribution of the materials provided to the Depositary in connection with any meeting of, or solicitation of consents or proxies from, holders of Deposited Securities, distribute to the Holders a notice that provides Holders with, or otherwise publicizes to Holders, instructions on how to retrieve such materials or receive such materials upon request (*e.g.*, by reference to a website containing the materials for retrieval or a contact for requesting copies of the materials).

The Depositary has been advised by the Company that under the Articles of Association of the Company as in effect on the date of the Deposit Agreement, voting at any meeting of shareholders of the Company is by show of hands unless (before or upon the declaration of the result of the show of hands) a poll is demanded. The Depositary will not join in demanding a poll, whether or not requested to do so by Holders of ADSs. Under the Articles of Association of the Company as in effect on the date of the Deposit Agreement, a poll may be demanded by (a) the chairman of the Company's board of directors, (b) not fewer than five shareholders present in person or by proxy and having the right to vote at the meeting, (c) any shareholder(s) present in person or by proxy and representing not less than 10% of the total voting rights of all the shareholders having the right to vote on the resolution (excluding any shares held in treasury), or (d) any shareholder(s) present in person or by proxy and holding shares in the Company conferring a right to vote on the resolution 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 (excluding any shares held in treasury).

Voting instructions may be given only in respect of a number of ADSs representing an integral number of Deposited Securities. Upon the timely receipt from a Holder of ADSs as of the ADS Record Date of voting instructions in the manner specified by the Depositary, the Depositary shall endeavor, insofar as practicable and permitted under applicable law, the provisions of the Deposit Agreement, Articles of Association of the Company and the provisions of the Deposited Securities, to vote, or cause the Custodian to vote, the Deposited Securities (in person or by proxy) represented by such Holder's ADSs as follows: (a) in the event voting takes place at a shareholders' meeting by a show of hands, the Depositary will instruct the Custodian to vote all Deposited Securities in accordance with the voting instructions received from a majority of Holders of ADSs who provided voting instructions, and (b) in the event voting takes place at a shareholders' meeting by poll, the Depositary will instruct the Custodian to vote the Deposited Securities in accordance with the voting instructions received from the Holders of ADSs. If voting is by poll and the Depositary does not receive voting instructions from a Holder as of the ADS Record Date on or before the date established by the Depositary for such purpose, such Holder shall be deemed, and the Depositary shall deem such Holder, to have instructed the Depositary to give a discretionary proxy to a person designated by the Company to vote the Deposited Securities; provided, however, that no such discretionary proxy shall be given by the Depositary with respect to any matter to be voted upon as to which the Company informs the

Depository that (a) the Company does not wish such proxy to be given, (b) substantial opposition exists, or (c) the rights of holders of Deposited Securities may be adversely affected.

Neither the Depository nor the Custodian shall under any circumstances exercise any discretion as to voting and neither the Depository nor the Custodian shall vote, attempt to exercise the right to vote, or in any way make use of, for purposes of establishing a quorum or otherwise, the Deposited Securities represented by ADSs, except pursuant to and in accordance with the voting instructions timely received from Holders or as otherwise contemplated in the Deposit Agreement. If the Depository timely receives voting instructions from a Holder which fail to specify the manner in which the Depository is to vote the Deposited Securities represented by such Holder's ADSs, the Depository will deem such Holder (unless otherwise specified in the notice distributed to Holders) to have instructed the Depository to vote in favor of the items set forth in such voting instructions. Deposited Securities represented by ADSs for which no timely voting instructions are received by the Depository from the Holder shall not be voted (except (a) in the case voting is by show of hands, in which case the Depository will instruct the Custodian to vote all Deposited Securities in accordance with the voting instructions received from a majority of Holders of ADSs who provided voting instructions, and (b) as contemplated in Section 4.10 of the Deposit Agreement). Notwithstanding anything else contained herein, the Depository shall, if so requested in writing by the Company, represent all Deposited Securities (whether or not voting instructions have been received in respect of such Deposited Securities from Holders as of the ADS Record Date) for the sole purpose of establishing quorum at a meeting of shareholders.

Notwithstanding anything else contained in the Deposit Agreement or any ADR, the Depository shall not have any obligation to take any action with respect to any meeting, or solicitation of consents or proxies, of holders of Deposited Securities if the taking of such action would violate U.S. laws. The Company agrees to take any and all actions reasonably necessary and as permitted by the laws of England and Wales to enable Holders and Beneficial Owners to exercise the voting rights accruing to the Deposited Securities and to deliver to the Depository an opinion of U.S. counsel addressing any actions requested to be taken if so requested by the Depository.

There can be no assurance that Holders generally or any Holder in particular will receive the notice described above with sufficient time to enable the Holder to return voting instructions to the Depository in a timely manner.

**(19) Changes Affecting Deposited Securities.** Upon any change in nominal or par value, split-up, cancellation, consolidation or any other reclassification of Deposited Securities, or upon any recapitalization, reorganization, merger, consolidation or sale of assets affecting the Company or to which it is a party, any property which shall be received by the Depository or the Custodian in exchange for, or in conversion of, or replacement of, or otherwise in respect of, such Deposited Securities shall, to the extent permitted by law, be treated as new Deposited Property under the Deposit Agreement, and the ADSs shall, subject to the provisions of the Deposit Agreement, any ADR(s) evidencing such ADSs and applicable law, represent the right to receive such additional or replacement Deposited Property. In giving effect to such change, split-up, cancellation, consolidation or other reclassification of Deposited Securities, recapitalization, reorganization, merger, consolidation or sale of assets, the Depository may, with



the Company's approval, and shall, if the Company shall so request, subject to the terms of the Deposit Agreement (including, without limitation, (a) the applicable fees and charges of, and expenses incurred by, the Depositary, and (b) applicable taxes) and receipt of an opinion of counsel to the Company satisfactory to the Depositary that such actions are not in violation of any applicable laws or regulations, (i) issue and deliver additional ADSs as in the case of a stock dividend on the Shares, (ii) amend the Deposit Agreement and the applicable ADRs, (iii) amend the applicable Registration Statement(s) on Form F-6 as filed with the Commission in respect of the ADSs, (iv) call for the surrender of outstanding ADRs to be exchanged for new ADRs, and (v) take such other actions as are appropriate to reflect the transaction with respect to the ADSs. The Company agrees to, jointly with the Depositary, amend the Registration Statement on Form F-6 as filed with the Commission to permit the issuance of such new form of ADRs. Notwithstanding the foregoing, in the event that any Deposited Property so received may not be lawfully distributed to some or all Holders, the Depositary may, with the Company's approval, and shall, if the Company requests, subject to receipt of an opinion of Company's counsel satisfactory to the Depositary that such action is not in violation of any applicable laws or regulations, sell such Deposited Property at public or private sale, at such place or places and upon such terms as it may deem proper and may allocate the net proceeds of such sales (net of applicable (a) fees and charges of, and expenses incurred by, the Depositary and (b) taxes) for the account of the Holders otherwise entitled to such Deposited Property upon an averaged or other practicable basis without regard to any distinctions among such Holders and distribute the net proceeds so allocated to the extent practicable as in the case of a distribution received in cash pursuant to Section 4.1 of the Deposit Agreement. The Depositary shall not be responsible for (i) any failure to determine that it may be lawful or practicable to make such Deposited Property available to Holders in general or to any Holder in particular, (ii) any foreign exchange exposure or loss incurred in connection with such sale, or (iii) any liability to the purchaser of such Deposited Property.

**(20) Exoneration.** Notwithstanding anything contained in the Deposit Agreement or any ADR, neither the Depositary nor the Company shall be obligated to do or perform any act which is inconsistent with the provisions of the Deposit Agreement or incur any liability (i) if the Depositary or the Company shall be prevented or forbidden from, or delayed in, doing or performing any act or thing required by the terms of the Deposit Agreement, by reason of any provision of any present or future law or regulation of the United States, England and Wales or any other country, or of any other governmental authority or regulatory authority or stock exchange, or on account of potential criminal or civil penalties or restraint, or by reason of any provision, present or future, of the Articles of Association of the Company or any provision of or governing any Deposited Securities, or by reason of any act of God or war or other circumstances beyond its control (including, without limitation, nationalization, expropriation, currency restrictions, work stoppage, strikes, civil unrest, acts of terrorism, revolutions, rebellions, explosions and computer failure), (ii) by reason of any exercise of, or failure to exercise, any discretion provided for in the Deposit Agreement or in the Articles of Association of the Company or provisions of or governing Deposited Securities, (iii) for any action or inaction in reliance upon the advice of or information from legal counsel, accountants, any person presenting Shares for deposit, any Holder, any Beneficial Owner or authorized representative thereof, or any other person believed by it in good faith to be competent to give such advice or information, (iv) for the inability by a Holder or Beneficial Owner to benefit from any distribution, offering, right or other benefit which is made available to holders of Deposited

Securities but is not, under the terms of the Deposit Agreement, made available to Holders of ADSs, or (v) for any consequential or punitive damages (including lost profits) for any breach of the terms of the Deposit Agreement.

The Depositary, its controlling persons, its agents, any Custodian and the Company, its controlling persons and its agents may rely and shall be protected in acting upon any written notice, request or other document believed by it to be genuine and to have been signed or presented by the proper party or parties.

No disclaimer of liability under the Securities Act is intended by any provision of the Deposit Agreement.

**(21) Standard of Care.** The Company and the Depositary assume no obligation and shall not be subject to any liability under the Deposit Agreement or any ADRs to any Holder(s) or Beneficial Owner(s), except that the Company and the Depositary agree to perform their respective obligations specifically set forth in the Deposit Agreement or the applicable ADRs without negligence or bad faith.

Without limitation of the foregoing, neither the Depositary, nor the Company, nor any of their respective controlling persons, or agents, shall be under any obligation to appear in, prosecute or defend any action, suit or other proceeding in respect of any Deposited Property or in respect of the ADSs, which in its opinion may involve it in expense or liability, unless indemnity satisfactory to it against all expense (including fees and disbursements of counsel) and liability be furnished as often as may be required (and no Custodian shall be under any obligation whatsoever with respect to such proceedings, the responsibility of the Custodian being solely to the Depositary).

The Depositary and its agents shall not be liable for any failure to carry out any instructions to vote any of the Deposited Securities, or for the manner in which any vote is cast or the effect of any vote, provided that any such action or omission is in good faith and without negligence and in accordance with the terms of the Deposit Agreement. The Depositary shall not incur any liability for any failure to accurately determine that any distribution or action may be lawful or reasonably practicable, for the content of any information submitted to it by the Company for distribution to the Holders or for any inaccuracy of any translation thereof, for any investment risk associated with acquiring an interest in the Deposited Property, for the validity or worth of the Deposited Property or for any tax consequences that may result from the ownership of ADSs, Shares or other Deposited Property, for the credit-worthiness of any third party, for allowing any rights to lapse upon the terms of the Deposit Agreement, for the failure or timeliness of any notice from the Company, or for any action of or failure to act by, or any information provided or not provided by, DTC or any DTC Participant.

The Depositary shall not be liable for any acts or omissions made by a successor depositary whether in connection with a previous act or omission of the Depositary or in connection with any matter arising wholly after the removal or resignation of the Depositary, provided that in connection with the issue out of which such potential liability arises the

Depository performed its obligations without negligence or bad faith while it acted as Depository.

The Depository shall not be liable for any acts or omissions made by a predecessor depository whether in connection with an act or omission of the Depository or in connection with any matter arising wholly prior to the appointment of the Depository or after the removal or resignation of the Depository, provided that in connection with the issue out of which such potential liability arises the Depository performed its obligations without negligence or bad faith while it acted as Depository.

**(22) Resignation and Removal of the Depository; Appointment of Successor Depository.** The Depository may at any time resign as Depository hereunder by written notice of resignation delivered to the Company, such resignation to be effective on the earlier of (i) the 90th day after delivery thereof to the Company (whereupon the Depository shall be entitled to take the actions contemplated in Section 6.2 of the Deposit Agreement), or (ii) the appointment by the Company of a successor depository and its acceptance of such appointment as hereinafter provided.

The Depository may at any time be removed by the Company by written notice of such removal, which removal shall be effective on the later of (i) the 90th day after delivery thereof to the Depository (whereupon the Depository shall be entitled to take the actions contemplated in Section 6.2 of the Deposit Agreement), or (ii) upon the appointment by the Company of a successor depository and its acceptance of such appointment as hereinafter provided.

In case at any time the Depository acting hereunder shall resign or be removed, the Company shall use its best efforts to appoint a successor depository, which shall be a bank or trust company having an office in the Borough of Manhattan, the City of New York. Every successor depository shall be required by the Company to execute and deliver to its predecessor and to the Company an instrument in writing accepting its appointment hereunder, and thereupon such successor depository, without any further act or deed (except as required by applicable law), shall become fully vested with all the rights, powers, duties and obligations of its predecessor (other than as contemplated in Sections 5.8 and 5.9 of the Deposit Agreement). The predecessor depository, upon payment of all sums due it and on the written request of the Company, shall, (i) execute and deliver an instrument transferring to such successor all rights and powers of such predecessor hereunder (other than as contemplated in Sections 5.8 and 5.9 of the Deposit Agreement), (ii) duly assign, transfer and deliver all of the Depository's right, title and interest to the Deposited Property to such successor, and (iii) deliver to such successor a list of the Holders of all outstanding ADSs and such other information relating to ADSs and Holders thereof as the successor may reasonably request. Any such successor depository shall promptly provide notice of its appointment to such Holders.

Any entity into or with which the Depository may be merged or consolidated shall be the successor of the Depository without the execution or filing of any document or any further act.

(23) **Amendment/Supplement.** Subject to the terms and conditions of Section 6.1 of the Deposit Agreement and applicable law, the ADRs outstanding at any time, the provisions of the Deposit Agreement and the form of ADR attached hereto and to be issued under the terms hereof may at any time and from time to time be amended or supplemented by written agreement between the Company and the Depositary in any respect which they may deem necessary or desirable without the prior written consent of the Holders or Beneficial Owners. Any amendment or supplement which shall impose or increase any fees or charges (other than charges in connection with foreign exchange control regulations, and taxes and other governmental charges, delivery and other such expenses), or which shall otherwise materially prejudice any substantial existing right of Holders or Beneficial Owners, shall not, however, become effective as to outstanding ADSs until the expiration of thirty (30) days after notice of such amendment or supplement shall have been given to the Holders of outstanding ADSs. Notice of any amendment to the Deposit Agreement or any ADR shall not need to describe in detail the specific amendments effectuated thereby, and failure to describe the specific amendments in any such notice shall not render such notice invalid, provided, however, that, in each such case, the notice given to the Holders identifies a means for Holders and Beneficial Owners to retrieve or receive the text of such amendment (*e.g.*, upon retrieval from the Commission's, the Depositary's or the Company's website or upon request from the Depositary). The parties hereto agree that any amendments or supplements which (i) are reasonably necessary (as agreed by the Company and the Depositary) in order for (a) the ADSs to be registered on Form F-6 under the Securities Act or (b) the ADSs to be settled solely in electronic book-entry form and (ii) do not in either such case impose or increase any fees or charges to be borne by Holders, shall be deemed not to materially prejudice any substantial rights of Holders or Beneficial Owners. Every Holder and Beneficial Owner at the time any amendment or supplement so becomes effective shall be deemed, by continuing to hold such ADSs, to consent and agree to such amendment or supplement and to be bound by the Deposit Agreement and the ADR, if applicable, as amended or supplemented thereby. In no event shall any amendment or supplement impair the right of the Holder to surrender such ADS and receive therefor the Deposited Securities represented thereby, except in order to comply with mandatory provisions of applicable law. Notwithstanding the foregoing, if any governmental body should adopt new laws, rules or regulations which would require an amendment of, or supplement to, the Deposit Agreement to ensure compliance therewith, the Company and the Depositary may amend or supplement the Deposit Agreement and any ADRs at any time in accordance with such changed laws, rules or regulations. Such amendment or supplement to the Deposit Agreement and any ADRs in such circumstances may become effective before a notice of such amendment or supplement is given to Holders or within any other period of time as required for compliance with such laws, rules or regulations.

(24) **Termination.** The Depositary shall, at any time at the written direction of the Company, terminate the Deposit Agreement by distributing notice of such termination to the Holders of all ADSs then outstanding at least thirty (30) days prior to the date fixed in such notice for such termination. If ninety (90) days shall have expired after (i) the Depositary shall have delivered to the Company a written notice of its election to resign, or (ii) the Company shall have delivered to the Depositary a written notice of the removal of the Depositary, and, in either case, a successor depositary shall not have been appointed and accepted its appointment as provided in Section 5.4 of the Deposit Agreement of the Deposit Agreement, the Depositary may terminate the Deposit Agreement by distributing notice of such termination to the Holders of all

ADSs then outstanding at least thirty (30) days prior to the date fixed in such notice for such termination. The date so fixed for termination of the Deposit Agreement in any termination notice so distributed by the Depositary to the Holders of ADSs is referred to as the “Termination Date”. Until the Termination Date, the Depositary shall continue to perform all of its obligations under the Deposit Agreement, and the Holders and Beneficial Owners will be entitled to all of their rights under the Deposit Agreement.

If any ADSs shall remain outstanding after the Termination Date, the Registrar and the Depositary shall not, after the Termination Date, have any obligation to perform any further acts under the Deposit Agreement, except that the Depositary shall, subject, in each case, to the terms and conditions of the Deposit Agreement, continue to (i) collect dividends and other distributions pertaining to Deposited Securities, (ii) sell Deposited Property received in respect of Deposited Securities, (iii) deliver Deposited Securities, together with any dividends or other distributions received with respect thereto and the net proceeds of the sale of any other Deposited Property, in exchange for ADSs surrendered to the Depositary (after deducting, or charging, as the case may be, in each case, the fees and charges of, and expenses incurred by, the Depositary, and all applicable taxes or governmental charges for the account of the Holders and Beneficial Owners, in each case upon the terms set forth in Section 5.9 of the Deposit Agreement), and (iv) take such actions as may be required under applicable law in connection with its role as Depositary under the Deposit Agreement.

At any time after the Termination Date, the Depositary may sell the Deposited Property then held under the Deposit Agreement and shall after such sale hold un-invested the net proceeds of such sale, together with any other cash then held by it under the Deposit Agreement, in an un-segregated account and without liability for interest, for the pro rata benefit of the Holders whose ADSs have not theretofore been surrendered. After making such sale, the Depositary shall be discharged from all obligations under the Deposit Agreement except (i) to account for such net proceeds and other cash (after deducting, or charging, as the case may be, in each case, the fees and charges of, and expenses incurred by, the Depositary, and all applicable taxes or governmental charges for the account of the Holders and Beneficial Owners, in each case upon the terms set forth in Section 5.9 of the Deposit Agreement), and (ii) as may be required at law in connection with the termination of the Deposit Agreement. After the Termination Date, the Company shall be discharged from all obligations under the Deposit Agreement, except for its obligations to the Depositary under Sections 5.8, 5.9 and 7.6 of the Deposit Agreement. The obligations under the terms of the Deposit Agreement of Holders and Beneficial Owners of ADSs outstanding as of the Termination Date shall survive the Termination Date and shall be discharged only when the applicable ADSs are presented by their Holders to the Depositary for cancellation under the terms of the Deposit Agreement (except as specifically provided in the Deposit Agreement).

**(25) Compliance with U.S. Securities Laws.** Notwithstanding anything in the Deposit Agreement to the contrary, the withdrawal or delivery of Deposited Securities will not be suspended by the Company or the Depositary except as would be permitted by Instruction I.A.(1) of the General Instructions to Form F-6 Registration Statement, as amended from time to time, under the Securities Act.



(26) **Pre-Release Transactions.** Subject to the further terms and provisions of Section 5.10 of the Deposit Agreement, the Depositary, its Affiliates and their agents, on their own behalf, may own and deal in any class of securities of the Company and its Affiliates and in ADSs. In its capacity as Depositary, the Depositary shall not lend Shares or ADSs; provided, however, that the Depositary may (i) issue ADSs prior to the receipt of Shares pursuant to Section 2.3 of the Deposit Agreement and (ii) deliver Shares prior to the receipt of ADSs for withdrawal of Deposited Securities pursuant to Section 2.7 of the Deposit Agreement, including ADSs which were issued under (i) above but for which Shares may not have been received (each such transaction a “Pre-Release Transaction”). The Depositary may receive ADSs in lieu of Shares under (i) above and receive Shares in lieu of ADSs under (ii) above. Each such Pre-Release Transaction will be (a) subject to a written agreement whereby the person or entity (the “Applicant”) to whom ADSs or Shares are to be delivered (w) represents that at the time of the Pre-Release Transaction the Applicant or its customer owns the Shares or ADSs that are to be delivered by the Applicant under such Pre-Release Transaction, (x) agrees to indicate the Depositary as owner of such Shares or ADSs in its records and to hold such Shares or ADSs in trust for the Depositary until such Shares or ADSs are delivered to the Depositary or the Custodian, (y) unconditionally guarantees to deliver to the Depositary or the Custodian, as applicable, such Shares or ADSs, and (z) agrees to any additional restrictions or requirements that the Depositary deems appropriate, (b) at all times fully collateralized with cash, U.S. government securities or such other collateral as the Depositary deems appropriate, (c) terminable by the Depositary on not more than five (5) business days’ notice and (d) subject to such further indemnities and credit regulations as the Depositary deems appropriate. The Depositary will normally limit the number of ADSs and Shares involved in such Pre-Release Transactions at any one time to thirty percent (30%) of the ADSs outstanding (without giving effect to ADSs outstanding under (i) above), provided, however, that the Depositary reserves the right to change or disregard such limit from time to time as it deems appropriate.

The Depositary may also set limits with respect to the number of ADSs and Shares involved in Pre-Release Transactions with any one person on a case-by-case basis as it deems appropriate. The Depositary may retain for its own account any compensation received by it in conjunction with the foregoing. Collateral provided pursuant to (b) above, but not the earnings thereon, shall be held for the benefit of the Holders (other than the Applicant).

(27) **Governing Law and Jurisdiction.** The Deposit Agreement and the ADRs shall be interpreted in accordance with, and all rights hereunder and thereunder and provisions hereof and thereof shall be governed by, the laws of the State of New York applicable to contracts made and to be wholly performed in that State. Notwithstanding anything contained in the Deposit Agreement, any ADR or any present or future provisions of the laws of the State of New York, the rights of holders of Shares and of any other Deposited Securities and the obligations and duties of the Company in respect of the holders of Shares and other Deposited Securities, as such, shall be governed by the laws of England and Wales (or, if applicable, such other laws as may govern the Deposited Securities).

**EACH OF THE PARTIES TO THE DEPOSIT AGREEMENT (INCLUDING, WITHOUT LIMITATION, EACH HOLDER AND BENEFICIAL OWNER) IRREVOCABLY WAIVES, TO THE FULLEST EXTENT PERMITTED BY**

**APPLICABLE LAW, ANY AND ALL RIGHT TO TRIAL BY JURY IN ANY LEGAL PROCEEDING AGAINST THE COMPANY AND/OR THE DEPOSITARY ARISING OUT OF, OR RELATING TO, THE DEPOSIT AGREEMENT, ANY ADR AND ANY TRANSACTIONS CONTEMPLATED THEREIN (WHETHER BASED ON CONTRACT, TORT, COMMON LAW OR OTHERWISE).**

**(ASSIGNMENT AND TRANSFER SIGNATURE LINES)**

FOR VALUE RECEIVED, the undersigned Holder hereby sell(s), assign(s) and transfer(s) unto \_\_\_\_\_ whose taxpayer identification number is \_\_\_\_\_ and whose address including postal zip code is \_\_\_\_\_, the within ADR and all rights thereunder, hereby irrevocably constituting and appointing \_\_\_\_\_ attorney-in-fact to transfer said ADR on the books of the Depositary with full power of substitution in the premises.

Dated: \_\_\_\_\_

Name: \_\_\_\_\_

By: \_\_\_\_\_

Title: \_\_\_\_\_

NOTICE: The signature of the Holder to this assignment must correspond with the name as written upon the face of the within instrument in every particular, without alteration or enlargement or any change whatsoever.

If the endorsement be executed by an attorney, executor, administrator, trustee or guardian, the person executing the endorsement must give his/her full title in such capacity and proper evidence of authority to act in such capacity, if not on file with the Depositary, must be forwarded with this ADR.

\_\_\_\_\_  
SIGNATURE GUARANTEED

All endorsements or assignments of ADRs must be guaranteed by a member of a Medallion Signature Program approved by the Securities Transfer Association, Inc.

**Legends**

[The ADRs issued in respect of Partial Entitlement American Depositary Shares shall bear the following legend on the face of the ADR: "This ADR evidences ADSs representing 'partial entitlement' Shares of [Company] and as such do not entitle the holders thereof to the same per-share entitlement as other Shares (which are 'full entitlement' Shares) issued and outstanding at such time. The ADSs represented by this ADR shall entitle holders to distributions and entitlements identical to other ADSs when the Shares represented by such ADSs become 'full entitlement' Shares."]



**EXHIBIT B**  
**FEE SCHEDULE**

**ADS FEES AND RELATED CHARGES**

All capitalized terms used but not otherwise defined herein shall have the meaning given to such terms in the Deposit Agreement.

**I. ADS Fees**

The following ADS fees are payable under the terms of the Deposit Agreement:

<b>Service</b>	<b>Rate</b>	<b>By Whom Paid</b>
(1) Issuance of ADSs ( <i>e.g.</i> , an issuance upon a deposit of Shares, upon a change in the ADS(s)-to-Share(s) ratio, or for any other reason), excluding issuances as a result of distributions described in paragraph (4) below.	Up to U.S. \$5.00 per 100 ADSs (or fraction thereof) issued.	Person receiving ADSs.
(2) Cancellation of ADSs ( <i>e.g.</i> , a cancellation of ADSs for delivery of deposited Shares, upon a change in the ADS(s)-to-Share(s) ratio, or for any other reason).	Up to U.S. \$5.00 per 100 ADSs (or fraction thereof) cancelled.	Person whose ADSs are being cancelled.
(3) Distribution of cash dividends or other cash distributions ( <i>e.g.</i> , upon a sale of rights and other entitlements).	Up to U.S. \$5.00 per 100 ADSs (or fraction thereof) held.	Person to whom the distribution is made.
(4) Distribution of ADSs pursuant to (i) stock dividends or other free stock distributions, or (ii) an exercise of rights to purchase additional ADSs.	Up to U.S. \$5.00 per 100 ADSs (or fraction thereof) held.	Person to whom the distribution is made.
(5) Distribution of securities other than ADSs or rights to purchase additional ADSs ( <i>e.g.</i> , spin-off shares).	Up to U.S. \$5.00 per 100 ADSs (or fraction thereof) held.	Person to whom the distribution is made.

6) ADS Services.	Up to U.S. \$5.00 per 100 ADSs (or fraction thereof) held on the applicable record date(s) established by the Depositary.	Person holding ADSs on the applicable record date(s) established by the Depositary.
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## **II. Charges**

The Company, Holders, Beneficial Owners, persons receiving ADSs upon issuance and persons whose ADSs are being cancelled shall be responsible for the following ADS charges under the terms of the Deposit Agreement:

- (i) taxes (including applicable interest and penalties) and other governmental charges;
- (ii) such registration fees as may from time to time be in effect for the registration of Shares or other Deposited Securities on the share register and applicable to transfers of Shares or other Deposited Securities to or from the name of the Custodian, the Depositary or any nominees upon the making of deposits and withdrawals, respectively;
- (iii) such cable, telex and facsimile transmission and delivery expenses as are expressly provided in the Deposit Agreement to be at the expense of the person depositing Shares or withdrawing Deposited Securities or of the Holders and Beneficial Owners of ADSs;
- (iv) the expenses and charges incurred by the Depositary in the conversion of foreign currency;
- (v) such fees and expenses as are incurred by the Depositary in connection with compliance with exchange control regulations and other regulatory requirements applicable to Shares, Deposited Securities, ADSs and ADRs; and
- (vi) the fees and expenses incurred by the Depositary, the Custodian, or any nominee in connection with the servicing or delivery of Deposited Property.



**VERONA PHARMA PLC  
2017 INCENTIVE AWARD PLAN**

**ARTICLE I.  
PURPOSE**

The Plan's purpose is to enhance the Company's ability to attract, retain and motivate persons who make (or are expected to make) important contributions to the Company by providing these individuals with equity ownership opportunities. Capitalized terms used in the Plan are defined in Article XI.

**ARTICLE II.  
ELIGIBILITY**

Service Providers are eligible to be granted Awards under the Plan, subject to the limitations described herein.

**ARTICLE III.  
ADMINISTRATION AND DELEGATION**

3.1 Administration. The Plan is administered by the Administrator. The Administrator has authority to determine which Service Providers receive Awards, grant Awards, set Award terms and conditions, and designate whether such Awards will cover Ordinary Shares or ADSs, subject to the conditions and limitations in the Plan. The Administrator also has the authority to take all actions and make all determinations under the Plan, to interpret the Plan and Award Agreements and to adopt, amend and repeal Plan administrative rules, guidelines and practices as it deems advisable. The Administrator may correct defects and ambiguities, supply omissions and reconcile inconsistencies in the Plan or any Award as it deems necessary or appropriate to administer the Plan and any Awards. The Administrator's determinations under the Plan are in its sole discretion and will be final and binding on all persons having or claiming any interest in the Plan or any Award.

3.2 Appointment of Committees. To the extent Applicable Laws permit, the Board may delegate any or all of its powers under the Plan to one or more Committees or officers of the Company or any of its Subsidiaries. The Board may abolish any Committee or re-vest in itself any previously delegated authority at any time.

**ARTICLE IV.  
SHARES AVAILABLE FOR AWARDS**

4.1 Number of Shares. Subject to adjustment under Article VIII and the terms of this Article IV, Awards may be made under the Plan covering up to the Overall Share Limit. As of the Plan's effective date under Section 10.3, the Company will cease granting awards under the Prior Plans; however, Prior Plan Awards will remain subject to the terms of the applicable Prior Plan. Shares issued under the Plan may consist of authorized but unissued Shares, Shares purchased on the open market, treasury Shares or ADSs.

4.2 Share Recycling. If all or any part of an Award or Prior Plan Award expires, lapses or is terminated, exchanged for cash, surrendered, repurchased, canceled without having been fully exercised or forfeited, in any case, in a manner that results in the Company acquiring Shares covered by the Award or Prior Plan Award at a price not greater than the price (as adjusted to reflect any Equity Restructuring)

paid by the Participant for such Shares or not issuing any Shares covered by the Award or Prior Plan Award, the unused Shares covered by the Award or Prior Plan Award will, as applicable, become or again be available for Award grants under the Plan. Further, Shares delivered (either by actual delivery or attestation) to the Company by a Participant to satisfy the applicable exercise or purchase price of an Award or Prior Plan Award and/or to satisfy any applicable tax withholding obligation (including Shares retained by the Company from the Award or Prior Plan Award being exercised or purchased and/or creating the tax obligation) will, as applicable, become or again be available for Award grants under the Plan. The payment of Dividend Equivalents in cash in conjunction with any outstanding Awards or Prior Plan Awards shall not count against the Overall Share Limit.

4.3 Incentive Option Limitations. Notwithstanding anything to the contrary herein, no more than 5,000,000 Shares may be issued pursuant to the exercise of Incentive Options.

4.4 Substitute Awards. In connection with an entity's merger or consolidation with the Company or the Company's acquisition of an entity's property or stock, the Administrator may grant Awards in substitution for any options or other equity or equity-based awards granted before such merger or consolidation by such entity or its affiliate. Substitute Awards may be granted on such terms as the Administrator deems appropriate, notwithstanding limitations on Awards in the Plan. Substitute Awards will not count against the Overall Share Limit (nor shall Shares subject to a Substitute Award be added to the Shares available for Awards under the Plan as provided above), except that Shares acquired by exercise of substitute Incentive Options will count against the maximum number of Shares that may be issued pursuant to the exercise of Incentive Options under the Plan. Additionally, in the event that a company acquired by the Company or any Subsidiary or with which the Company or any Subsidiary combines has shares available under a pre-existing plan approved by shareholders and not adopted in contemplation of such acquisition or combination, the shares available for grant pursuant to the terms of such pre-existing plan (as adjusted, to the extent appropriate, using the exchange ratio or other adjustment or valuation ratio or formula used in such acquisition or combination to determine the consideration payable to the holders of common stock of the entities party to such acquisition or combination) may be used for Awards under the Plan and shall not reduce the Shares authorized for grant under the Plan (and Shares subject to such Awards shall not be added to the Shares available for Awards under the Plan as provided above); provided that Awards using such available shares shall not be made after the date awards or grants could have been made under the terms of the pre-existing plan, absent the acquisition or combination, and shall only be made to individuals who were not Employees or Directors prior to such acquisition or combination.

## **ARTICLE V. OPTIONS AND SHARE APPRECIATION RIGHTS**

5.1 General. The Administrator may grant Options or Share Appreciation Rights to Service Providers subject to the limitations in the Plan, including any limitations in the Plan that apply to Incentive Options. The Administrator will determine the number of Shares covered by each Option and Share Appreciation Right, the exercise price of each Option and Share Appreciation Right and the conditions and limitations applicable to the exercise of each Option and Share Appreciation Right. A Share Appreciation Right will entitle the Participant (or other person entitled to exercise the Share Appreciation Right) to receive from the Company upon exercise of the exercisable portion of the Share Appreciation Right an amount determined by multiplying the excess, if any, of the Fair Market Value of one Share on the date of exercise over the exercise price per Share of the Share Appreciation Right by the number of Shares with respect to which the Share Appreciation Right is exercised, subject to any limitations of the Plan or that the Administrator may impose and payable in cash, Shares valued at Fair Market Value or a combination of the two as the Administrator may determine or provide in the Award Agreement.

5.2 Exercise Price. The Administrator will establish each Option's and Share Appreciation Right's exercise price and specify the exercise price in the Award Agreement. The exercise price will not be less than 100% of the Fair Market Value on the grant date of the Option or Share Appreciation Right.

5.3 Duration. Each Option or Share Appreciation Right will be exercisable at such times and as specified in the Award Agreement, provided that the term of an Option or Share Appreciation Right will not exceed ten years. Notwithstanding the foregoing and unless determined otherwise by the Company, in the event that on the last business day of the term of an Option or Share Appreciation Right (other than an Incentive Option) (i) the exercise of the Option or Share Appreciation Right is prohibited by Applicable Law, as determined by the Company, or (ii) Shares may not be purchased or sold by the applicable Participant due to any Company insider trading policy (including blackout periods) or a "lock-up" agreement undertaken in connection with an issuance of securities by the Company, the term of the Option or Share Appreciation Right shall be extended until the date that is thirty (30) days after the end of the legal prohibition, black-out period or lock-up agreement, as determined by the Company; provided, however, in no event shall the extension last beyond the ten year term of the applicable Option or Share Appreciation Right. Notwithstanding the foregoing, if the Participant, prior to the end of the term of an Option or Share Appreciation Right, violates the non-competition, non-solicitation, confidentiality or other similar restrictive covenant provisions of any employment contract, confidentiality and nondisclosure agreement or other agreement between the Participant and the Company or any of its Subsidiaries, the right of the Participant and the Participant's transferees to exercise any Option or Share Appreciation Right issued to the Participant shall terminate immediately upon such violation, unless the Company otherwise determines. In addition, if, prior to the end of the term of an Option or Share Appreciation Right, the Participant is given notice by the Company or any of its Subsidiaries of the Participant's Termination of Service by the Company or any of its Subsidiaries for Cause, and the effective date of such Termination of Service is subsequent to the date of the delivery of such notice, the right of the Participant and the Participant's transferees to exercise any Option or Share Appreciation Right issued to the Participant shall be suspended from the time of the delivery of such notice until the earlier of (i) such time as it is determined or otherwise agreed that the Participant's service as a Service Provider will not be terminated for Cause as provided in such notice or (ii) the effective date of the Participant's Termination of Service by the Company or any of its Subsidiaries for Cause (in which case the right of the Participant and the Participant's transferees to exercise any Option or Share Appreciation Right issued to the Participant will terminate immediately upon the effective date of such Termination of Service).

5.4 Exercise. Options and Share Appreciation Rights may be exercised by delivering to the Company a written notice of exercise, in a form the Administrator approves (which may be electronic), signed by the person authorized to exercise the Option or Share Appreciation Right, together with, as applicable, payment in full (i) as specified in Section 5.5 for the number of Shares for which the Award is exercised and (ii) as specified in Section 9.5 for any applicable taxes. Unless the Administrator otherwise determines, an Option or Share Appreciation Right may not be exercised for a fraction of a Share.

5.5 Payment Upon Exercise. Subject to Section 10.8, any Company insider trading policy (including blackout periods) and Applicable Laws, the exercise price of an Option must be paid by:

(a) cash, wire transfer of immediately available funds or by check payable to the order of the Company, provided that the Company may limit the use of one of the foregoing payment forms if one or more of the payment forms below is permitted;

(b) if there is a public market for Shares at the time of exercise, unless the Company otherwise determines, (A) delivery (including telephonically to the extent permitted by the Company) of an irrevocable and unconditional undertaking by a broker acceptable to the Company to deliver promptly

to the Company sufficient funds to pay the exercise price, or (B) the Participant's delivery to the Company of a copy of irrevocable and unconditional instructions to a broker acceptable to the Company to deliver promptly to the Company cash or a check sufficient to pay the exercise price; provided that such amount is paid to the Company at such time as may be required by the Administrator;

(c) to the extent permitted by the Administrator, delivery (either by actual delivery or attestation) of Shares owned by the Participant valued at their Fair Market Value;

(d) to the extent permitted by the Administrator, surrendering Shares then issuable upon the Option's exercise valued at their Fair Market Value on the exercise date;

(e) to the extent permitted by the Administrator, delivery of a promissory note or any other property that the Administrator determines is good and valuable consideration; or

(f) to the extent permitted by the Company, any combination of the above payment forms approved by the Administrator.

## **ARTICLE VI. RESTRICTED SHARES; RESTRICTED SHARE UNITS**

6.1 General. The Administrator may grant Restricted Shares, or the right to purchase Restricted Shares, to any Service Provider, subject to the Company's right to repurchase all or part of such shares at their issue price or other stated or formula price from the Participant (or to require forfeiture of such shares) if conditions the Administrator specifies in the Award Agreement are not satisfied before the end of the applicable restriction period or periods that the Administrator establishes for such Award. In addition, the Administrator may grant to Service Providers Restricted Share Units, which may be subject to vesting and forfeiture conditions during the applicable restriction period or periods, as set forth in an Award Agreement. The Administrator will determine and set forth in the Award Agreement the terms and conditions for each Restricted Share and Restricted Share Unit Award, subject to the conditions and limitations contained in the Plan.

### 6.2 Restricted Shares.

(a) Dividends. Participants holding Restricted Shares will be entitled to all ordinary cash dividends paid with respect to such Shares, unless the Administrator provides otherwise in the Award Agreement. In addition, unless the Administrator provides otherwise, if any dividends or distributions are paid in Shares, or consist of a dividend or distribution to holders of Restricted Shares of property other than an ordinary cash dividend, the Shares or other property will be subject to the same restrictions on transferability and forfeitability as the Restricted Shares with respect to which they were paid.

(b) Certificates. The Company may require that the Participant deposit in escrow with the Company (or its designee) any certificates issued in respect of Restricted Shares, together with a stock transfer form endorsed in blank.

### 6.3 Restricted Share Units.

(a) Settlement. The Administrator may provide that settlement of Restricted Share Units will occur upon or as soon as reasonably practicable after the Restricted Share Units vest or will instead be deferred, on a mandatory basis or at the Participant's election.



(b) Shareholder Rights. A Participant will have no rights of a shareholder with respect to Shares subject to any Restricted Share Unit unless and until the Shares are delivered in settlement of the Restricted Share Unit.

(c) Dividend Equivalents. If the Administrator provides, a grant of Restricted Share Units may provide a Participant with the right to receive Dividend Equivalents. Dividend Equivalents may be paid currently or credited to an account for the Participant, settled in cash or Shares and subject to the same restrictions on transferability and forfeitability as the Restricted Share Units with respect to which the Dividend Equivalents are granted and subject to other terms and conditions as set forth in the Award Agreement.

#### **ARTICLE VII. OTHER SHARE OR CASH BASED AWARDS**

Other Share or Cash Based Awards may be granted to Participants, including Awards entitling Participants to receive Shares to be delivered in the future and including annual or other periodic or long-term cash bonus awards (whether based on specified Performance Criteria or otherwise), in each case subject to any conditions and limitations in the Plan. Such Other Share or Cash Based Awards will 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. Other Share or Cash Based Awards may be paid in Shares, cash or other property, as the Administrator determines. Subject to the provisions of the Plan, the Administrator will determine the terms and conditions of each Other Share or Cash Based Award, including any purchase price, performance goal (which may be based on the Performance Criteria), transfer restrictions, and vesting conditions, which will be set forth in the applicable Award Agreement.

#### **ARTICLE VIII. ADJUSTMENTS FOR CHANGES IN SHARES AND CERTAIN OTHER EVENTS**

8.1 Equity Restructuring. In connection with any Equity Restructuring, notwithstanding anything to the contrary in this Article VIII, the Administrator will equitably adjust each outstanding Award as it deems appropriate to reflect the Equity Restructuring, which may include adjusting the number and type of securities subject to each outstanding Award and/or the Award's exercise price or grant price (if applicable), granting new Awards to Participants, and making a cash payment to Participants. The adjustments provided under this Section 8.1 will be nondiscretionary and final and binding on the affected Participant and the Company; provided that the Administrator will determine whether an adjustment is equitable.

8.2 Corporate Transactions. In the event of any Equity Restructuring, dividend or other distribution (whether in the form of cash, Shares, other securities, or other property), capitalization, share issue, offer, subdivision, reorganization, merger, consolidation, combination, amalgamation, repurchase, recapitalization, liquidation, dissolution, or sale, transfer, exchange or other disposition of all or substantially all of the assets of the Company, or sale or exchange of Shares or other securities of the Company, Change in Control, issuance of warrants or other rights to purchase Shares or other securities of the Company, other similar corporate transaction or event, other unusual or nonrecurring transaction or event affecting the Company or its financial statements or any change in any Applicable Laws or accounting principles (any "*Corporate Event*"), the Administrator, on such terms and conditions as it deems appropriate, either by the terms of the Award or by action taken prior to the occurrence of such transaction or event (except that action to give effect to a change in Applicable Law or accounting principles may be made within a reasonable period of time after such change) and either automatically or



upon the Participant's request, is hereby authorized to take any one or more of the following actions whenever the Administrator determines that such action is appropriate in order to (x) prevent dilution or enlargement of the benefits or potential benefits intended by the Company to be made available under the Plan or with respect to any Award granted or issued under the Plan, (y) to facilitate such transaction or event or (z) give effect to such changes in Applicable Laws or accounting principles:

(a) To provide for the cancellation of any such Award in exchange for either an amount of cash or other property with a value equal to the amount that could have been obtained upon the exercise or settlement of the vested portion of such Award or realization of the Participant's rights under the vested portion of such Award, as applicable; provided that, if the amount that could have been obtained upon the exercise or settlement of the vested portion of such Award or realization of the Participant's rights, in any case, is equal to or less than zero, then the Award may be terminated without payment;

(b) To provide that such Award shall vest and, to the extent applicable, be exercisable as to all shares covered thereby, notwithstanding anything to the contrary in the Plan or the provisions of such Award;

(c) To provide that such Award be assumed by the successor or survivor corporation, or a parent or subsidiary thereof, or shall be substituted for by awards covering the equity securities of the successor or survivor corporation, or a parent or subsidiary thereof, with appropriate adjustments as to the number and kind of shares and/or applicable exercise or purchase price, in all cases, as determined by the Administrator;

(d) To make adjustments in the number and type of shares (or other securities or property) subject to outstanding Awards and/or with respect to which Awards may be granted under the Plan (including, but not limited to, adjustments of the limitations in Article IV hereof on the maximum number and kind of shares which may be issued) and/or in the terms and conditions of (including the grant or exercise price), and the criteria included in, outstanding Awards;

(e) To replace such Award with other rights or property selected by the Administrator; and/or

(f) To provide that the Award will terminate and cannot vest, be exercised or become payable after the applicable transaction or event.

8.3 Administrative Stand Still. In the event of any pending Corporate Event or other similar transaction, for administrative convenience, the Administrator may refuse to permit the exercise of any Award for up to sixty days before or after such transaction.

8.4 General. Except as expressly provided in the Plan or the Administrator's action under the Plan, no Participant will have any rights due to any subdivision or consolidation of Shares of any class, dividend payment, increase or decrease in the number of Shares of any class, issue, rights issue, offer or dissolution, liquidation, merger, or consolidation of the Company or other corporation. Except as expressly provided with respect to an Equity Restructuring under Section 8.1 above or the Administrator's action under the Plan, no issuance by the Company of Shares of any class, or securities convertible into Shares of any class, will affect, and no adjustment will be made regarding, the number of Shares subject to an Award or the Award's grant or exercise price. The existence of the Plan, any Award Agreements and the Awards granted hereunder will not affect or restrict in any way the Company's right or power to make or authorize (i) any adjustment, recapitalization, reorganization or other change in the Company's capital structure or its business, (ii) any Corporate Event or (iii) sale or issuance of securities,

including securities with rights superior to those of the Shares or securities convertible into or exchangeable for Shares. The Administrator may treat Participants and Awards (or portions thereof) differently under this Article VIII.

#### **ARTICLE IX. GENERAL PROVISIONS APPLICABLE TO AWARDS**

9.1 Transferability. Except as the Administrator may determine or provide in an Award Agreement or otherwise for Awards other than Incentive Options, Awards may not be sold, assigned, transferred, pledged or otherwise encumbered, either voluntarily or by operation of law, except by will or the laws of descent and distribution, or, subject to the Administrator's consent, pursuant to a domestic relations order, and, during the life of the Participant, will be exercisable only by the Participant. References to a Participant, to the extent relevant in the context, will include references to a Participant's authorized transferee that the Administrator specifically approves.

9.2 Documentation. Each Award will be evidenced in an Award Agreement, which may be written or electronic, as the Administrator determines. Each Award may contain terms and conditions in addition to those set forth in the Plan.

9.3 Discretion. Except as the Plan otherwise provides, each Award may be made alone or in addition or in relation to any other Award. The terms of each Award to a Participant need not be identical, and the Administrator need not treat Participants or Awards (or portions thereof) uniformly.

9.4 Termination of Status. The Administrator will determine how the disability, death, retirement, authorized leave of absence or any other change or purported change in a Participant's Service Provider status affects an Award and the extent to which, and the period during which, the Participant, the Participant's legal representative, conservator, guardian or Designated Beneficiary may exercise rights under the Award, if applicable.

9.5 Withholding. Each Participant must pay the Company, or make provision satisfactory to the Administrator for payment of, any taxes (which includes any social security contributions or the like) required by law to be withheld or paid by the Company or by an Subsidiary that is the employing entity of the Participant in connection with such Participant's Awards by the date of the event creating the tax liability. The Company may deduct an amount sufficient to satisfy such tax obligations based on the minimum statutory withholding rates (or such other rate as may be determined by the Company after considering any accounting consequences or costs) from any payment of any kind otherwise due to a Participant. Subject to Section 10.8 and any Company insider trading policy (including blackout periods), Participants may satisfy such tax obligations (i) in cash, by wire transfer of immediately available funds, by check made payable to the order of the Company, provided that the Company may limit the use of the foregoing payment forms if one or more of the payment forms below is permitted, (ii) to the extent permitted by the Administrator, in whole or in part by delivery of Shares, including Shares retained from the Award creating the tax obligation, valued at their Fair Market Value, (iii) if there is a public market for Shares at the time the tax obligations are satisfied, unless the Company otherwise determines, (A) delivery (including telephonically to the extent permitted by the Company) of an irrevocable and unconditional undertaking by a broker acceptable to the Company to deliver promptly to the Company sufficient funds to satisfy the tax obligations, or (B) delivery by the Participant to the Company of a copy of irrevocable and unconditional instructions to a broker acceptable to the Company to deliver promptly to the Company cash or a check sufficient to satisfy the tax withholding, provided that such amount is paid to the Company at such time as may be required by the Administrator, or (iv) to the extent permitted by the Company, any combination of the foregoing payment forms approved by the Administrator. If any tax withholding obligation will be satisfied under clause (ii) of the immediately preceding sentence by the

Company's retention of Shares from the Award creating the tax obligation and there is a public market for Shares at the time the tax obligation is satisfied, the Company may elect to instruct any brokerage firm determined acceptable to the Company for such purpose to sell on the applicable Participant's behalf some or all of the Shares retained and to remit the proceeds of the sale to the Company or its designee, and each Participant's acceptance of an Award under the Plan will constitute the Participant's authorization to the Company and instruction and authorization to such brokerage firm to complete the transactions described in this sentence.

9.6 Amendment of Award; Repricing. The Administrator may amend, modify or terminate any outstanding Award, including by substituting another Award of the same or a different type, changing the exercise or settlement date, and converting an Incentive Option to a Non-Qualified Option. The Participant's consent to such action will be required unless (i) the action, taking into account any related action, does not materially and adversely affect the Participant's rights under the Award, or (ii) the change is permitted under Article VIII or pursuant to Section 10.6. Notwithstanding the foregoing or anything in the Plan to the contrary, the Administrator may not, except pursuant to Article VIII, without the approval of the shareholders of the Company, reduce the exercise price per share of outstanding Options or Share Appreciation Rights or cancel outstanding Options or Share Appreciation Rights in exchange for cash, other Awards or Options or Share Appreciation Rights with an exercise price per share that is less than the exercise price per share of the original Options or Share Appreciation Rights.

9.7 Conditions on Delivery of Shares. The Company will not be obligated to deliver any Shares under the Plan or remove restrictions from Shares previously delivered under the Plan until (i) all Award conditions have been met or removed to the Company's satisfaction, (ii) as determined by the Company, all other legal matters regarding the issuance and delivery of such Shares have been satisfied, including any applicable securities laws and stock exchange or stock market rules and regulations, and (iii) the Participant has executed and delivered to the Company such representations or agreements as the Administrator deems necessary or appropriate to satisfy any Applicable Laws. The Company's inability to obtain authority from any regulatory body having jurisdiction, which the Administrator determines is necessary to the lawful issuance and sale of any securities, will relieve the Company of any liability for failing to issue or sell such Shares as to which such requisite authority has not been obtained.

9.8 Acceleration. The Administrator may at any time provide that any Award will become immediately vested and fully or partially exercisable, free of some or all restrictions or conditions, or otherwise fully or partially realizable.

9.9 Additional Terms of Incentive Options. The Administrator may grant Incentive Options only to employees of the Company, any of its present or future parent or subsidiary corporations, as defined in Sections 424(e) or (f) of the Code, respectively, and any other entities the employees of which are eligible to receive Incentive Options under the Code. If an Incentive Option is granted to a Greater Than 10% Shareholder, the exercise price will not be less than 110% of the Fair Market Value on the Option's grant date, and the term of the Option will not exceed five years. All Incentive Options will be subject to and construed consistently with Section 422 of the Code. By accepting an Incentive Option, the Participant agrees to give prompt notice to the Company of dispositions or other transfers (other than in connection with a Change in Control) of Shares acquired under the Option made within (i) two years from the grant date of the Option or (ii) one year after the transfer of such Shares to the Participant, specifying the date of the disposition or other transfer and the amount the Participant realized, in cash, other property, assumption of indebtedness or other consideration, in such disposition or other transfer. Neither the Company nor the Administrator will be liable to a Participant, or any other party, if an Incentive Option fails or ceases to qualify as an "incentive stock option" under Section 422 of the Code. Any Incentive Option or portion thereof that fails to qualify as an "incentive stock option" under Section 422 of the Code for any reason, including becoming exercisable with respect to Shares having a

fair market value exceeding the \$100,000 limitation under Treasury Regulation Section 1.422-4, will be a Non-Qualified Option.

## **ARTICLE X. MISCELLANEOUS**

10.1 No Right to Employment or Other Status. No person will have any claim or right to be granted an Award, and the grant of an Award will not be construed as giving a Participant the right to continued employment or any other relationship with the Company. The Company expressly reserves the right at any time to dismiss or otherwise terminate its relationship with a Participant free from any liability or claim under the Plan or any Award, except as expressly provided in an Award Agreement.

10.2 No Rights as Shareholder; Certificates. Subject to the Award Agreement, no Participant or Designated Beneficiary will have any rights as a shareholder with respect to any Shares to be distributed under an Award until becoming the record holder of such Shares. Notwithstanding any other provision of the Plan, unless the Administrator otherwise determines or Applicable Laws require, the Company will not be required to deliver to any Participant certificates evidencing Shares issued in connection with any Award and instead such Shares may be recorded in the books of the Company (or, as applicable, its transfer agent or stock plan administrator). The Company may place legends on certificates issued under the Plan that the Administrator deems necessary or appropriate to comply with Applicable Laws.

10.3 Effective Date and Term of Plan. Unless earlier terminated by the Board, the Plan will become effective on the day prior to the NASDAQ Listing Date and will remain in effect until the tenth anniversary of the effective date, but Awards previously granted may extend beyond that date in accordance with the Plan. If the Plan is not approved by the Company's shareholders, the Plan will not become effective, no Awards will be granted under the Plan and the Prior Plans will continue in full force and effect in accordance with their terms.

10.4 Amendment of Plan. The Administrator may amend, suspend or terminate the Plan at any time; provided that no amendment, other than an increase to the Overall Share Limit, may materially and adversely affect any Award outstanding at the time of such amendment without the affected Participant's consent. No Awards may be granted under the Plan during any suspension period or after Plan termination. Awards outstanding at the time of any Plan suspension or termination will continue to be governed by the Plan and the Award Agreement, as in effect before such suspension or termination. The Board will obtain shareholder approval of any Plan amendment to the extent necessary to comply with Applicable Laws.

10.5 Provisions for Foreign Participants. The Administrator may modify Awards granted to Participants who are foreign nationals or employed outside the United States or establish subplans or procedures under the Plan to address differences in laws, rules, regulations or customs of such foreign jurisdictions with respect to tax, securities, currency, employee benefit or other matters.

10.6 Section 409A. The following provisions only apply to Participants subject to tax in the United States.

(a) General. The Company intends that all Awards be structured to comply with, or be exempt from, Section 409A, such that no adverse tax consequences, interest, or penalties under Section 409A apply. Notwithstanding anything in the Plan or any Award Agreement to the contrary, the Administrator may, without a Participant's consent, amend this Plan or Awards, adopt policies and procedures, or take any other actions (including amendments, policies, procedures and retroactive actions)

as are necessary or appropriate to preserve the intended tax treatment of Awards, including any such actions intended to (A) exempt this Plan or any Award from Section 409A, or (B) comply with Section 409A, including regulations, guidance, compliance programs and other interpretative authority that may be issued after an Award's grant date. The Company makes no representations or warranties as to an Award's tax treatment under Section 409A or otherwise. The Company will have no obligation under this Section 10.6 or otherwise to avoid the taxes, penalties or interest under Section 409A with respect to any Award and will have no liability to any Participant or any other person if any Award, compensation or other benefits under the Plan are determined to constitute noncompliant "nonqualified deferred compensation" subject to taxes, penalties or interest under Section 409A.

(b) Separation from Service. If an Award constitutes "nonqualified deferred compensation" under Section 409A, any payment or settlement of such Award upon a termination of a Participant's Service Provider relationship will, to the extent necessary to avoid taxes under Section 409A, be made only upon the Participant's "separation from service" (within the meaning of Section 409A), whether such "separation from service" occurs upon or after the termination of the Participant's Service Provider relationship. For purposes of this Plan or any Award Agreement relating to any such payments or benefits, references to a "termination," "termination of employment" or like terms means a "separation from service."

(c) Payments to Specified Employees. Notwithstanding any contrary provision in the Plan or any Award Agreement, any payment(s) of "nonqualified deferred compensation" required to be made under an Award to a "specified employee" (as defined under Section 409A and as the Administrator determines) due to his or her "separation from service" will, to the extent necessary to avoid taxes under Section 409A(a)(2)(B)(i) of the Code, be delayed for the six-month period immediately following such "separation from service" (or, if earlier, until the specified employee's death) and will instead be paid (as set forth in the Award Agreement) on the day immediately following such six-month period or as soon as administratively practicable thereafter (without interest). Any payments of "nonqualified deferred compensation" under such Award payable more than six months following the Participant's "separation from service" will be paid at the time or times the payments are otherwise scheduled to be made.

10.7 Limitations on Liability. Notwithstanding any other provisions of the Plan, no individual acting as a director, officer, other employee or agent of the Company or any Subsidiary will be liable to any Participant, former Participant, spouse, beneficiary, or any other person for any claim, loss, liability, or expense incurred in connection with the Plan or any Award, and such individual will not be personally liable with respect to the Plan because of any contract or other instrument executed in his or her capacity as an Administrator, director, officer, other employee or agent of the Company or any Subsidiary. The Company will indemnify and hold harmless each director, officer, other employee and agent of the Company or any Subsidiary that has been or will be granted or delegated any duty or power relating to the Plan's administration or interpretation, against any cost or expense (including attorneys' fees) or liability (including any sum paid in settlement of a claim with the Administrator's approval) arising from any act or omission concerning this Plan unless arising from such person's own fraud or bad faith.

10.8 Lock-Up Period. The Company may, at the request of any underwriter representative or otherwise, in connection with registering the offering of any Company securities under the Securities Act, prohibit Participants from, directly or indirectly, selling or otherwise transferring any Shares or other Company securities during a period of up to one hundred eighty days following the effective date of a Company registration statement filed under the Securities Act, or such longer period as determined by the underwriter.



10.9 Data Privacy. As a condition for receiving any Award, each Participant explicitly and unambiguously consents to the collection, use and transfer, in electronic or other form, of personal data as described in this section by and among the Company and its Subsidiaries and affiliates exclusively for implementing, administering and managing the Participant's participation in the Plan. The Company and its Subsidiaries and affiliates may hold certain personal information about a Participant, including the Participant's name, address and telephone number; birthdate; social security, insurance number or other identification number; salary; nationality; job title(s); any Shares held in the Company or its Subsidiaries and affiliates; and Award details, to implement, manage and administer the Plan and Awards (the "**Data**"). The Company and its Subsidiaries and affiliates may transfer the Data amongst themselves as necessary to implement, administer and manage a Participant's participation in the Plan, and the Company and its Subsidiaries and affiliates may transfer the Data to third parties assisting the Company with Plan implementation, administration and management. These recipients may be located in the Participant's country, or elsewhere, and the Participant's country may have different data privacy laws and protections than the recipients' country. By accepting an Award, each Participant authorizes such recipients to receive, possess, use, retain and transfer the Data, in electronic or other form, to implement, administer and manage the Participant's participation in the Plan, including any required Data transfer to a broker or other third party with whom the Company or the Participant may elect to deposit any Shares. The Data related to a Participant will be held only as long as necessary to implement, administer, and manage the Participant's participation in the Plan. A Participant may, at any time, view the Data that the Company holds regarding such Participant, request additional information about the storage and processing of the Data regarding such Participant, recommend any necessary corrections to the Data regarding the Participant or refuse or withdraw the consents in this Section 10.9 in writing, without cost, by contacting the local human resources representative. The Company may cancel Participant's ability to participate in the Plan and, in the Administrator's discretion, the Participant may forfeit any outstanding Awards if the Participant refuses or withdraws the consents in this Section 10.9. For more information on the consequences of refusing or withdrawing consent, Participants may contact their local human resources representative.

10.10 Severability. If any portion of the Plan or any action taken under it is held illegal or invalid for any reason, the illegality or invalidity will not affect the remaining parts of the Plan, and the Plan will be construed and enforced as if the illegal or invalid provisions had been excluded, and the illegal or invalid action will be null and void.

10.11 Governing Documents. If any contradiction occurs between the Plan and any Award Agreement or other written agreement between a Participant and the Company (or any Subsidiary) that the Administrator has approved, the Plan will govern, unless it is expressly specified in such Award Agreement or other written document that a specific provision of the Plan will not apply.

10.12 Governing Law. The Plan and all Awards will be governed by and interpreted in accordance with the laws of the United Kingdom, disregarding any state's choice-of-law principles requiring the application of a jurisdiction's laws other than the United Kingdom.

10.13 Claw-back Provisions. All Awards (including any proceeds, gains or other economic benefit the Participant actually or constructively receives upon receipt or exercise of any Award or the receipt or resale of any Shares underlying the Award) will be subject to any Company claw-back policy, including any claw-back policy adopted to comply with Applicable Laws (including the Dodd-Frank Wall Street Reform and Consumer Protection Act and any rules or regulations promulgated thereunder) as set forth in such claw-back policy or the Award Agreement.

10.14 Titles and Headings. The titles and headings in the Plan are for convenience of reference only and, if any conflict, the Plan's text, rather than such titles or headings, will control.

10.15 Conformity to Securities Laws. Participant acknowledges that the Plan is intended to conform to the extent necessary with Applicable Laws. Notwithstanding anything herein to the contrary, the Plan and all Awards will be administered only in conformance with Applicable Laws. To the extent Applicable Laws permit, the Plan and all Award Agreements will be deemed amended as necessary to conform to Applicable Laws.

10.16 Relationship to Other Benefits. No payment under the Plan will be taken into account in determining any benefits under any pension, retirement, savings, profit sharing, group insurance, welfare or other benefit plan of the Company or any Subsidiary except as expressly provided in writing in such other plan or an agreement thereunder.

10.17 Broker-Assisted Sales. In the event of a broker-assisted sale of Shares in connection with the payment of amounts owed by a Participant under or with respect to the Plan or Awards, including amounts to be paid under the final sentence of Section 9.5: (a) any Shares to be sold through the broker-assisted sale will be sold on the day the payment first becomes due, or as soon thereafter as practicable; (b) such Shares may be sold as part of a block trade with other Participants in the Plan in which all participants receive an average price; (c) the applicable Participant will be responsible for all broker's fees and other costs of sale, and by accepting an Award, each Participant agrees to indemnify and hold the Company harmless from any losses, costs, damages, or expenses relating to any such sale; (d) to the extent the Company or its designee receives proceeds of such sale that exceed the amount owed, the Company will pay such excess in cash to the applicable Participant as soon as reasonably practicable; (e) the Company and its designees are under no obligation to arrange for such sale at any particular price; and (f) in the event the proceeds of such sale are insufficient to satisfy the Participant's applicable obligation, the Participant may be required to pay immediately upon demand to the Company or its designee an amount in cash sufficient to satisfy any remaining portion of the Participant's obligation.

## **ARTICLE XI. DEFINITIONS**

As used in the Plan, the following words and phrases will have the following meanings:

11.1 "**ADSS**" means American Depositary Shares, representing Ordinary Shares on deposit with a U.S. banking institution selected by the Company and which are registered pursuant to a Form F-6.

11.2 "**Administrator**" means the Board or a Committee to the extent that the Board's powers or authority under the Plan have been delegated to such Committee.

11.3 "**Applicable Laws**" shall mean any applicable law, including without limitation: (a) the requirements relating to the administration of equity incentive plans under U.S. federal and state securities, tax and other applicable laws, rules and regulations, the applicable rules of any stock exchange or quotation system on which the Shares are listed or quoted and the applicable laws and rules of any foreign country or other jurisdiction where Awards are granted; and (b) corporate, securities, tax or other laws, statutes, rules, requirements or regulations, whether U.S. federal, state, local or foreign, applicable in the United Kingdom, United States or any other relevant jurisdiction.

11.4 "**Award**" means, individually or collectively, a grant under the Plan of Options, Share Appreciation Rights, Restricted Shares, Restricted Share Units or Other Share or Cash Based Awards.

11.5 "**Award Agreement**" means a written agreement evidencing an Award, which may be electronic, that contains such terms and conditions as the Administrator determines, consistent with and subject to the terms and conditions of the Plan.

11.6 “**Board**” means the Board of Directors of the Company.

11.7 “**Cause**” means (i) if a Participant is a party to a written employment or consulting agreement with the Company or any of its Subsidiaries or an Award Agreement in which the term “cause” is defined (a “**Relevant Agreement**”), “Cause” as defined in the Relevant Agreement, and (ii) if no Relevant Agreement exists, (A) the Administrator’s determination that the Participant failed to substantially perform the Participant’s duties (other than a failure resulting from the Participant’s Disability); (B) the Administrator’s determination that the Participant failed to carry out, or comply with any lawful and reasonable directive of the Board or the Participant’s immediate supervisor; (C) the occurrence of any act or omission by the Participant that could reasonably be expected to result in (or has resulted in) the Participant’s conviction, plea of no contest, plea of nolo contendere, or imposition of unadjudicated probation for any felony or indictable offense or crime involving moral turpitude; (D) the Participant’s unlawful use (including being under the influence) or possession of illegal drugs on the premises of the Company or any of its Subsidiaries or while performing the Participant’s duties and responsibilities for the Company or any of its Subsidiaries; or (E) the Participant’s commission of an act of fraud, embezzlement, misappropriation, misconduct, or breach of fiduciary duty against the Company or any of its Subsidiaries.

11.8 “**Change in Control**” means and includes each of the following:

- (i) a Sale; or
- (ii) a Takeover.

The Administrator shall have full and final authority, which shall be exercised in its sole discretion, to determine conclusively whether a Change in Control has occurred pursuant to the above definition, the date of the occurrence of such Change in Control and any incidental matters relating thereto; provided that any exercise of authority in conjunction with a determination of whether a Change in Control is a “change in control event” as defined in Treasury Regulation Section 1.409A-3(i)(5) shall be consistent with such regulation.

11.9 “**Code**” means the Internal Revenue Code of 1986, as amended, and the regulations issued thereunder.

11.10 “**Committee**” means one or more committees or subcommittees of the Board, which may include one or more Company directors or executive officers, to the extent Applicable Laws permit. To the extent required to comply with the provisions of Rule 16b-3, it is intended that each member of the Committee will be, at the time the Committee takes any action with respect to an Award that is subject to Rule 16b-3, a “non-employee director” within the meaning of Rule 16b-3; however, a Committee member’s failure to qualify as a “non-employee director” within the meaning of Rule 16b-3 will not invalidate any Award granted by the Committee that is otherwise validly granted under the Plan.

11.11 “**Company**” means Verona Pharma plc, registered in England and Wales with company number 05375156, or any successor.

11.12 “**Consultant**” means any person, including any adviser, engaged by the Company or its parent or Subsidiary to render services to such entity if the consultant or adviser: (i) renders bona fide services to the Company; (ii) renders services not in connection with the offer or sale of securities in a capital-raising transaction and does not directly or indirectly promote or maintain a market for the Company’s securities; and (iii) is a natural person.



11.13 “**Control**” shall have the meaning given in section 995 (2) of the UK Income Tax Act 2007, unless otherwise specified.

11.14 “**Designated Beneficiary**” means the beneficiary or beneficiaries the Participant designates, in a manner the Administrator determines, to receive amounts due or exercise the Participant’s rights if the Participant dies or becomes incapacitated. Without a Participant’s effective designation, “Designated Beneficiary” will mean the Participant’s estate.

11.15 “**Director**” means a Board member.

11.16 “**Disability**” means a permanent and total disability under Section 22(e)(3) of the Code, as amended.

11.17 “**Dividend Equivalents**” means a right granted to a Participant under the Plan to receive the equivalent value (in cash or Shares) of dividends paid on Shares.

11.18 “**Employee**” means any employee of the Company or its Subsidiaries.

11.19 “**Equity Restructuring**” means a nonreciprocal transaction between the Company and its shareholders, such as a share dividend, share split, spin-off, rights offering or recapitalization through a large, nonrecurring cash dividend, that affects the number or kind of Shares (or other Company securities) or the price of Shares (or other Company securities) and causes a change in the per share value of the Shares underlying outstanding Awards.

11.20 “**Exchange Act**” means the Securities Exchange Act of 1934, as amended.

11.21 “**Fair Market Value**” means, as of any date, the value of Shares determined as follows: (i) if the Shares are listed on one or more established stock exchanges, its Fair Market Value will be the closing sales price for Shares as quoted on any exchange (as determined by the Administrator) for the last day preceding such date during which a sale occurred, as reported in The Wall Street Journal or another source the Administrator deems reliable; (ii) if the Shares are not traded on a stock exchange but is quoted on a national market or other quotation system, the closing sales price on the last date preceding such date during which a sale occurred, as reported in The Wall Street Journal or another source the Administrator deems reliable; or (iii) without an established market for the Shares, the Administrator will determine the Fair Market Value in its discretion. Notwithstanding the foregoing, with respect to any Award granted on the date of the effectiveness of the Company’s first registration statement filed under the Securities Act, the Fair Market Value shall mean the price of a Share as set forth in the Company’s final prospectus relating to such registration statement.

11.22 “**Greater Than 10% Shareholder**” means an individual then owning (within the meaning of Section 424(d) of the Code) more than 10% of the total combined voting power of all classes of equity securities of the Company or its parent or subsidiary corporation, as defined in Section 424(e) and (f) of the Code, respectively.

11.23 “**Incentive Option**” means an Option intended to qualify as an “incentive stock option” as defined in Section 422 of the Code.

11.24 “**NASDAQ Listing Date**” means the first date upon which the Shares are listed (or approved for listing) upon notice of issuance on the NASDAQ Global Market.

11.25 “**Non-Qualified Option**” means an Option not intended or not qualifying as an Incentive Option.

11.26 “**Option**” means an option to purchase Shares.

11.27 “**Ordinary Share**” means an ordinary share of £0.05 each in the capital of the Company.

11.28 “**Other Share or Cash Based Awards**” means cash awards, awards of Shares, and other awards valued wholly or partially by referring to, or are otherwise based on, Shares or other property.

11.29 “**Overall Share Limit**” means the sum of (i) 6,333,000 Shares; (ii) any Shares which are subject to Prior Plan Awards which become available for issuance under the Plan pursuant to Article IV and (iii) an annual increase on the first day of each calendar year beginning January 1, 2018 and ending on and including January 1, 2027, equal to the least of (A) 4% of the aggregate number of Shares outstanding on the final day of the immediately preceding calendar year and (B) such smaller number of Shares as is determined by the Board.

11.30 “**Participant**” means a Service Provider who has been granted an Award.

11.31 “**Performance Criteria**” mean the criteria (and adjustments) that the Administrator may select for an Award to establish performance goals for a performance period, which may include 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. The Committee may provide for exclusion of the impact of an event or occurrence which the Committee determines should appropriately be excluded, including (a) restructurings, discontinued operations, extraordinary items, and other unusual, infrequently occurring or non-recurring charges or events, (b) asset write-downs, (c) litigation or claim judgments or settlements, (d) acquisitions or divestitures, (e) reorganization or change in the corporate structure or capital structure of the Company, (f) an event either not directly related to the operations of the Company, Subsidiary, division, business segment or business unit or not within the reasonable control of management, (g) foreign exchange gains and losses, (h) a

change in the fiscal year of the Company, (i) the refinancing or repurchase of bank loans or debt securities, (j) unbudgeted capital expenditures, (k) the issuance or repurchase of equity securities and other changes in the number of outstanding shares, (l) conversion of some or all of convertible securities to Shares, (m) any business interruption event (n) the cumulative effects of tax or accounting changes in accordance with U.S. generally accepted accounting principles, or (o) the effect of changes in other laws or regulatory rules affecting reported results.

11.32 “**Plan**” means this 2017 Incentive Award Plan.

11.33 “**Prior Plans**” means, collectively, the Verona Pharma plc EMI Option Scheme, the Verona Pharma plc Unapproved Share Option Scheme and any prior equity incentive plans of the Company or its predecessor.

11.34 “**Prior Plan Award**” means an award outstanding under the Prior Plans as of the Plan’s effective date in Section 10.3.

11.35 “**Restricted Shares**” means Shares awarded to a Participant under Article VI subject to certain vesting conditions and other restrictions.

11.36 “**Restricted Share Unit**” means an unfunded, unsecured right to receive, on the applicable settlement date, one Share or an amount in cash or other consideration determined by the Administrator to be of equal value as of such settlement date, subject to certain vesting conditions and other restrictions.

11.37 “**Rule 16b-3**” means Rule 16b-3 promulgated under the Exchange Act.

11.38 “**Sale**” shall mean the sale of all or substantially all of the assets of the Company.

11.39 “**Section 409A**” means Section 409A of the Code and all regulations, guidance, compliance programs and other interpretative authority thereunder.

11.40 “**Securities Act**” means the Securities Act of 1933, as amended.

11.41 “**Service Provider**” means an Employee, Consultant or Director.

11.42 “**Share**” means an Ordinary Share or the number of ADSs equal to an Ordinary Share.

11.43 “**Share Appreciation Right**” means a Share Appreciation right granted under Article V.

11.44 “**Subsidiary**” means any entity (other than the Company), whether domestic or foreign, in an unbroken chain of entities beginning with the Company if each of the entities other than the last entity in the unbroken chain beneficially owns, at the time of the determination, securities or interests representing at least 50% of the total combined voting power of all classes of securities or interests in one of the other entities in such chain.

11.45 “**Substitute Awards**” shall mean Awards granted or Shares issued by the Company in assumption of, or in substitution or exchange for, awards previously granted, or the right or obligation to make future awards, in each case by a company acquired by the Company or any Subsidiary or with which the Company or any Subsidiary combines.

(a) “**Takeover**” shall mean if any person (or a group of persons acting in concert) (the “**Acquiring Person**”):

- to:-
- (i) obtains Control of the Company as the result of making a general offer
  - (A) acquire all of the issued ordinary share capital of the Company, which is made on a condition that, if it is satisfied, the Acquiring Person will have Control of the Company; or
  - (B) acquire all of the shares in the Company which are of the same class as the Shares; or
  - (ii) obtains Control of the Company as a result of a compromise or arrangement sanctioned by a court under Section 899 of the UK Companies Act 2006, or sanctioned under any other similar law of another jurisdiction; or
  - (iii) becomes bound or entitled under Sections 979 to 985 of the UK Companies Act 2006 (or similar law of another jurisdiction) to acquire shares of the same class as the Shares; or
  - (iv) obtains Control of the Company in any other way.

11.46 “*Termination of Service*” means the date the Participant ceases to be a Service Provider.

\* \* \* \* \*

**VERONA PHARMA PLC  
2017 INCENTIVE AWARD PLAN**

**OPTION GRANT NOTICE**

Capitalized terms not specifically defined in this Option Grant Notice (the “**Grant Notice**”) have the meanings given to them in the 2017 Incentive Award Plan (as amended from time to time, the “**Plan**”) of Verona Pharma plc (the “**Company**”).

The Company has granted to the participant listed below (“**Participant**”) the option described in this Grant Notice (the “**Option**”), subject to the terms and conditions of the Plan and the Option Agreement attached as **Exhibit A** (the “**Agreement**”), both of which are incorporated into this Grant Notice by reference.

**Participant:**

**Grant Date:**

**Exercise Price per Share:**

**Shares Subject to the Option:**

**Final Expiration Date:**

**Vesting Commencement Date:**

**Vesting Schedule:** [To be specified in individual award agreements]

**Type of Option** [Incentive Option/Non-Qualified Option]

By Participant’s signature below, Participant agrees to be bound by the terms of this Grant Notice, the Plan and the Agreement. Participant has reviewed the Plan, this Grant Notice and the Agreement in their entirety, has had an opportunity to obtain the advice of counsel prior to executing this Grant Notice and fully understands all provisions of the Plan, this Grant Notice and the Agreement. Participant hereby agrees to accept as binding, conclusive and final all decisions or interpretations of the Administrator upon any questions arising under the Plan, this Grant Notice or the Agreement.

**VERONA PHARMA PLC**

**PARTICIPANT**

By: \_\_\_\_\_

Name: \_\_\_\_\_

Title: \_\_\_\_\_

\_\_\_\_\_

[Participant Name]

**OPTION AGREEMENT**

Capitalized terms not specifically defined in this Agreement have the meanings specified in the Grant Notice or, if not defined in the Grant Notice, in the Plan.

**ARTICLE XII.  
GENERAL**

12.1 Grant of Option. The Company has granted to Participant the Option effective as of the grant date set forth in the Grant Notice (the “**Grant Date**”).

12.2 Incorporation of Terms of Plan. The Option is subject to the terms and conditions set forth in this Agreement and the Plan, which is incorporated herein by reference. In the event of any inconsistency between the Plan and this Agreement, the terms of the Plan will control.

**ARTICLE XIII.  
PERIOD OF EXERCISABILITY**

13.1 Commencement of Exercisability. The Option will vest and become exercisable according to the vesting schedule in the Grant Notice (the “**Vesting Schedule**”) except that any fraction of a Share as to which the Option would be vested or exercisable will be accumulated and will vest and become exercisable only when a whole Share has accumulated. Notwithstanding anything in the Grant Notice, the Plan or this Agreement to the contrary, (i) unless the Administrator otherwise determines, the Option will immediately expire and be forfeited as to any portion that is not vested and exercisable as of Participant’s Termination of Service for any reason and (ii) upon a Change in Control, the Option will vest and become exercisable in full immediately prior to such Change in Control, so long as Participant remains continuously a Service Provider from the date hereof through the date of the Change in Control.

13.2 Duration of Exercisability. The Vesting Schedule is cumulative. Any portion of the Option which vests and becomes exercisable will remain vested and exercisable until the Option expires. The Option will be forfeited immediately upon its expiration.

13.3 Expiration of Option. The Option may not be exercised to any extent by anyone after, and will expire on, the first of the following to occur:

- (a) The final expiration date in the Grant Notice;
  - (b) Except as the Administrator may otherwise approve, the expiration of three (3) months from the date of Participant’s Termination of Service, unless Participant’s Termination of Service is for Cause or by reason of Participant’s death or Disability;
  - (c) Except as the Administrator may otherwise approve, the expiration of one (1) year from the date of Participant’s Termination of Service by reason of Participant’s death or Disability; and
  - (d) Except as the Administrator may otherwise approve, Participant’s Termination of Service for Cause.
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#### **ARTICLE XIV. EXERCISE OF OPTION**

14.1 Person Eligible to Exercise. During Participant's lifetime, only Participant may exercise the Option. After Participant's death, any exercisable portion of the Option may, prior to the time the Option expires, be exercised by Participant's Designated Beneficiary as provided in the Plan.

14.2 Partial Exercise. Any exercisable portion of the Option or the entire Option, if then wholly exercisable, may be exercised, in whole or in part, according to the procedures in the Plan at any time prior to the time the Option or portion thereof expires, except that the Option may only be exercised for whole Shares.

14.3 Tax Withholding.

(a) The Company has the right and option, but not the obligation, to treat Participant's failure to provide timely payment in accordance with the Plan of any withholding tax arising in connection with the Option as Participant's election to satisfy all or any portion of the withholding tax by requesting the Company retain Shares otherwise issuable under the Option.

(b) Participant acknowledges that Participant is ultimately liable and responsible for all taxes owed in connection with the Option, regardless of any action the Company or any Subsidiary takes with respect to any tax withholding obligations that arise in connection with the Option. Neither the Company nor any Subsidiary makes any representation or undertaking regarding the treatment of any tax withholding in connection with the awarding, vesting or exercise of the Option or the subsequent sale of Shares. The Company and the Subsidiaries do not commit and are under no obligation to structure the Option to reduce or eliminate Participant's tax liability.

#### **ARTICLE XV. OTHER PROVISIONS**

15.1 Adjustments. Participant acknowledges that the Option is subject to adjustment, modification and termination in certain events as provided in this Agreement and the Plan.

15.2 Notices. Any notice to be given under the terms of this Agreement to the Company must be in writing and addressed to the Company in care of the Company's Secretary at the Company's principal office or the Secretary's then-current email address or facsimile number. Any notice to be given under the terms of this Agreement to Participant must be in writing and addressed to Participant (or, if Participant is then deceased, to the person entitled to exercise the Option) at Participant's last known mailing address, email address or facsimile number in the Company's personnel files. By a notice given pursuant to this Section, either party may designate a different address for notices to be given to that party. Any notice will be deemed duly given when actually received, when sent by email, when sent by certified mail (return receipt requested) and deposited with postage prepaid in a post office or branch post office regularly maintained by the United States Postal Service, when delivered by a nationally recognized express shipping company or upon receipt of a facsimile transmission confirmation.

15.3 Titles. Titles are provided herein for convenience only and are not to serve as a basis for interpretation or construction of this Agreement.

15.4 Conformity to Securities Laws. Participant acknowledges that the Plan, the Grant Notice and this Agreement are intended to conform to the extent necessary with all Applicable Laws and, to the extent Applicable Laws permit, will be deemed amended as necessary to conform to Applicable Laws.

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15.5 Successors and Assigns. The Company may assign any of its rights under this Agreement to single or multiple assignees, and this Agreement will inure to the benefit of the successors and assigns of the Company. Subject to the restrictions on transfer set forth in the Plan, this Agreement will be binding upon and inure to the benefit of the heirs, legatees, legal representatives, successors and assigns of the parties hereto.

15.6 Limitations Applicable to Section 16 Persons. Notwithstanding any other provision of the Plan or this Agreement, if Participant is subject to Section 16 of the Exchange Act, the Plan, the Grant Notice, this Agreement and the Option will be subject to any additional limitations set forth in any applicable exemptive rule under Section 16 of the Exchange Act (including any amendment to Rule 16b-3) that are requirements for the application of such exemptive rule. To the extent Applicable Laws permit, this Agreement will be deemed amended as necessary to conform to such applicable exemptive rule.

15.7 Entire Agreement. The Plan, the Grant Notice and this Agreement (including any exhibit hereto) constitute the entire agreement of the parties and supersede in their entirety all prior undertakings and agreements of the Company and Participant with respect to the subject matter hereof.

15.8 Agreement Severable. In the event that any provision of the Grant Notice or this Agreement is held illegal or invalid, the provision will be severable from, and the illegality or invalidity of the provision will not be construed to have any effect on, the remaining provisions of the Grant Notice or this Agreement.

15.9 Limitation on Participant's Rights. Participation in the Plan confers no rights or interests other than as herein provided. This Agreement creates only a contractual obligation on the part of the Company as to amounts payable and may not be construed as creating a trust. Neither the Plan nor any underlying program, in and of itself, has any assets. Participant will have only the rights of a general unsecured creditor of the Company with respect to amounts credited and benefits payable, if any, with respect to the Option, and rights no greater than the right to receive the Shares as a general unsecured creditor with respect to the Option, as and when exercised pursuant to the terms hereof.

15.10 Not a Contract of Employment. Nothing in the Plan, the Grant Notice or this Agreement confers upon Participant any right to continue in the employ or service of the Company or any Subsidiary or interferes with or restricts in any way the rights of the Company and its Subsidiaries, which rights are hereby expressly reserved, to discharge or terminate the services of Participant at any time for any reason whatsoever, with or without Cause, except to the extent expressly provided otherwise in a written agreement between the Company or a Subsidiary and Participant.

15.11 Counterparts. The Grant Notice may be executed in one or more counterparts, including by way of any electronic signature, subject to Applicable Law, each of which will be deemed an original and all of which together will constitute one instrument.

15.12 Incentive Options. If the Option is designated as an Incentive Option:

(a) Participant acknowledges that to the extent the aggregate fair market value of shares (determined as of the time the option with respect to the shares is granted) with respect to which options intended to qualify as "incentive stock options" under Section 422 of the Code, including the Option, are exercisable for the first time by Participant during any calendar year exceeds \$100,000 or if for any other reason such options do not qualify or cease to qualify for treatment as "incentive stock options" under Section 422 of the Code, such options (including the Option) will be treated as non-qualified options. Participant further acknowledges that the rule set forth in the preceding sentence will

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be applied by taking the Option and other options into account in the order in which they were granted, as determined under Section 422(d) of the Code. Participant also acknowledges that if the Option is exercised more than three (3) months after Participant's Termination of Service, other than by reason of death or disability, the Option will be taxed as a Non-Qualified Option.

(b) Participant will give prompt written notice to the Company of any disposition or other transfer of any Shares acquired under this Agreement if such disposition or other transfer is made (a) within two (2) years from the Grant Date or (b) within one (1) year after the transfer of such Shares to Participant. Such notice will specify the date of such disposition or other transfer and the amount realized, in cash, other property, assumption of indebtedness or other consideration, by Participant in such disposition or other transfer.

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<p style="text-align: center;"><b>VERONA PHARMA PLC</b> <b>2017 INCENTIVE AWARD PLAN</b></p>
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**RESTRICTED SHARE GRANT NOTICE**

Capitalized terms not specifically defined in this Restricted Share Grant Notice (the “*Grant Notice*”) have the meanings given to them in the 2017 Incentive Award Plan (as amended from time to time, the “*Plan*”) of Verona Pharma plc (the “*Company*”).

The Company has granted to the participant listed below (“*Participant*”) the Restricted Shares described in this Grant Notice (the “*Restricted Shares*”), subject to the terms and conditions of the Plan and the Restricted Share Agreement attached as **Exhibit A** (the “*Agreement*”), both of which are incorporated into this Grant Notice by reference.

**Participant:**

**Grant Date:**

**Number of Restricted Shares:**

**Vesting Commencement Date:**

**Vesting Schedule:** [To be specified in individual award agreements]

By Participant’s signature below, Participant agrees to be bound by the terms of this Grant Notice, the Plan and the Agreement. Participant has reviewed the Plan, this Grant Notice and the Agreement in their entirety, has had an opportunity to obtain the advice of counsel prior to executing this Grant Notice and fully understands all provisions of the Plan, this Grant Notice and the Agreement. Participant hereby agrees to accept as binding, conclusive and final all decisions or interpretations of the Administrator upon any questions arising under the Plan, this Grant Notice or the Agreement.

**VERONA PHARMA PLC**

**PARTICIPANT**

By: \_\_\_\_\_

Name: \_\_\_\_\_

Title: \_\_\_\_\_

\_\_\_\_\_

[Participant Name]

**RESTRICTED SHARE AGREEMENT**

Capitalized terms not specifically defined in this Agreement have the meanings specified in the Grant Notice or, if not defined in the Grant Notice, in the Plan.

**ARTICLE XVI.  
GENERAL**

16.1 Issuance of Restricted Shares. The Company will issue the Restricted Shares to the Participant effective as of the grant date set forth in the Grant Notice and will cause (a) a certificate or certificates representing the Restricted Shares to be registered in Participant's name or (b) the Restricted Shares to be held in book-entry form. If a certificate representing the Restricted Shares is issued, the certificate will be delivered to, and held in accordance with this Agreement by, the Company or its authorized representatives and will bear the restrictive legends required by this Agreement. If the Restricted Shares are held in book-entry form, then the book-entry will indicate that the Restricted Shares are subject to the restrictions of this Agreement.

16.2 Incorporation of Terms of Plan. The Restricted Shares are subject to the terms and conditions set forth in this Agreement and the Plan, which is incorporated herein by reference. In the event of any inconsistency between the Plan and this Agreement, the terms of the Plan will control.

**ARTICLE XVII.  
VESTING, FORFEITURE AND ESCROW**

17.1 Vesting. The Restricted Shares will become vested Shares (the "*Vested Shares*") according to the vesting schedule in the Grant Notice except that any fraction of a Share that would otherwise become a Vested Share will be accumulated and will become a Vested Share only when a whole Vested Share has accumulated.

17.2 Forfeiture. In the event of Participant's Termination of Service for any reason, Participant will immediately and automatically forfeit to the Company any Shares that are not Vested Shares (the "*Unvested Shares*") at the time of Participant's Termination of Service, except as otherwise determined by the Administrator or provided in a binding written agreement between Participant and the Company. Upon forfeiture of Unvested Shares, the Company will become the legal and beneficial owner of the Unvested Shares and all related interests and Participant will have no further rights with respect to the Unvested Shares.

17.3 Escrow.

(a) Unvested Shares will be held by the Company or its authorized representatives until (i) they are forfeited, (ii) they become Vested Shares or (iii) this Agreement is no longer in effect. By accepting this Award, Participant appoints the Company and its authorized representatives as Participant's attorney(s)-in-fact to take all actions necessary to effect any transfer of forfeited Unvested Shares (and Retained Distributions (as defined below), if any, paid on such forfeited Unvested Shares) to the Company as may be required pursuant to the Plan or this Agreement and to execute such representations or other documents or assurances as the Company or such representatives deem necessary or advisable in connection with any such transfer. The Company, or its authorized representative, will not be liable for any good faith act or omission with respect to the holding in escrow or transfer of the Restricted Shares.

(b) All cash dividends and other distributions made or declared with respect to

Unvested Shares ("***Retained Distributions***") will be held by the Company until the time (if ever) when the Unvested Shares to which such Retained Distributions relate become Vested Shares. The Company will establish a separate Retained Distribution bookkeeping account ("***Retained Distribution Account***") for each Unvested Share with respect to which Retained Distributions have been made or declared in cash and credit the Retained Distribution Account (without interest) on the date of payment with the amount of such cash made or declared with respect to the Unvested Share. Retained Distributions (including any Retained Distribution Account balance) will immediately and automatically be forfeited upon forfeiture of the Unvested Share with respect to which the Retained Distributions were paid or declared.

(c) As soon as reasonably practicable following the date on which an Unvested Share becomes a Vested Share, the Company will (i) cause the certificate (or a new certificate without the legend required by this Agreement, if Participant so requests) representing the Share to be delivered to Participant or, if the Share is held in book-entry form, cause the notations indicating the Share is subject to the restrictions of this Agreement to be removed and (ii) pay to Participant the Retained Distributions relating to the Share.

17.4 **Rights as Shareholder.** Except as otherwise provided in this Agreement or the Plan, upon issuance of the Restricted Shares by the Company, Participant will have all the rights of a shareholder with respect to the Restricted Shares, including the right to vote the Restricted Shares and to receive dividends or other distributions paid or made with respect to the Restricted Shares.

#### **ARTICLE XVIII. TAXATION AND TAX WITHHOLDING**

18.1 **Representation.** Participant represents to the Company that Participant has reviewed with Participant's own tax advisors the tax consequences of the Restricted Shares and the transactions contemplated by the Grant Notice and this Agreement. Participant is relying solely on such advisors and not on any statements or representations of the Company or any of its agents.

18.2 **Section 83(b) Election.** If Participant makes an election under Section 83(b) of the Code with respect to the Restricted Shares, Participant will deliver a copy of the election to the Company promptly after filing the election with the Internal Revenue Service.

18.3 **Tax Withholding.**

(a) The Company has the right and option, but not the obligation, to treat Participant's failure to provide timely payment in accordance with the Plan of any withholding tax arising in connection with the Restricted Shares as Participant's election to satisfy all or any portion of the withholding tax by requesting the Company retain Shares otherwise deliverable under the Award.

(b) Participant acknowledges that Participant is ultimately liable and responsible for all taxes owed in connection with the Restricted Shares, regardless of any action the Company or any Subsidiary takes with respect to any tax withholding obligations that arise in connection with the Restricted Shares. Neither the Company nor any Subsidiary makes any representation or undertaking regarding the treatment of any tax withholding in connection with the awarding, vesting or payment of the Restricted Shares or the subsequent sale of the Restricted Shares. The Company and the Subsidiaries do not commit and are under no obligation to structure this Award to reduce or eliminate Participant's tax liability.

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**ARTICLE XIX.  
RESTRICTIVE LEGENDS AND TRANSFERABILITY**

19.1 Legends. Any certificate representing a Restricted Share will bear the following legend until the Restricted Share becomes a Vested Share:

THE SHARES REPRESENTED BY THIS CERTIFICATE ARE  
SUBJECT TO FORFEITURE IN FAVOR OF THE COMPANY AND  
MAY BE TRANSFERRED ONLY IN ACCORDANCE WITH THE  
TERMS OF A RESTRICTED SHARE AGREEMENT BETWEEN THE  
COMPANY AND THE SHAREHOLDER, A COPY OF WHICH IS ON  
FILE WITH THE SECRETARY OF THE COMPANY.

19.2 Transferability. The Restricted Shares and any Retained Distributions are subject to the restrictions on transfer in the Plan and may not be sold, assigned or transferred in any manner unless and until they become Vested Shares. Any attempted transfer or disposition of Unvested Shares or related Retained Distributions prior to the time the Unvested Shares become Vested Shares will be null and void. The Company will not be required to (a) transfer on its books any Restricted Share that has been sold or otherwise transferred in violation of this Agreement or (b) treat as owner of such Restricted Share or accord the right to vote or pay dividends to any purchaser or other transferee to whom such Restricted Share has been so transferred. The Company may issue appropriate "stop transfer" instructions to its transfer agent, if any, or make appropriate notations to the same effect in its records.

**ARTICLE XX.  
OTHER PROVISIONS**

20.1 Adjustments. Participant acknowledges that the Restricted Shares are subject to adjustment, modification and termination in certain events as provided in this Agreement and the Plan.

20.2 Notices. Any notice to be given under the terms of this Agreement to the Company must be in writing and addressed to the Company in care of the Company's Secretary at the Company's principal office or the Secretary's then-current email address or facsimile number. Any notice to be given under the terms of this Agreement to Participant must be in writing and addressed to Participant at Participant's last known mailing address, email address or facsimile number in the Company's personnel files. By a notice given pursuant to this Section, either party may designate a different address for notices to be given to that party. Any notice will be deemed duly given when actually received, when sent by email, when sent by certified mail (return receipt requested) and deposited with postage prepaid in a post office or branch post office regularly maintained by the United States Postal Service, when delivered by a nationally recognized express shipping company or upon receipt of a facsimile transmission confirmation.

20.3 Titles. Titles are provided herein for convenience only and are not to serve as a basis for interpretation or construction of this Agreement.

20.4 Conformity to Securities Laws. Participant acknowledges that the Plan, the Grant Notice and this Agreement are intended to conform to the extent necessary with all Applicable Laws and, to the extent Applicable Laws permit, will be deemed amended as necessary to conform to Applicable Laws.

20.5 Successors and Assigns. The Company may assign any of its rights under this Agreement to single or multiple assignees, and this Agreement will inure to the benefit of the successors and assigns of the Company. Subject to the restrictions on transfer set forth in this Agreement or the

Plan, this Agreement will be binding upon and inure to the benefit of the heirs, legatees, legal representatives, successors and assigns of the parties hereto.

20.6 Limitations Applicable to Section 16 Persons. Notwithstanding any other provision of the Plan or this Agreement, if Participant is subject to Section 16 of the Exchange Act, the Plan, the Grant Notice, this Agreement and the Restricted Shares will be subject to any additional limitations set forth in any applicable exemptive rule under Section 16 of the Exchange Act (including any amendment to Rule 16b-3) that are requirements for the application of such exemptive rule. To the extent Applicable Laws permit, this Agreement will be deemed amended as necessary to conform to such applicable exemptive rule.

20.7 Entire Agreement. The Plan, the Grant Notice and this Agreement (including any exhibit hereto) constitute the entire agreement of the parties and supersede in their entirety all prior undertakings and agreements of the Company and Participant with respect to the subject matter hereof.

20.8 Agreement Severable. In the event that any provision of the Grant Notice or this Agreement is held illegal or invalid, the provision will be severable from, and the illegality or invalidity of the provision will not be construed to have any effect on, the remaining provisions of the Grant Notice or this Agreement.

20.9 Limitation on Participant's Rights. Participation in the Plan confers no rights or interests other than as herein provided. This Agreement creates only a contractual obligation on the part of the Company as to amounts payable and may not be construed as creating a trust. Neither the Plan nor any underlying program, in and of itself, has any assets. Participant will have only the rights of a general unsecured creditor of the Company with respect to amounts credited and benefits payable, if any, with respect to the Award.

20.10 Not a Contract of Employment. Nothing in the Plan, the Grant Notice or this Agreement confers upon Participant any right to continue in the employ or service of the Company or any Subsidiary or interferes with or restricts in any way the rights of the Company and its Subsidiaries, which rights are hereby expressly reserved, to discharge or terminate the services of Participant at any time for any reason whatsoever, with or without cause, except to the extent expressly provided otherwise in a written agreement between the Company or a Subsidiary and Participant.

20.11 Counterparts. The Grant Notice may be executed in one or more counterparts, including by way of any electronic signature, subject to Applicable Law, each of which will be deemed an original and all of which together will constitute one instrument.

\* \* \* \* \*

**VERONA PHARMA PLC  
2017 INCENTIVE AWARD PLAN**

**PERFORMANCE RESTRICTED SHARE UNIT GRANT NOTICE**

Capitalized terms not specifically defined in this Performance Restricted Share Unit Grant Notice (the “*Grant Notice*”) have the meanings given to them in the 2017 Incentive Award Plan (as amended from time to time, the “*Plan*”) of Verona Pharma plc (the “*Company*”).

The Company has granted to the participant listed below (“*Participant*”) the Performance Restricted Share Units described in this Grant Notice (the “*PRSUs*”), subject to the terms and conditions of the Plan and the Performance Restricted Share Unit Agreement attached as **Exhibit A** (the “*Agreement*”), both of which are incorporated into this Grant Notice by reference.

**Participant:**

**Grant Date:**

**Number of PRSUs:**

**Vesting Commencement Date:**

**Vesting Schedule:** [To be specified in individual award agreements]

By Participant’s signature below, Participant agrees to be bound by the terms of this Grant Notice, the Plan and the Agreement. Participant has reviewed the Plan, this Grant Notice and the Agreement in their entirety, has had an opportunity to obtain the advice of counsel prior to executing this Grant Notice and fully understands all provisions of the Plan, this Grant Notice and the Agreement. Participant hereby agrees to accept as binding, conclusive and final all decisions or interpretations of the Administrator upon any questions arising under the Plan, this Grant Notice or the Agreement.

**VERONA PHARMA PLC**

**PARTICIPANT**

By: \_\_\_\_\_

Name: \_\_\_\_\_

Title: \_\_\_\_\_

\_\_\_\_\_

[Participant Name]

**PERFORMANCE RESTRICTED SHARE UNIT AGREEMENT**

Capitalized terms not specifically defined in this Agreement have the meanings specified in the Grant Notice or, if not defined in the Grant Notice, in the Plan.

**ARTICLE XXI.  
GENERAL**

**21.1 Award of PRSUs and Dividend Equivalents.**

(a) The Company has granted the PRSUs to Participant effective as of the grant date set forth in the Grant Notice (the “**Grant Date**”). Each PRSU represents the right to receive one Share or, at the option of the Company, an amount of cash, in either case, as set forth in this Agreement. Participant will have no right to the distribution of any Shares or payment of any cash until the time (if ever) the PRSUs have vested.

(b) The Company hereby grants to Participant, with respect to each PRSU, a Dividend Equivalent for ordinary cash dividends paid to substantially all holders of outstanding Shares with a record date after the Grant Date and prior to the date the applicable PRSU is settled, forfeited or otherwise expires. Each Dividend Equivalent entitles Participant to receive the equivalent value of any such ordinary cash dividends paid on a single Share. The Company will establish a separate Dividend Equivalent bookkeeping account (a “**Dividend Equivalent Account**”) for each Dividend Equivalent and credit the Dividend Equivalent Account (without interest) on the applicable dividend payment date with the amount of any such cash paid.

**21.2 Incorporation of Terms of Plan.** The PRSUs are subject to the terms and conditions set forth in this Agreement and the Plan, which is incorporated herein by reference. In the event of any inconsistency between the Plan and this Agreement, the terms of the Plan will control.

**21.3 Unsecured Promise.** The PRSUs and Dividend Equivalents will at all times prior to settlement represent an unsecured Company obligation payable only from the Company’s general assets.

**ARTICLE XXII.  
VESTING; FORFEITURE AND SETTLEMENT**

**22.1 Vesting; Forfeiture.** The PRSUs will vest according to the vesting schedule in the Grant Notice except that any fraction of an PRSU that would otherwise be vested will be accumulated and will vest only when a whole PRSU has accumulated. In the event of Participant’s Termination of Service for any reason, all unvested PRSUs will immediately and automatically be cancelled and forfeited, except as otherwise determined by the Administrator or provided in a binding written agreement between Participant and the Company. Dividend Equivalents (including any Dividend Equivalent Account balance) will vest or be forfeited, as applicable, upon the vesting or forfeiture of the PRSU with respect to which the Dividend Equivalent (including the Dividend Equivalent Account) relates.

**22.2 Settlement.**

(a) PRSUs and Dividend Equivalents (including any Dividend Equivalent Account balance) will be paid in Shares or cash at the Company’s option as soon as administratively practicable after the vesting of the applicable PRSU, but in no event more than sixty (60) days after the PRSU’s vesting date. Notwithstanding the foregoing, the Company may delay any payment under this Agreement



that the Company reasonably determines would violate Applicable Law until the earliest date the Company reasonably determines the making of the payment will not cause such a violation.

(b) If an PRSU is paid in cash, the amount of cash paid with respect to the PRSU will equal the Fair Market Value of a Share on the day immediately preceding the payment date. If a Dividend Equivalent is paid in Shares, the number of Shares paid with respect to the Dividend Equivalent will equal the quotient, rounded down to the nearest whole Share, of the Dividend Equivalent Account balance divided by the Fair Market Value of a Share on the day immediately preceding the payment date.

### **ARTICLE XXIII. TAXATION AND TAX WITHHOLDING**

23.1 Representation. Participant represents to the Company that Participant has reviewed with Participant's own tax advisors the tax consequences of this Award and the transactions contemplated by the Grant Notice and this Agreement. Participant is relying solely on such advisors and not on any statements or representations of the Company or any of its agents.

#### **23.2 Tax Withholding.**

(a) The Company has the right and option, but not the obligation, to treat Participant's failure to provide timely payment in accordance with the Plan of any withholding tax arising in connection with the PRSUs or Dividend Equivalents as Participant's election to satisfy all or any portion of the withholding tax by requesting the Company retain Shares otherwise issuable under the Award.

(b) Participant acknowledges that Participant is ultimately liable and responsible for all taxes owed in connection with the PRSUs and the Dividend Equivalents, regardless of any action the Company or any Subsidiary takes with respect to any tax withholding obligations that arise in connection with the PRSUs or Dividend Equivalents. Neither the Company nor any Subsidiary makes any representation or undertaking regarding the treatment of any tax withholding in connection with the awarding, vesting or payment of the PRSUs or the Dividend Equivalents or the subsequent sale of Shares. The Company and the Subsidiaries do not commit and are under no obligation to structure the PRSUs or Dividend Equivalents to reduce or eliminate Participant's tax liability.

### **ARTICLE XXIV. OTHER PROVISIONS**

24.1 Adjustments. Participant acknowledges that the PRSUs, the Shares subject to the PRSUs and the Dividend Equivalents are subject to adjustment, modification and termination in certain events as provided in this Agreement and the Plan.

24.2 Notices. Any notice to be given under the terms of this Agreement to the Company must be in writing and addressed to the Company in care of the Company's Secretary at the Company's principal office or the Secretary's then-current email address or facsimile number. Any notice to be given under the terms of this Agreement to Participant must be in writing and addressed to Participant at Participant's last known mailing address, email address or facsimile number in the Company's personnel files. By a notice given pursuant to this Section, either party may designate a different address for notices to be given to that party. Any notice will be deemed duly given when actually received, when sent by email, when sent by certified mail (return receipt requested) and deposited with postage prepaid in a post office or branch post office regularly maintained by the United States Postal Service, when delivered by a nationally recognized express shipping company or upon receipt of a facsimile transmission confirmation.

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24.3 Titles. Titles are provided herein for convenience only and are not to serve as a basis for interpretation or construction of this Agreement.

24.4 Conformity to Securities Laws. Participant acknowledges that the Plan, the Grant Notice and this Agreement are intended to conform to the extent necessary with all Applicable Laws and, to the extent Applicable Laws permit, will be deemed amended as necessary to conform to Applicable Laws.

24.5 Successors and Assigns. The Company may assign any of its rights under this Agreement to single or multiple assignees, and this Agreement will inure to the benefit of the successors and assigns of the Company. Subject to the restrictions on transfer set forth in the Plan, this Agreement will be binding upon and inure to the benefit of the heirs, legatees, legal representatives, successors and assigns of the parties hereto.

24.6 Limitations Applicable to Section 16 Persons. Notwithstanding any other provision of the Plan or this Agreement, if Participant is subject to Section 16 of the Exchange Act, the Plan, the Grant Notice, this Agreement, the PRSUs and the Dividend Equivalents will be subject to any additional limitations set forth in any applicable exemptive rule under Section 16 of the Exchange Act (including any amendment to Rule 16b-3) that are requirements for the application of such exemptive rule. To the extent Applicable Laws permit, this Agreement will be deemed amended as necessary to conform to such applicable exemptive rule.

24.7 Entire Agreement. The Plan, the Grant Notice and this Agreement (including any exhibit hereto) constitute the entire agreement of the parties and supersede in their entirety all prior undertakings and agreements of the Company and Participant with respect to the subject matter hereof.

24.8 Agreement Severable. In the event that any provision of the Grant Notice or this Agreement is held illegal or invalid, the provision will be severable from, and the illegality or invalidity of the provision will not be construed to have any effect on, the remaining provisions of the Grant Notice or this Agreement.

24.9 Limitation on Participant's Rights. Participation in the Plan confers no rights or interests other than as herein provided. This Agreement creates only a contractual obligation on the part of the Company as to amounts payable and may not be construed as creating a trust. Neither the Plan nor any underlying program, in and of itself, has any assets. Participant will have only the rights of a general unsecured creditor of the Company with respect to amounts credited and benefits payable, if any, with respect to the PRSUs and Dividend Equivalents, and rights no greater than the right to receive cash or the Shares as a general unsecured creditor with respect to the PRSUs and Dividend Equivalents, as and when settled pursuant to the terms of this Agreement.

24.10 Not a Contract of Employment. Nothing in the Plan, the Grant Notice or this Agreement confers upon Participant any right to continue in the employ or service of the Company or any Subsidiary or interferes with or restricts in any way the rights of the Company and its Subsidiaries, which rights are hereby expressly reserved, to discharge or terminate the services of Participant at any time for any reason whatsoever, with or without Cause, except to the extent expressly provided otherwise in a written agreement between the Company or a Subsidiary and Participant.

24.11 Counterparts. The Grant Notice may be executed in one or more counterparts, including by way of any electronic signature, subject to Applicable Law, each of which will be deemed an original and all of which together will constitute one instrument.

\* \* \* \* \*

<p style="text-align: center;"><b>VERONA PHARMA PLC</b> <b>2017 INCENTIVE AWARD PLAN</b></p>
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**RESTRICTED SHARE UNIT GRANT NOTICE**

Capitalized terms not specifically defined in this Restricted Share Unit Grant Notice (the “*Grant Notice*”) have the meanings given to them in the 2017 Incentive Award Plan (as amended from time to time, the “*Plan*”) of Verona Pharma plc (the “*Company*”).

The Company has granted to the participant listed below (“*Participant*”) the Restricted Share Units described in this Grant Notice (the “*RSUs*”), subject to the terms and conditions of the Plan and the Restricted Share Unit Agreement attached as **Exhibit A** (the “*Agreement*”), both of which are incorporated into this Grant Notice by reference.

**Participant:**

**Grant Date:**

**Number of RSUs:**

**Vesting Commencement Date:**

**Vesting Schedule:** [To be specified in individual award agreements]

By Participant’s signature below, Participant agrees to be bound by the terms of this Grant Notice, the Plan and the Agreement. Participant has reviewed the Plan, this Grant Notice and the Agreement in their entirety, has had an opportunity to obtain the advice of counsel prior to executing this Grant Notice and fully understands all provisions of the Plan, this Grant Notice and the Agreement. Participant hereby agrees to accept as binding, conclusive and final all decisions or interpretations of the Administrator upon any questions arising under the Plan, this Grant Notice or the Agreement.

**VERONA PHARMA PLC**

**PARTICIPANT**

By: \_\_\_\_\_

Name: \_\_\_\_\_

Title: \_\_\_\_\_

\_\_\_\_\_

[Participant Name]

**RESTRICTED SHARE UNIT AGREEMENT**

Capitalized terms not specifically defined in this Agreement have the meanings specified in the Grant Notice or, if not defined in the Grant Notice, in the Plan.

**ARTICLE XXV.  
GENERAL**

**25.1 Award of RSUs and Dividend Equivalents.**

(a) The Company has granted the RSUs to Participant effective as of the grant date set forth in the Grant Notice (the “**Grant Date**”). Each RSU represents the right to receive one Share or, at the option of the Company, an amount of cash, in either case, as set forth in this Agreement. Participant will have no right to the distribution of any Shares or payment of any cash until the time (if ever) the RSUs have vested.

(b) The Company hereby grants to Participant, with respect to each RSU, a Dividend Equivalent for ordinary cash dividends paid to substantially all holders of outstanding Shares with a record date after the Grant Date and prior to the date the applicable RSU is settled, forfeited or otherwise expires. Each Dividend Equivalent entitles Participant to receive the equivalent value of any such ordinary cash dividends paid on a single Share. The Company will establish a separate Dividend Equivalent bookkeeping account (a “**Dividend Equivalent Account**”) for each Dividend Equivalent and credit the Dividend Equivalent Account (without interest) on the applicable dividend payment date with the amount of any such cash paid.

**25.2 Incorporation of Terms of Plan.** The RSUs are subject to the terms and conditions set forth in this Agreement and the Plan, which is incorporated herein by reference. In the event of any inconsistency between the Plan and this Agreement, the terms of the Plan will control.

**25.3 Unsecured Promise.** The RSUs and Dividend Equivalents will at all times prior to settlement represent an unsecured Company obligation payable only from the Company’s general assets.

**ARTICLE XXVI.  
VESTING; FORFEITURE AND SETTLEMENT**

**26.1 Vesting; Forfeiture.** The RSUs will vest according to the vesting schedule in the Grant Notice except that any fraction of an RSU that would otherwise be vested will be accumulated and will vest only when a whole RSU has accumulated. In the event of Participant’s Termination of Service for any reason, all unvested RSUs will immediately and automatically be cancelled and forfeited, except as otherwise determined by the Administrator or provided in a binding written agreement between Participant and the Company. Dividend Equivalents (including any Dividend Equivalent Account balance) will vest or be forfeited, as applicable, upon the vesting or forfeiture of the RSU with respect to which the Dividend Equivalent (including the Dividend Equivalent Account) relates.

**26.2 Settlement.**

(a) RSUs and Dividend Equivalents (including any Dividend Equivalent Account balance) will be paid in Shares or cash at the Company’s option as soon as administratively practicable after the vesting of the applicable RSU, but in no event more than sixty (60) days after the RSU’s vesting date. Notwithstanding the foregoing, the Company may delay any payment under this Agreement that the

Company reasonably determines would violate Applicable Law until the earliest date the Company reasonably determines the making of the payment will not cause such a violation.

(b) If an RSU is paid in cash, the amount of cash paid with respect to the RSU will equal the Fair Market Value of a Share on the day immediately preceding the payment date. If a Dividend Equivalent is paid in Shares, the number of Shares paid with respect to the Dividend Equivalent will equal the quotient, rounded down to the nearest whole Share, of the Dividend Equivalent Account balance divided by the Fair Market Value of a Share on the day immediately preceding the payment date.

## **ARTICLE XXVII. TAXATION AND TAX WITHHOLDING**

27.1 Representation. Participant represents to the Company that Participant has reviewed with Participant's own tax advisors the tax consequences of this Award and the transactions contemplated by the Grant Notice and this Agreement. Participant is relying solely on such advisors and not on any statements or representations of the Company or any of its agents.

### 27.2 Tax Withholding.

(a) The Company has the right and option, but not the obligation, to treat Participant's failure to provide timely payment in accordance with the Plan of any withholding tax arising in connection with the RSUs or Dividend Equivalents as Participant's election to satisfy all or any portion of the withholding tax by requesting the Company retain Shares otherwise issuable under the Award.

(b) Participant acknowledges that Participant is ultimately liable and responsible for all taxes owed in connection with the RSUs and the Dividend Equivalents, regardless of any action the Company or any Subsidiary takes with respect to any tax withholding obligations that arise in connection with the RSUs or Dividend Equivalents. Neither the Company nor any Subsidiary makes any representation or undertaking regarding the treatment of any tax withholding in connection with the awarding, vesting or payment of the RSUs or the Dividend Equivalents or the subsequent sale of Shares. The Company and the Subsidiaries do not commit and are under no obligation to structure the RSUs or Dividend Equivalents to reduce or eliminate Participant's tax liability.

## **ARTICLE XXVIII. OTHER PROVISIONS**

28.1 Adjustments. Participant acknowledges that the RSUs, the Shares subject to the RSUs and the Dividend Equivalents are subject to adjustment, modification and termination in certain events as provided in this Agreement and the Plan.

28.2 Notices. Any notice to be given under the terms of this Agreement to the Company must be in writing and addressed to the Company in care of the Company's Secretary at the Company's principal office or the Secretary's then-current email address or facsimile number. Any notice to be given under the terms of this Agreement to Participant must be in writing and addressed to Participant at Participant's last known mailing address, email address or facsimile number in the Company's personnel files. By a notice given pursuant to this Section, either party may designate a different address for notices to be given to that party. Any notice will be deemed duly given when actually received, when sent by email, when sent by certified mail (return receipt requested) and deposited with postage prepaid in a post office or branch post office regularly maintained by the United States Postal Service, when delivered by a nationally recognized express shipping company or upon receipt of a facsimile transmission confirmation.

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28.3 Titles. Titles are provided herein for convenience only and are not to serve as a basis for interpretation or construction of this Agreement.

28.4 Conformity to Securities Laws. Participant acknowledges that the Plan, the Grant Notice and this Agreement are intended to conform to the extent necessary with all Applicable Laws and, to the extent Applicable Laws permit, will be deemed amended as necessary to conform to Applicable Laws.

28.5 Successors and Assigns. The Company may assign any of its rights under this Agreement to single or multiple assignees, and this Agreement will inure to the benefit of the successors and assigns of the Company. Subject to the restrictions on transfer set forth in the Plan, this Agreement will be binding upon and inure to the benefit of the heirs, legatees, legal representatives, successors and assigns of the parties hereto.

28.6 Limitations Applicable to Section 16 Persons. Notwithstanding any other provision of the Plan or this Agreement, if Participant is subject to Section 16 of the Exchange Act, the Plan, the Grant Notice, this Agreement, the RSUs and the Dividend Equivalents will be subject to any additional limitations set forth in any applicable exemptive rule under Section 16 of the Exchange Act (including any amendment to Rule 16b-3) that are requirements for the application of such exemptive rule. To the extent Applicable Laws permit, this Agreement will be deemed amended as necessary to conform to such applicable exemptive rule.

28.7 Entire Agreement. The Plan, the Grant Notice and this Agreement (including any exhibit hereto) constitute the entire agreement of the parties and supersede in their entirety all prior undertakings and agreements of the Company and Participant with respect to the subject matter hereof.

28.8 Agreement Severable. In the event that any provision of the Grant Notice or this Agreement is held illegal or invalid, the provision will be severable from, and the illegality or invalidity of the provision will not be construed to have any effect on, the remaining provisions of the Grant Notice or this Agreement.

28.9 Limitation on Participant's Rights. Participation in the Plan confers no rights or interests other than as herein provided. This Agreement creates only a contractual obligation on the part of the Company as to amounts payable and may not be construed as creating a trust. Neither the Plan nor any underlying program, in and of itself, has any assets. Participant will have only the rights of a general unsecured creditor of the Company with respect to amounts credited and benefits payable, if any, with respect to the RSUs and Dividend Equivalents, and rights no greater than the right to receive cash or the Shares as a general unsecured creditor with respect to the RSUs and Dividend Equivalents, as and when settled pursuant to the terms of this Agreement.

28.10 Not a Contract of Employment. Nothing in the Plan, the Grant Notice or this Agreement confers upon Participant any right to continue in the employ or service of the Company or any Subsidiary or interferes with or restricts in any way the rights of the Company and its Subsidiaries, which rights are hereby expressly reserved, to discharge or terminate the services of Participant at any time for any reason whatsoever, with or without Cause, except to the extent expressly provided otherwise in a written agreement between the Company or a Subsidiary and Participant.

28.11 Counterparts. The Grant Notice may be executed in one or more counterparts, including by way of any electronic signature, subject to Applicable Law, each of which will be deemed an original and all of which together will constitute one instrument.

\* \* \* \* \*





EXECUTION COPY



**Verona Pharma**

May 1, 2017

Armi Desiree Elisabeth Luthman  
306 Windy Run Road  
Doylestown, Pennsylvania 18901  
USA

**Re: Offer of Employment**

Dear Desiree:

On behalf of Verona Pharma, Inc. (the "Company" or "Verona Pharma"), I am pleased to offer you the position of Vice President, Regulatory Affairs. This offer letter agreement (the "Agreement") sets forth the terms of employment the Company is offering you. If you accept this offer, we anticipate that your first day of employment will be mid-June 2017 ("Commencement Date").

**1. DUTIES.** As the Company's Vice President, Regulatory Affairs, you will be responsible for the development and implementation of regulatory strategy, and prepare, coordinate, manage and maintain regulatory submissions in accordance with applicable regulations by FDA, EMA and select countries; provide regulatory review of key documents; interface with external regulatory groups and act as liaison between Regulatory Affairs and other functional areas; represent Regulatory Affairs in cross-functional team meetings; author and review standard operating procedures (SOPs) in area of expertise; ensure SOPs are in compliance with current regulatory requirements and provide regulatory support for corporate quality assurance efforts. You will also participate in the oversight of the currently outsourced pharmacovigilance function and perform the other duties associated with this position. You will report to the Chief Executive Officer (the "Manager") of Verona Pharma plc, the Company's parent company (the "Parent"). You will perform your services at the Company's office in White Plains, New York and will attend such office on average not less than two full days per week. In the event that the Company asks you to relocate, the Company will reimburse your relocation expenses on terms to be mutually agreed upon prior to the relocation. You shall devote your full time and attention to the business affairs of the Company.

**2. BASE SALARY.** You will receive an annual base salary of \$265,000 for all hours worked, less payroll deductions and withholdings, earned and payable in substantially equal installments in accordance with the Company's payroll policy from time to time in effect.



3. **BONUS.** You will be eligible to participate in the Company's annual bonus plan, with a target bonus of 25% of your base salary, subject to the terms of such plan and on such other terms and conditions as may be determined by the Company. You must be employed on the date of payment of the bonus in order to be eligible for the bonus.

4. **STOCK OPTIONS.** Subject to the approval of the board of directors of the Parent, and as soon as reasonably practicable after the Commencement Date having regard to the Parent's Share Dealing Policy, you will be granted, pursuant to, and subject to, Parent's equity incentive plan, an option to subscribe for a total of 20,000 American Depositary Shares in the capital of Parent (the "Stock Option"). The definitive terms of the Stock Option will be governed by the equity incentive plan, which requires, as a condition of the grant, that you enter into a written option agreement, which will contain the definitive terms of the Stock Option. The Stock Option shall vest in equal proportions over three years from the date of grant, or earlier in the event of a change in control of Parent (as defined in the equity incentive plan or option agreement), in each case subject to your continued employment through such date or such change in control.

5. **BENEFITS.** You will be entitled to participate in the Company's 401(k) plan and healthcare plan generally available from time to time to employees of the Company, subject to the terms of such plans. In addition, the Company will procure short-term disability insurance for you in accordance with New York state law. You will be entitled to four (4) weeks of paid time off per year, earned and accrued on a pro rata basis throughout the year, provided that except with the prior written approval of the Manager, you may carry over five days of accrued but unused time into the first quarter of the subsequent year. You will not be paid for any accrued but unused time upon termination of employment.

6. **EXPENSES.** You shall be entitled to reimbursement for all ordinary and reasonable out-of-pocket business expenses which are reasonably incurred by you in furtherance of the Company's business and in accordance with the standard policies of the Company and Parent, provided that you produce to the Company such evidence of actual payment as the Company may require.

7. **SEVERANCE BENEFITS.**

(a) **Termination By The Company Without Cause or Termination by the Employee for Good Reason.** If this Agreement is terminated by the Company without Cause (as defined below) or by the Employee for Good Reason (as defined below), and if you sign an agreement acceptable to the Company that (i) waives any rights you may otherwise have against the Company and Parent, (ii) releases the Company and Parent from any actions, suits, claims, proceedings and demands you may have relating to the period of your employment with the Company and/or the termination of your employment, and (iii) contains certain other obligations which will be set forth at the time of the termination, the Company shall provide you with the following severance benefits: (1) continuation of your base salary less payroll deductions and withholding for a period of eight (8) weeks; (2) continued payment, or reimbursement, as the case may be, of your COBRA premiums at the rate in effect upon termination for a period of eight (8) weeks; and (3) a pro-rated portion of the annual bonus you otherwise would have earned for the year in which termination occurs, if any, based upon actual performance for such year.

**(b) Termination By The Company With Cause, By Reason of Death or Disability or By Resignation.** If this Agreement is terminated by the Company at any time with Cause, by reason of your death or disability, or if you terminate your employment with the Company under this Agreement, you shall not be entitled to any severance pay, severance benefits, accelerated vesting or any compensation or benefits from the Company whatsoever.

**(c) Definitions:**

A. **Cause.** "Cause" for purposes of this Agreement shall mean if you: (1) shall have committed any felony or any other act involving fraud, theft, misappropriation, dishonesty, or embezzlement; (2) shall have committed intentional acts that materially impair the goodwill or business of the Company or Parent or cause material damage to Company's or Parent's property, goodwill, or business; (3) shall have refused to, or willfully failed to, perform your material duties hereunder; or (4) shall have violated any written policies or procedures of the Company or Parent.

B. **Good Reason.** "Good Reason" for purposes of this Agreement shall mean if (i) the Company moves or relocates the Employee and the Employee is unable to achieve on reasonable terms approximately equivalent living circumstances to his situation in the New York metropolitan area, (ii) the Employee is demoted or assigned duties of less seniority than his duties under this Agreement, or (iii) the Company decreases by 15% or more the Employee's base salary and target bonus under this Agreement. In order for the Employee to terminate his Employment for "Good Reason" under this paragraph, immediately after becoming aware of the breach or other event giving rise to the Employee's right to terminate, the Employee must have provided the Company with written notice of his right to terminate pursuant to this paragraph and the Company must have failed to cure the breach or other event so specified, if curable, within thirty days after receiving such notice.

C. **Release Requirement and Timing of Severance Payments.** In order to receive the severance benefits under paragraph (a) above, as applicable, you must sign and tender the release as described above not later than sixty (60) days following your last day of employment, or such earlier date as required by the Company, and if you fail or refuse to do so, you shall forfeit the right to such termination compensation as would otherwise be due and payable. If the severance payments are otherwise subject to Section 409A of the Internal Revenue Code of 1986, as amended (the "Code"), they shall begin on the first pay period following the date that is sixty (60) days after your employment terminates and shall otherwise begin on the first pay period after the release becomes effective (with the initial salary continuation payment to include any unpaid salary continuation payments from the date your employment terminated), subject to your executing and tendering the release on the terms as set forth in the immediately preceding sentence. The pro-rated bonus, if any, shall be paid when such bonus would have been paid absent the termination of your employment and in all cases in the calendar year following the fiscal year to which the bonus relates.

**8. COMPANY POLICIES AND CONFIDENTIALITY AGREEMENT.** As an employee of the Company, you will be expected to abide by all of the applicable policies and procedures of the Company and Parent. As a condition of your employment, you agree to sign and to abide by the terms of a Protective Agreement with the Company, which is attached hereto as Exhibit A.

**9. NEW YORK WAGE THEFT PREVENTION ACT NOTICE.** Attached as Exhibit B a notice containing certain information regarding your pay as required by the New York Wage Theft Prevention Act.

**10. AT-WILL EMPLOYMENT.** As an employee of the Company, you may terminate your employment at any time and for any reason whatsoever simply by notifying the Company. Similarly, the Company may terminate your employment at any time and for any reason whatsoever, with or without cause or advance notice. Your at-will employment relationship with the Company cannot be changed except in writing signed by the Manager.

**11. ENTIRE AGREEMENT.** This Agreement, including Exhibit A, constitutes the complete, final and exclusive embodiment of the entire agreement between you and the Company with respect to the terms and conditions of your employment specified herein. If you enter into this Agreement, you are doing so voluntarily, and without reliance upon any promise, warranty or representation, written or oral, other than those expressly contained herein. This Agreement supersedes any other such promises, warranties, representations or agreements. This Agreement may not be amended or modified except by a written instrument signed by you and the CEO.

**12. GOVERNING LAW.** This Agreement will be governed by and construed in accordance with the laws of the State of New York.

**13. DISPUTE RESOLUTION.** To ensure the timely and economical resolution of disputes that arise in connection with your employment with the Company, you and the Company agree that any and all disputes, claims, or causes of action arising from or relating to the enforcement, breach, performance or interpretation of this Agreement, your employment, or the termination of your employment, shall be resolved to the fullest extent permitted by law by final, binding and confidential arbitration, by a single arbitrator, in New York, New York, conducted by Judicial Arbitration and Mediation Services, Inc. ("JAMS") under the applicable JAMS employment rules. **By agreeing to this arbitration procedure, both you and the Company waive the right to resolve any such dispute through a trial by jury or judge or administrative proceeding.** Judgment upon the award rendered by the arbitrator may be entered in any court having jurisdiction thereof in the State of New York. In reaching his or her decision, the arbitrator shall have no authority (a) to authorize or require the parties to engage in discovery (provided, however, that the arbitrator may schedule the time by which the parties must exchange copies of the exhibits that, and the names of the witnesses whom, the parties intend to present at the hearing) (b) to interpret or enforce the Protective Agreement (which shall not be covered by the dispute resolutions contained in this paragraph), (c) to change or modify any provision of this Agreement, (d) to base any part of his or her decision on the common law principle of constructive termination, or (e) to award punitive damages or any other damages not measured by the prevailing party's actual damages and may not make any ruling, finding or award that does not conform to this Agreement. Each party shall bear his, her or its own legal fees, costs and expenses of arbitration and one-half (1/2) of the costs of the arbitrator.

**14. SECTION 409A.** You and the Company intend that the payments and benefits provided for in this letter either be exempt from Section 409A of the Code, or be provided for in a manner that complies with Section 409A of the Code, and any ambiguity herein shall be interpreted so as to be consistent with the intent of this Section 14. In no event whatsoever shall the Company be liable for any additional tax, interest or penalty that may be imposed on you by Section 409A of the Code or damages for failing to comply with Section 409A of the Code. Notwithstanding anything contained herein to the contrary, all payments and benefits under Section 7 above shall be paid or provided only at the time of a termination of your employment that constitutes a "separation from service" from the Company within the meaning of Section 409A of the Code and the regulations and guidance promulgated thereunder (determined after applying the presumptions set forth in Treas. Reg. Section 1.409A-1(h)(1)). Further, if you are a "specified employee" as such term is defined under Section 409A of the Code and the regulations and guidance promulgated thereunder, any payments described in Section 7 above shall be delayed for a period of six (6) months following your separation of employment to the extent and up to an amount necessary to ensure such payments are not subject to the penalties and interest under Section 409A of the Code. In addition, (i) in-kind benefits and reimbursements provided under this Agreement during any calendar year shall not affect in-kind benefits or reimbursements to be provided in any other calendar year, other than an arrangement providing for the reimbursement of medical expenses referred to in Section 105(b) of the Code, and are not subject to liquidation or exchange for another benefit and (ii) reimbursement requests must be timely submitted by you and, if timely submitted, reimbursement payments shall be promptly made to you following such submission, but in no event later than December 31<sup>st</sup> of the calendar year following the calendar year in which the expense was incurred. In no event shall you be entitled to any reimbursement payments after December 31<sup>st</sup> of the calendar year following the calendar year in which the expense was incurred. The reimbursement provisions in this Section 14 shall only apply to in-kind benefits and reimbursements that would result in taxable compensation income to you.

**15. AUTHORIZATION TO WORK AND BACKGROUND CHECK.** Your employment with the Company is contingent upon satisfactory results from any pre-employment background checks that we may deem necessary, including, but not limited to, a credit check, criminal background check, drug screening and confirmation of your legal authorization to work in the United States. Our offer is also contingent upon you not being subject to any limitation, obligation or agreement, whether imposed by contract, statute or otherwise, that would preclude your employment by the Company or in any way restrict your ability to perform your duties as an employee. If you have provided the Company with any false information with respect to your employment history, educational background or other credentials, the offer of employment contained herein shall be withdrawn or, if you have already been hired, your employment shall be immediately terminated.

If you choose to accept this Agreement under the terms described above, please sign below and return this letter to me no later than May 15, 2017.

We look forward to your favorable reply, and to a productive and enjoyable work relationship.

Very truly yours,

Verona Pharma, Inc.

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Name: Jan-Anders Karlsson  
Position: Director

*Accepted and Agreed to by:*

---

Employee Name: Armi Desiree Elisabeth Luthman

Date: \_\_\_\_\_

Exhibit A

Protective Agreement

(attached)

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Exhibit B

New York Wage Theft Prevention Act Notice  
(attached)

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Agreement Date : 19 October 2017 Confirmation No : R-380019

## Business Centre Details

LONDON, London Bridge - More London

Sales Manager Max Chapman

## Client Details

Company Name VERONA PHARMA PLC

Phone 02032834000

Email piers.morgan@veronapharma.com

## Office Payment Details (exc.VAT and exc. services)

Office Number	Number of people	Price per Office
145A	6	£ 11,000.00
151	1	£ 2,858.00

Service Provision :	Start Date	1 January 2018	End Date	31 January 2020
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All agreements end on the last calendar day of the month.

## Terms and Conditions

We are IW Group Services (UK) Limited [the Provider], please click the link below for terms and conditions.

By signing our service Agreement, you agree to provide information and sign relevant documents to allow the Provider to claim any relief on business rates which at the Provider's risk is already included in your service fee with reference to the Business Centre within 2 working days of such request. The Provider has appointed Gerald Eve LLP Rating Payment Management Services to administer such information.

[Download the terms and conditions](#)[Download the house rules](#)

This website is secure. Your personal details are protected at all times.

[Print Agreement](#)

## **1. This Agreement**

1.1 Nature of this agreement: This agreement is the commercial equivalent of an agreement for accommodation(s) in a hotel. The whole of the Centre remains in the Provider's possession and control. THE CLIENT ACCEPTS THAT THIS AGREEMENT CREATES NO TENANCY INTEREST, LEASEHOLD ESTATE OR OTHER REAL PROPERTY INTEREST IN THE CLIENT'S FAVOUR WITH RESPECT TO THE ACCOMMODATION(S). The Provider is giving the Client the right to share with the Provider the use of the Centre on these terms and conditions, as supplemented by the House Rules, so that the Provider can provide the services to the Client. This Agreement is personal to the Client and cannot be transferred to anyone else without prior consent from the Provider unless such transfer is required by law. The Provider will not unreasonably withhold its consent to assignment to a parent, subsidiary or affiliate of Client provided that Client and assignee execute the Provider's form of Assignment of License Agreement which will require assignee to assume all Client obligations and will not release the Client. This agreement is composed of the front page describing the accommodation(s), the present terms and conditions, the House Rules and the Service Price Guide (where available).

1.2 Comply with House Rules: The Client must comply with any House Rules which the Provider imposes generally on users of the Centre. The House Rules vary from country to country and from Centre to Centre and these can be requested locally.

1.3 AUTOMATIC RENEWAL: THIS AGREEMENT LASTS FOR THE PERIOD STATED IN IT AND THEN **WILL BE EXTENDED AUTOMATICALLY FOR SUCCESSIVE PERIODS EQUAL TO THE CURRENT TERM BUT NO LESS THAN 3 MONTHS** (UNLESS LEGAL RENEWAL TERM LIMITS APPLY) UNTIL TERMINATED BY THE CLIENT OR BY THE PROVIDER PURSUANT TO SECTION 1.4. ALL PERIODS SHALL RUN TO THE LAST DAY OF THE MONTH IN WHICH THEY WOULD OTHERWISE EXPIRE. THE FEES ON ANY RENEWAL WILL BE AT THE THEN PREVAILING MARKET RATE. THIS CLAUSE DOES NOT APPLY TO MONTH TO MONTH AGREEMENTS.

1.4 **CANCELLATION:** EITHER THE PROVIDER OR THE CLIENT CAN TERMINATE THIS AGREEMENT AT THE END DATE STATED IN IT, OR AT THE END OF ANY EXTENSION OR RENEWAL PERIOD, BY GIVING AT LEAST THREE MONTHS WRITTEN NOTICE TO THE OTHER. HOWEVER, IF THIS AGREEMENT, EXTENSION OR RENEWAL IS FOR THREE MONTHS OR LESS AND EITHER THE PROVIDER OR THE CLIENT WISHES TO TERMINATE IT, THE NOTICE PERIOD IS TWO MONTHS IF THIS AGREEMENT, EXTENSION OR RENEWAL IS FOR TWO MONTHS OR LESS, NOTICE MUST BE GIVEN WITHIN ONE WEEK OF THE START DATE OF THE CURRENT TERM. IF THE CLIENT IS ON A MONTH TO MONTH AGREEMENT EITHER PARTY MAY TERMINATE THIS AGREEMENT BY GIVING NO LESS THAN ONE MONTHS' NOTICE TO THE OTHER (EFFECTIVE FROM THE START OF ANY CALENDAR MONTH).

1.5 Ending this agreement immediately: To the maximum extent permitted by applicable law, the Provider may put an end to this agreement immediately by giving the Client notice and without need to follow any additional procedure if (a) the Client becomes insolvent, bankrupt, goes into liquidation or becomes unable to pay its debts as they fall due, or (b) the Client is in breach of one of its obligations which cannot be put right or which the Provider have given the Client notice to put right and which the Client has failed to put right within fourteen (14) days of that notice, or (c) its conduct, or that of someone at the Centre with its permission or invitation, is incompatible with ordinary office use and (i) such conduct is repeated despite the Client having been given a warning or (ii) such conduct is material enough (in the Provider's opinion) to warrant immediate termination.

If the Provider puts an end to this agreement for any of these reasons it does not put an end to any outstanding obligations, including additional services used, requested or required under the agreement and the monthly office fee for the remainder of the period for which this agreement would have lasted if the Provider had not ended it.

1.6 If the Centre is no longer available: In the event that the Provider is permanently unable to provide the services and accommodation(s) at the Centre stated in this agreement then this agreement will end and the Client will only have to pay monthly office fees up to the date it ends and for the additional services the Client has used. The Provider will try to find suitable alternative accommodation(s) for the Client at another Provider Centre.

1.7 When this agreement ends the Client is to vacate the accommodation(s) immediately, leaving the accommodation(s) in the same condition as it was when the Client took it. Upon the Client's departure or if the Client, at its option, chooses to relocate to different rooms within the Centre, the Provider will charge an Office Restoration Service fee to cover normal cleaning and testing and to return the accommodation(s) to its original state. This fee will differ by country and is listed in the House Rules. The Provider reserves the right to charge additional reasonable fees for any repairs needed above and beyond normal wear and tear. If the Client leaves any property in the Centre the Provider may dispose of it at the Client's cost in any way the Provider chooses without owing the Client any responsibility for it or any proceeds of sale. If the Client continues to use the accommodation(s) when

this agreement has ended the Client is responsible for any loss, claim or liability the Provider incurs as a result of the Client's failure to vacate on time. The Provider may, at its discretion, permit the Client an extension subject to a surcharge on the monthly office fee.

1.8 Employees: While this agreement is in force and for a period of six months after it ends, neither the Provider nor the Client may knowingly solicit or offer employment to any of the other's staff employed in the Centre. This obligation applies to any employee employed at the Centre up to that employee's termination of employment, and for three months thereafter. It is stipulated that the breaching party shall pay the non-breaching party the equivalent of six months' salary for any employee concerned. Nothing in this clause shall prevent either party from employing an individual who responds in good faith and independently to an advertisement which is made to the public at large.

1.9 Notices: All formal notices must be in writing, which may include by email, to the address first written above.

1.10 Confidentiality: The terms of this agreement are confidential. Neither the Provider nor the Client must disclose them without the other's consent unless required to do so by law or an official authority. This obligation continues for a period of 3 years after this agreement ends.

1.11 Applicable law: This agreement is interpreted and enforced in accordance with the law of the place where the relevant Centre is located. All dispute resolution proceedings will be conducted in the country, state or province where the Centre is located. If any provision of these terms and conditions is held void or unenforceable under the applicable law, the other provisions shall remain in force. In the case of Japan all agreements will be interpreted and enforced by the Tokyo District Court, and in the case of France, any dispute regarding this agreement will be settled by the relevant courts of the Paris jurisdiction.

## **2. Services and Obligations**

2.1 Office accommodation(s): The Provider is to provide the number of serviced office accommodation(s) for which the Client has agreed to pay in the Centre stated in this agreement. This agreement lists the accommodation(s) the Provider has initially allocated for the Client's use. The Client will have a non-exclusive right to the rooms allocated to it. Occasionally the Provider may need to allocate different accommodation(s), but these accommodation(s) will be of reasonably equivalent size and the Provider will notify the Client with respect to such different accommodation(s) in advance.

2.2 Office Services: The Provider is to provide during normal opening hours the services, if requested, described in the relevant service description (which is available on request). If the Provider decides that a request for any particular service is excessive, it reserves the right to charge an additional fee.

2.3 THE PROVIDER'S IT: WHILST THE PROVIDER HAS INTERNET SECURITY PROTOCOLS, THE PROVIDER DOES NOT MAKE ANY REPRESENTATIONS AS TO THE SECURITY OF THE PROVIDER'S NETWORK (OR THE INTERNET) OR OF ANY INFORMATION THAT THE CLIENT PLACES ON IT. The Client should adopt whatever security measures (such as encryption) it believes are appropriate to its circumstances. The Provider cannot guarantee that a particular degree of availability will be attained in connection with the Client's use of the Provider's network (or the internet). The Client's sole and exclusive remedy shall be the remedy of such failure by the Provider within a reasonable time after written notice.

## **3. Providing the Services**

3.1 Access to the accommodation(s): The Provider may need to enter the Client's accommodation(s) and may do so at any time. However, unless there is an emergency or the Client has given notice to terminate, the Provider will attempt to notify the Client verbally or electronically in advance when the Provider needs access to carry out testing, repair or works other than routine inspection, cleaning and maintenance. The Provider will also endeavour to respect reasonable security procedures to protect the confidentiality of the Client's business.

3.2 Availability at the start of this agreement: If for any reason the Provider cannot provide the accommodation(s) stated in this agreement by the date when this agreement is due to start it has no liability to the Client for any loss or damages but the Client may cancel this agreement without penalty. The Provider will not charge the Client the monthly office fee for accommodation(s) the Client cannot use until it becomes available. The Provider may delay the start date of this agreement provided it provides to the Client alternative accommodation(s) that shall be at least of equivalent size to the accommodation(s) stated in this agreement.

#### **4. Accommodation(s)**

4.1 The Client must not alter any part of its accommodation and must take good care of all parts of the centre, its equipment, fixtures, fittings and furnishings which the Client uses. The Client is liable for any damage caused by it or those in the Centre with the Client's permission or at the Client's invitation whether express or implied, including but not limited to all employees, contractors, agents or other persons present on the premises.

4.2 Office equipment: The Client must not install any cabling, IT or telecom connections without the Provider's consent, which the Provider may refuse at its absolute discretion.

As a condition to the Provider's consent, the Client must permit the Provider to oversee any installations (for example IT or electrical systems) and to verify that such installations do not interfere with the use of the accommodation(s) by other Clients or the Provider or any landlord of the building.

4.3 Insurance: It is the Client's responsibility to arrange insurance for its own property which it brings in to the Centre and for its own liability to its employees and to third parties. The Provider strongly recommends that the Client put such insurance in place.

#### **5. Use**

5.1 The Client must only use the accommodation(s) for office purposes. Office use of a "retail" or "medical" nature, involving frequent visits by members of the public, is not permitted.

5.2 The Client must not carry on a business that competes with the Provider's business of providing serviced office accommodation(s) or its ancillary services.

5.3 The Client's name and address: The Client may only carry on that business in its name or some other name that the Provider previously agrees.

5.4 Use of the Centre Address: The Client may use the Centre address as its business address. Any other uses are prohibited without the Provider's prior written consent.

#### **6. Compliance**

6.1 Comply with the law: The Client and the Provider must comply with all relevant laws and regulations in the conduct of its business in relation to this agreement. The Client must do nothing illegal in connection with its use of the Business Centre. The Client must not do anything that may interfere with the use of the Centre by the Provider or by others, (including but not limited to political campaigning or immoral activity), cause any nuisance or annoyance, increase the insurance premiums the Provider has to pay, or cause loss or damage to the Provider (including damage to reputation) or to the owner of any interest in the building which contains the Centre the Client is using. Both the Client and the Provider shall comply at all times with all relevant anti-bribery and anti-corruption laws. 6.2 If the Provider has been advised by any government authority or other legislative body that it has reasonable suspicion that the Client is conducting criminal activities from the Centre then the Provider shall be entitled to terminate this agreement with immediate effect. The Provider confirms that in providing the services it has not employed or used any labour in contravention of the requirements of any anti-slavery laws.

6.3 The Client acknowledges that (a) the terms of this clause are a material inducement in the Provider's execution of this agreement and (b) any violation by the Client of this clause shall constitute a material default by the Client hereunder, entitling the Provider to terminate this agreement, without further notice or procedure.

6.4 The Provider may collect and process personal data from and of the Client to administer contractual relationship, ensure compliance with applicable laws and regulations, and enable the Provider to provide its services and to manage its business. The Client acknowledges and accepts that such personal data may be transferred or made accessible to all entities of the Provider's group, wherever located, for the purposes of providing the services herein.

#### **7. The Provider's Liability**

7.1. The extent of the Provider's liability: To the maximum extent permitted by applicable law, the Provider is not liable to the Client in respect of any loss or damage the Client suffers in connection with this agreement, with the services or with the Client's accommodation(s) unless the Provider has acted deliberately or negligently in causing that loss or damage. The Provider is not liable for any loss as a result of the Provider's failure to provide a service as a result of mechanical breakdown, strike, termination of the Provider's interest in the building containing the Centre or otherwise unless the Provider does so deliberately or is negligent. In no event shall the Provider be liable for any loss or damage until the Client provides the Provider written notice and gives the Provider a reasonable time to put it right. If the Provider is liable for failing to provide the Client with any service under this

agreement then subject to the exclusions and limits set out immediately below the Provider will pay any actual and reasonable expenses the Client has incurred in obtaining that service from an alternative source. If the Client believes the Provider has failed to deliver a service consistent with these terms and conditions the Client shall provide the Provider written notice of such failure and give the Provider a reasonable period to put it right.

**7.2. EXCLUSION OF CONSEQUENTIAL LOSSES, ETC.: THE PROVIDER WILL NOT IN ANY CIRCUMSTANCES HAVE ANY LIABILITY FOR LOSS OF BUSINESS, LOSS OF PROFITS, LOSS OF ANTICIPATED SAVINGS, LOSS OF OR DAMAGE TO DATA, THIRD PARTY CLAIMS OR ANY CONSEQUENTIAL LOSS UNLESS the Provider OTHERWISE AGREES IN WRITING. THE PROVIDER STRONGLY ADVISES THE CLIENT TO INSURE AGAINST ALL SUCH POTENTIAL LOSS, DAMAGE, EXPENSE OR LIABILITY.**

7.3. Financial limits to the Provider's liability: In all cases, the Provider's liability to the Client is subject to the following limits:

- Without limit for personal injury or death;
- Up to a maximum of £1 million / USD\$2 million / €1.3 million (or local equivalent) for any one event or series of connected events for damage to the Client's personal property;
- Up to a maximum equal to 125% of the total fees paid between the date the Client moved into its accommodation(s) and the date on which the claim in question arises or £50,000 / USD\$100,000 / €66,000 (or local equivalent) whichever is the higher, in respect of any other loss or damage.

#### **8. Fees**

8.1 Taxes and duty charges: The Client agrees to pay promptly (i) all sales, use, excise, consumption and any other taxes and license fees which it is required to pay to any governmental authority (and, at the Provider's request, will provide to the Provider evidence of such payment) and (ii) any taxes paid by the Provider to any governmental authority that are attributable to the accommodation(s), including, without limitation, any gross receipts, rent and occupancy taxes, tangible personal property taxes, stamp tax or other documentary taxes and fees.

8.2 Service Retainer/Deposit: The Client will be required to pay a service retainer/deposit equivalent to two months' of the monthly office fee (plus VAT/Tax where applicable) upon entering into this agreement unless a different amount is specified on the front of this agreement. This will be held by the Provider without generating interest as security for performance of all the Client's obligations under this agreement. The service retainer/deposit or any balance will be returned to the Client when the Client has settled its account which includes deducting outstanding fees and other costs due to the Provider.

8.3 The Provider may require the Client to pay an increased retainer if outstanding fees exceed the service retainer/deposit held and/or the Client frequently fails to pay the Provider when due.

8.4 Payment: The Provider is continually striving to reduce its environmental impact and supports its clients in doing the same. Therefore the Provider will send all invoices electronically (where allowed by law) and the Client will make payments via an automated method such as Direct Debit or Credit Card, wherever local banking systems permit unless another form of payment is offered to the Client as a qualified and current Key Account.

8.5 Late payment: If the Client does not pay fees when due, a fee will be charged on all overdue balances. This fee will differ by country and is listed in the House Rules. If the Client disputes any part of an invoice the Client must pay the amount not in dispute by the due date or be subject to late fees. The Provider also reserves the right to withhold services (including for the avoidance of doubt, denying the Client access to its accommodation(s)) while there are any outstanding fees and/or interest or the Client is in breach of this agreement.

8.6 Insufficient Funds: The Client will pay a fee for any returned cheque or any other declined payments due to insufficient funds. This fee will differ by country and is listed in the House Rules.

8.7 If this agreement is for a term of more than 12 months, the Provider will increase the monthly office fee on each anniversary of the start date. This increase will be by the local Consumer Price Index or such other broadly equivalent index where a consumer price index is not available locally. If there is a negative index rate, prices will not be decreased. Renewals are calculated separately from annual indexation increases. Month to Month agreements will use the above stated index or the current month to month office price, whichever is the greater.

8.8 Standard services: The monthly office fee and any recurring services requested by the Client are payable monthly in advance. Unless otherwise agreed in writing, these recurring services will be

provided by the Provider at the specified rates for the duration of this Agreement (including any renewal). Specific due dates will differ by country and are listed in the House Rules. Where a daily rate applies, the charge for any such month will be 30 times the daily fee. For a period of less than a month the fee will be applied on a daily basis.

8.9 Pay-as-you-use and Additional Variable Services: Fees for pay-as-you-use services, plus applicable taxes, in accordance with the Provider's published rates which may change from time to time, are invoiced in arrears and payable the month following the calendar month in which the additional services were provided. Specific due dates will differ by country and are listed in the House Rules.

8.10 Discounts, Promotions and Offers: If the Client benefited from a special discount, promotion or offer, the Provider may discontinue that discount, promotion or offer without notice if the Client materially breaches these terms and conditions.

*Global Terms & Conditions, Iveber, Jan-17*





Client Details			
Company Name:	VERONA PHARMA PLC	Centre:	3 More London
Contact Name:	Piers Morgan	Reference No.:	6995616

Office Details (excluding VAT/GST/tax and services)			
Office Number	Monthly Office Price		
	25 Months	____ Months	____ Months
	Option A	Option B	Option C
142	2,000.00		
144	6,063.00		
Total per Month	8,063.00		

GBP

Start Date of Renewal:	01 December 2017
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Comments:

*Superseding renewal following missed auto renewal in pick up period. CEO Approved.*

Please place an "X" in the shaded box next to your preferred option:

- Option A: I agree ☒
- Option B: I agree ☐
- Option C: I agree ☐
- I do not wish to renew ☐

SIGNED on your behalf (Client)

*PJM* *PJMorgan CB*

Date

*November 8, 2017*



**Exhibit 12.1**

I, Jan-Anders Karlsson, Ph.D., certify that:

1. I have reviewed this annual report on Form 20-F of Verona Pharma plc;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the company as of, and for, the periods presented in this report;
4. The company's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the company and have:
  - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - (b) [OMITTED]
  - (c) Evaluated the effectiveness of the company's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - (d) Disclosed in this report any change in the company's internal control over financial reporting that occurred during the period covered by the annual report that has materially affected, or is reasonably likely to materially affect, the company's internal control over financial reporting; and
5. The company's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the company's auditors and the audit committee of the company's board of directors (or persons performing the equivalent functions):
  - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the company's ability to record, process, summarize and report financial information; and
  - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the company's internal control over financial reporting.

Date: February 27, 2018

By: /s/ Jan-Anders Karlsson

Jan-Anders Karlsson, Ph.D.

Chief Executive Officer

(Principal Executive Officer)





**Exhibit 12.2**

I, Piers Morgan, certify that:

1. I have reviewed this annual report on Form 20-F of Verona Pharma plc;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the company as of, and for, the periods presented in this report;
4. The company's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the company and have:
  - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - (b) [OMITTED]
  - (c) Evaluated the effectiveness of the company's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - (d) Disclosed in this report any change in the company's internal control over financial reporting that occurred during the period covered by the annual report that has materially affected, or is reasonably likely to materially affect, the company's internal control over financial reporting; and
5. The company's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the company's auditors and the audit committee of the company's board of directors (or persons performing the equivalent functions):
  - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the company's ability to record, process, summarize and report financial information; and
  - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the company's internal control over financial reporting.

Date: February 27, 2018

By: /s/ Piers Morgan  
Piers Morgan  
Chief Financial Officer  
(Principal Financial Officer)



**CERTIFICATION PURSUANT TO  
18 U.S.C. SECTION 1350,  
AS ADOPTED PURSUANT TO  
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

I, Jan-Anders Karlsson, Ph.D., Chief Executive Officer of Verona Pharma plc (the "Company"), hereby certify, pursuant to 18 U.S.C. §1350, as adopted pursuant to §906 of the Sarbanes-Oxley Act of 2002, that, to the best of my knowledge:

1. The Annual Report on Form 20-F of the Company for the period ended December 31, 2017 (the "Report") fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and
2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: February 27, 2018

/s/ Jan-Anders Karlsson  
Jan-Anders Karlsson, Ph.D.  
Chief Executive Officer  
(Principal Executive Officer)



**CERTIFICATION PURSUANT TO  
18 U.S.C. SECTION 1350,  
AS ADOPTED PURSUANT TO  
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

I, Piers Morgan, Chief Financial Officer of Verona Pharma plc. (the "Company"), hereby certify, pursuant to 18 U.S.C. §1350, as adopted pursuant to §906 of the Sarbanes-Oxley Act of 2002, that, to the best of my knowledge:

1. The Annual Report on Form 20-F of the Company for the period ended December 31, 2017 (the "Report") fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and
2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: February 27, 2018

/s/ Piers Morgan

Piers Morgan  
Chief Financial Officer  
(Principal Financial Officer)





CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statement on Form S-8 (333-217521) of Verona Pharma plc of our report dated February 27, 2018 relating to the financial statements, which appears in this Form 20-F.

*PricewaterhouseCoopers LLP*

PricewaterhouseCoopers LLP  
Reading, United Kingdom  
February 27, 2018

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*PricewaterhouseCoopers LLP, 3 Forbury Place, 23 Forbury Road, Reading, Berkshire, RG1 3JH*  
*T: +44 (0) 1189 597 111, F: +44 (0) 1189 383 020, www.pwc.co.uk*

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