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

Form 6-K

Report of Foreign Private Issuer
Pursuant to Rule 13a-16 or 15d-16
under the Securities Exchange Act of 1934

October 2017

Commission file number: 001-36288

Akari Therapeutics, Plc

(Translation of registrant's name into English)

24 West 40th Street, 8th Floor
New York, NY 10018
(Address of principal executive offices)

Indicate by check mark whether the registrant files or will file annual reports under cover of Form 20-F or Form 40-F.

Form 20-F ☒ Form 40-F ☐

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulations S-T Rule 101(b)(1):_____

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulations S-T Rule 101(b)(7):_____

CONTENTS

On October 17, 2017, Akari Therapeutics, Plc (the “Company”), announced that it intended to make a public offering of its American Depositary Shares.

In connection with this proposed offering, the Company prepared a description of certain risk factors relating to the Company, its business and industry and other information that are being presented to potential investors. These risk factors and updated business and industry and other information update the risk factors, business and industry and other information included in the Company's Annual Report on Form 20-F for the fiscal year ended December 31, 2016, which was filed with the Securities and Exchange Commission (the “SEC”) on March 31, 2017.

The risk factors and updated business and industry and other information are attached hereto as Exhibit 99.1 and incorporated by reference herein. The offering is being made pursuant to an effective registration statement filed with the SEC. Before investing, please read the prospectus and the related prospectus supplement for the offered ADSs in the registration statement and other documents the Company has filed with the SEC for more complete information about the Company and the proposed offering.

This report shall not constitute an offer to sell or a solicitation of an offer to buy, nor shall there be any sales of these securities in any state or jurisdiction in which such an offer, solicitation or sale would be unlawful prior to registration or qualification under the securities law of any such state or jurisdiction.

The information contained in this report (including the exhibit hereto) is hereby incorporated by reference into all effective registration statements filed by the Company under the Securities Act of 1933.

Exhibit No.

99.1 Risk Factor, Business and Industry and Other Information update dated October 17, 2017.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Akari Therapeutics, Plc
(Registrant)

By: /s/ Robert M. Shaw
Name: Robert M. Shaw
General Counsel & Secretary

Date: October 17, 2017

THE COMPANY

Except as otherwise indicated herein or as the context otherwise requires, references to "Akari," "we," "us," "our," the "Company" and similar designations refer to Akari Therapeutics, PLC and its subsidiaries. When we refer to "you," we mean prospective investors in the Company.

Overview

We are a clinical-stage biopharmaceutical company focused on developing inhibitors of acute and chronic inflammation, specifically the complement system, the eicosanoid system and the bioamine system for the treatment of rare and orphan diseases. Each of these systems has scientifically well-supported causative roles in the diseases being targeted by us. We believe that blocking early mediators of inflammation will prevent initiation and continual amplification of the processes that cause certain diseases.

Ticks have undergone 300 million years of natural selection to produce inhibitors that bind tightly to key highly-conserved inflammatory mediators, are generally well tolerated in humans, and remain fully functional when a host is repeatedly exposed to the molecule. Our molecules are derived from these inhibitors.

Our lead product candidate, Coversin™, which is a second-generation complement inhibitor, acts on complement component-C5, preventing release of C5a and formation of C5b–9 (also known as the membrane attack complex, or MAC), and independently also inhibits leukotriene B4, or LTB4, activity, both elements that are co-located as part of the immune/inflammatory response. Coversin is a recombinant small protein (16,740 Da) derived from a protein originally discovered in the saliva of the Ornithodoros moubata tick, where it modulates the host immune system to allow the parasite to feed without alerting the host to its presence or provoking an immune response.

Coversin has received orphan drug status from the U.S. Food and Drug Administration, or the FDA, and the European Medicines Agency, or the EMA, for paroxysmal nocturnal haemoglobinuria, or PNH, and Guillain Barré Syndrome, or GBS. Orphan drug designation provides us with certain benefits and incentives, including a period of marketing exclusivity if regulatory approval of the drug is ultimately received for the designated indication. The receipt of orphan drug designation status does not change the regulatory requirements or process for obtaining marketing approval and the designation does not mean that marketing approval will be received. We intend to apply in the future for orphan drug designation in additional indications we deem appropriate. We have also received fast track designation for the investigation of Coversin for treatment of PNH in patients who have polymorphisms conferring eculizumab resistance.

Our initial clinical targets for Coversin are PNH and atypical Hemolytic Uremic Syndrome, or aHUS. We are also targeting patients with polymorphisms of the C5 molecule which interfere with correct binding of Soliris® (eculizumab), a first-generation C5 inhibitor currently approved for PNH and aHUS treatment, making these patients resistant to treatment with that drug. In addition to disease targets where complement dysregulation is the key driver, we are also targeting a range of inflammatory diseases where the inhibition of both C5 and LTB4 are implicated, including bullous pemphigoid (a blistering disease of the skin), or BP, and atopic keratoconjunctivitis, or AKC.

Other compounds in our pipeline include engineered versions of Coversin that potentially decrease the frequency of administration, improve potency, or allow for specific tissue targeting, as well as new proteins targeting LBT4 alone, as well as bioamine inhibitors (for example, anti-histamines). In general, these inhibitors act as ligand binding compounds, which may provide additional benefit versus other modes of inhibition. For example, off target effects are less likely with ligand capture. One example of this benefit is seen with LTB4 inhibition through ligand capture. LTB4 acts to amplify the inflammatory signal by bringing and activating white blood cells to the area of inflammation. Compounds that have targeted the production of leukotrienes will inhibit both the production of pro-inflammatory as well as anti-inflammatory leukotrienes—often diminishing the potential benefit of the drug on the inflammatory system. Coversin has demonstrated that, by capturing LTB4, it is limited to disrupting the white blood cell activation and attraction aspects, without interfering with the anti-inflammatory benefits of other leukotrienes.

Coversin is much smaller than typical antibodies currently used in therapeutic treatment. Coversin can be self-administered by subcutaneous injection, much like an insulin injection, which we believe will provide considerable benefits in terms of patient convenience. We believe that the subcutaneous formulation of Coversin may accelerate recruitment for our clinical trials, and, as an alternative to intravenous infusion, may accelerate patient uptake if Coversin is approved by regulatory authorities for commercial sale. Patient surveys contracted by us suggest that a majority of patients would prefer to self-inject daily than undergo intravenous infusions.

Recent Developments

FDA Fast Track Designation of Coversin for PNH

On March 29, 2017, we received notice from the FDA of fast track designation for the investigation of Coversin for the treatment of PNH in patients who have polymorphisms conferring eculizumab resistance. The fast track program was created by the FDA to facilitate the development and expedite the review of new drugs which show promise in treating a serious or life-threatening disease and address an unmet medical need. Drugs that receive this designation benefit from more frequent communications and meetings with the FDA to review the drug's development plan including the design of the proposed clinical trials, use of biomarkers and the extent of data needed for approval. Drugs with fast track designation may also qualify for priority review to expedite the FDA review process, if relevant criteria are met.

Phase II Open Label PNH Trials

In the fourth quarter of 2016, we commenced enrollment for a 90 day open-label Phase II, single-arm clinical trial in patients with PNH in five centers in the European Union. We initially enrolled and treated five patients with Coversin self-administered subcutaneous injections twice a day for approximately the first month and then switched to once daily injections. Of those five patients, four completed the 90 day trial while one patient with a suspected co-morbidity unrelated to treatment was withdrawn on day 43 of the trial. Recently, we enrolled three additional patients, pursuant to an amended protocol based on a revised dosing regime, one of whom has completed approximately eight weeks of treatment while the other two patients are still within their first month of treatment.

The primary endpoint in this trial is reduction in serum lactic dehydrogenase, or LDH, to ≤1.8 X the upper limit of normal, or ULN or 500 I U/L, whichever is the lower from day 1 (pre-dose) to day 28. Secondary endpoints are LDH at days 60 and 90, hemoglobin, CH50, quality of life, and transfusion independence. The objectives of our Phase II clinical trial are to validate the safety and efficacy of Coversin, confirm convenience of our dosing regimen, and study dose ranging to identify the correct treatment dose in advance of anticipated Phase III clinical trials.

Interim results from the trial with respect to the first five patients showed that Coversin was well tolerated and patients reported no difficulty with self administration. Those results showed that there were no serious adverse events, SAEs, related to Coversin. The most commonly reported adverse events were mild to moderate injection site reactions which declined towards the end of the 90-day trial. Those results further showed that patients developed low titre antibodies between 2 to 13 weeks after starting daily exposure to Coversin but the antibodies were non-neutralizing as determined by lytic assay. All four patients that completed the trial saw declines in lactate dehydrogenase, LDH, levels with two of the four patients meeting the primary endpoint which was assessed at day 28. A fifth patient withdrawn from the study did not meet the primary endpoint. For the four patients that completed the study, LDH as a multiple of ULN (xULN) was 1.4, 2.2, 2.5 and 1.4 at day 28; 1.5, 2.1, 1.8 and 1.5 at day 60; and 1.6, 2.4, 2.0 and 1.9 at day 90. Aspartate aminotransferase, or AST, levels provide another measure of cellular haemolysis; AST decreased following initiation of dosing. Three of the four patients that completed the study were updosed. Two of the patients were updosed from 30mg to 45mg once daily at days 40 and 54, respectively and a third patient was updosed to 22.5mg twice daily at day 24 and moved to 45mg once daily at day 67. One of the patients updosed did not see a decline in LDH with updosing although his haemoglobin level rose after day 67. All four patients that completed the study had a CH50 level below the limit of quantification (<8 CH50 U Eq/mL) after the two-day ablating dose phase indicating total blockade of the terminal complement pathway. None of the four patients required transfusion during the trial, while three of the four patients required transfusions during the three months preceding the trial.

With respect to the three recently enrolled patients, the first patient who completed more than 28 days of treatment had an LDH value of 1.5 times the ULN at day 28. The other two patients have not yet reached the primary endpoint measurement date. To date, there have been no drug-related serious adverse events. The data reported is taken from the current electronic case report forms.

In addition, an eculizumab-resistant PNH patient has been under treatment with subcutaneous Coversin for over 18 months under an open-label long term safety and efficacy trial. The patient continues to self-administer Coversin and continues to demonstrate complete complement inhibition without any change in dose. The four patients that completed the 90 day trial have since moved into our long term safety and efficacy trial and have been under treatment with subcutaneous Coversin for between six and nine months.

Following advice from a recent FDA Type B End-of-Phase II Meeting, we plan to advance Coversin, towards Phase III clinical trials in PNH commencing with CAPSTONE in the first quarter of 2018, a Phase III clinical trial of Coversin in naïve PNH patients in Europe, where Soliris is not the standard of care, with co-primary clinical endpoints based on hemoglobin and transfusion data. Subsequent to the commencement of CAPSTONE, at a date to be determined, we plan to commence ASSET, a Phase III clinical trial in PNH patients in the United States, where Soliris, is the current standard of care. Based on the FDA's advice, we may decide to engage in additional discussions with the FDA with respect to the protocol design of both CAPSTONE and ASSET.

Recent Preclinical Data

Recent preclinical studies with Coversin have demonstrated positive results in an animal model of aHUS conducted by Prof. Giuseppe Remuzzi and colleagues Marina Noris and Miriam Galbusera at the Mario Negri Institute for Pharmacological Research in Bergamo, Italy, and the Clinical Research Center for Rare Diseases "Aldo e Cele Dacco" of the same institute, a European center for the study of aHUS. In a well-established ex vivo model testing sera of patients with aHUS, Coversin demonstrated a statistically significant ($p<0.001$) reduction in MAC, deposition on endothelial cells when activated by sera of patients with active aHUS, at least as well as eculizumab. We are planning to initiate a Phase II clinical trial in aHUS in up to ten naïve patients at seven sites across Europe, beginning in the fourth quarter of 2017.

New data demonstrating Coversin C5 and LTB4 dual activity in eye and skin models

Results in a rodent model of Experimental Immune Conjunctivitis, or EIC, undertaken at the world leading Moorfields Hospital Institute of Ophthalmology, showed that Coversin demonstrated significant anti-inflammatory activity with both C5 and LTB4 inhibition believed to play a role. In this preclinical model of severe eye surface inflammation, Coversin, applied topically, resulted in a statistically significant reduction (64%, $p<0.001$) in late phase inflammation versus placebo.

In a preclinical mouse model of BP where both LTB4 and C5 are thought to be dysregulated, Coversin demonstrated a statistically significant reduction (~60%, $p=0.002$) in the affected area with Coversin compared to placebo and steroids.

Based on these results, while continuing to develop Coversin in PNH and aHUS, we also intend to focus on new indications for Coversin in diseases where both C5 and LTB4 are believed to be involved. We expect to commence enrollment of a Phase II open label clinical trial of Coversin in BP and a Phase I/II randomized, double masked, placebo-controlled clinical trial of Coversin in AKC in the first half of 2018 in Europe.

Class Action

On April 27, 2017, we issued a press release stating that Edison Investment Research Ltd., or Edison, has withdrawn its report issued April 26, 2017 titled "Akari's Coversin matches Soliris in Phase II", or the "Edison Report", because it contains material inaccuracies, including without limitation, with respect to our interim analysis of our ongoing Phase II PNH trial of Coversin. Investors were cautioned not to rely upon any information contained in the Edison Report and instead were directed to our press release issued on April 24, 2017 that discusses the interim analysis of our ongoing Phase II PNH trial and other matters. Our Board of Directors established an *ad hoc* special committee of the Board to review the involvement, if any, of our personnel with the Edison Report, which was later retracted. Edison was retained by the Company to produce research reports about us. While that review was pending, Dr. Gur Roshwalb, our former Chief Executive Officer, was placed on administrative leave and Dr. Ray Prudo in his role as Executive Chairman temporarily assumed Dr. Roshwalb's duties in his absence. Following that review, we determined that the Edison Report was reviewed and approved by Dr. Roshwalb, in contravention of Company policy. On May 29, 2017, Dr. Roshwalb submitted his resignation as Chief Executive Officer and member of our Board of Directors, effective immediately.

On May 12, 2017, a putative securities class action captioned *Derek Da Ponte v. Akari Therapeutics, PLC, Gur Roshwalb, and Dov Elefant (Case 1:17-cv-03577)* was filed in the U.S. District Court for the Southern District of New York against us, our former Chief Executive Officer and our Chief Financial Officer. The plaintiff asserted claims alleging violations of Sections 10(b) and 20(a) of the Securities Exchange Act of 1934, or the Exchange Act, based primarily on our press releases or statements issued between April 24, 2017 and May 11, 2017 concerning the Phase II PNH trial of Coversin and the Edison Report about us and actions taken by us after the report was issued. The purported class covers the period from March 30, 2017 to May 11, 2017. The complaint seeks unspecified damages and costs and fees. On May 19, 2017, an almost identical class action complaint captioned *Shamoon v. Akari Therapeutics, PLC, Gur Roshwalb, and Dov Elefant (Case 1:17-cv-03783)* was filed in the same court. On July 11-12, 2017, candidates to be lead plaintiff filed motions to consolidate the cases and appoint a lead plaintiff. On August 10, 2017, the court issued a stipulated order: (i) consolidating the class actions under the caption *In re: Akari Therapeutics, PLC Securities Litigation (Case 1:17-cv-03577)*; (ii) ordering plaintiffs to file and serve a consolidated amended complaint within 60 days after the appointment of lead plaintiff and lead plaintiff's counsel; and (iii) ordering defendants to move, answer, otherwise respond to the consolidated amended complaint within 45 days of being served with it. By order dated September 7, 2017, the court appointed lead plaintiffs for the class and lead plaintiffs' counsel. We intend to vigorously defend ourselves against this lawsuit. At this time, we are unable to estimate the ultimate outcome of this legal matter and its impact on us.

Appointment of New Chief Executive Officer

On August 28, 2017, Dr. David Horn Solomon became our new Chief Executive Officer and joined our board as a Class A director.

Preliminary Financial Data for the Nine Months ended September 30, 2017

Our consolidated financial statements for the nine months ended September 30, 2017 are not yet available. Accordingly, the information presented below reflects our preliminary financial data subject to the completion of our financial closing procedures. As a result, this preliminary financial data may differ from the actual results that will be reflected in our consolidated financial statements for the year when they are completed and publicly disclosed. This preliminary financial data may change and those changes may be material. Accordingly, you should not place undue reliance upon these preliminary estimates. Please see "Note Regarding Forward-Looking Statements."

Our expectations with respect to our unaudited consolidated financial data for the period discussed below are based upon management estimates and are the responsibility of management. Our independent registered public accounting firm BDO USA LLP, has not audited, reviewed, compiled or performed any procedures with respect to this preliminary financial data. Accordingly, BDO USA LLP does not express an opinion or any other form of assurance with respect thereto. We believe that the following information about our cash and cash equivalents is helpful to an investor's understanding of our operating performance.

Cash and Cash Equivalents and Short Term Investments

As of September 30, 2017, we had cash and cash equivalents of approximately $21.0 million.

Corporate Information

Our legal and commercial name is Akari Therapeutics, PLC.

We were originally established as a private limited company under the laws of England and Wales on October 7, 2004 under the name Freshname No. 333 Limited. On January 19, 2005, we changed our name to Morria Biopharmaceuticals Limited and on February 3, 2005, we completed a reverse merger with Morria Biopharmaceuticals Inc., or Morria, a Delaware corporation, in which Morria became our wholly-owned subsidiary and we re-registered as a non-traded public limited company under the laws of England and Wales. Morria was dedicated to the discovery and development of novel, first-in-class, non-steroidal, synthetic anti-inflammatory drugs. On March 22, 2011, we incorporated an Israeli subsidiary, Morria Biopharma Ltd. On June 25, 2013, we changed our name to Celsus Therapeutics PLC and on October 13, 2013 Morria was renamed Celsus Therapeutics Inc. On September 25, 2015, we further changed our name to "Akari Therapeutics, PLC". As of the date of this report on Form 6-K, Celsus Therapeutics Inc. and Morria Biopharma Ltd. do not conduct any operations.

On September 18, 2015, we completed an acquisition of the entire capital stock of Volution Immuno Pharmaceuticals SA, or Volution, a private Swiss company, from RPC Pharma Limited, or RPC, Volution's sole shareholder, in exchange for our ordinary shares, in accordance with the terms of a Share Exchange Agreement, dated as of July 10, 2015. In connection with the acquisition, our name was changed to Akari Therapeutics, PLC.

Our principal office is located at 24 West 40th Street, 8th Floor, New York and our telephone number is (646) 350-0702.

Our website address is www.akaritx.com. The information contained on, or that can be accessed from, our website does not form part of this report on Form 6-K.

Implications of Being an Emerging Growth Company

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and therefore we may take advantage of certain exemptions from various public company reporting requirements, including but not limited to, not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. We have chosen to irrevocably opt out of the extended transition periods available under the JOBS Act for complying with new or revised accounting standards.

Implications of being a Foreign Private Issuer

On July 1, 2016, we became a foreign private issuer having previously lost this status at the end of 2014. As a foreign private issuer, we are not subject to the same requirements that are imposed upon U.S. domestic issuers by the SEC. Under the Exchange Act, we are subject to reporting obligations that, in certain respects, are less detailed and less frequent than those of U.S. domestic reporting companies. For example, we will not be required to issue proxy statements that comply with the requirements applicable to U.S. domestic reporting companies. We will also have four months after the end of each fiscal year to file our annual reports with the SEC and will not be required to file current reports as frequently or promptly as U.S. domestic reporting companies. Furthermore, our officers, directors, and principal shareholders will be exempt from the requirements to report transactions in our equity securities and from the short-swing profit liability provisions contained in Section 16 of the Exchange Act. These exemptions and leniencies, along with other corporate governance exemptions resulting from our ability to rely on home country rules, will reduce the frequency and scope of information and protections to which you may otherwise have been eligible in relation to a U.S. domestic reporting companies. If we were to lose our foreign private issuer status, the regulatory and compliance costs to us under U.S. securities laws as a U.S. domestic issuer will be significantly more than costs we incur as a foreign private issuer.

RISK FACTORS

Except for the historical information contained herein or incorporated by reference, this Report on Form 6-K and the information incorporated by reference contains forward-looking statements that involve risks and uncertainties. These statements include projections about our accounting and finances, plans and objectives for the future, future operating and economic performance and other statements regarding future performance. These statements are not guarantees of future performance or events. Our actual results could differ materially from those discussed in our Annual Report on Form 20-F. Factors that could cause or contribute to these differences include, but are not limited to, those discussed in Item 4 entitled "Information on the Company", as well as those discussed in Item 5 entitled "Operating and Financial Review and Prospects" and elsewhere throughout our Annual Report on Form 20-F and in any documents incorporated in our Annual Report on Form 20-F by reference.

You should consider carefully the following risk factors, together with all of the other information included or incorporated in our Annual Report on Form 20-F. If any of the following risks, either alone or taken together, or other risks not presently known to us or that we currently believe to not be significant, develop into actual events, then our business, financial condition, results of operations or prospects could be materially adversely affected. If that happens, the market price of our American Depositary Shares, or ADSs, could decline, and shareholders may lose all or part of their investment.

Risks Relating to Our Financial Position and Our Business

We have a history of operating losses and cannot give assurance of future revenues or operating profits; investors may lose their entire investment.

We do not expect to generate revenue or profitability that is necessary to finance our operations in the short term. We incurred net losses of $18,140,997, $45,317,532 and $12,904,527 for the years ended December 31, 2016 and 2015 and for the six months ended June 30, 2017, respectively. In addition, our accumulated deficit as of December 31, 2016 and 2015 and June 30, 2017 was $74,937,610, $56,796,613 and $87,842,137 respectively. Losses have principally resulted from costs incurred for manufacturing, our clinical trials, research and development programs and general and administrative expenses. We have funded our operations primarily through the private placement of equity securities. As of June 30, 2017, we had cash and cash equivalents of $30,118,882.

To date, we have not commercialized any products or generated any revenues from the sale of products, and absent the realization of sufficient revenues from product sales, we may never attain profitability in the future. We expect to incur significant losses for the foreseeable future as we continue to conduct research and development, clinical testing, regulatory compliance activities and, if Coversin™ or other future product candidates receive regulatory approval, sales and marketing activities.

Our failure to become and remain profitable would depress the market price of the ADSs and could impair our ability to raise capital, expand our business, diversify our product offerings or continue our operations. If we continue to suffer losses as we have in the past, investors may not receive any return on their investment and may lose their entire investment.

We will require additional capital to fund our operations, and if we are unable to obtain such capital, we will be unable to successfully develop and commercialize any product candidates.

As of June 30, 2017, we had cash and cash equivalents of $30,118,882. We will require additional capital in order to develop and commercialize our current product candidates or any product candidates that we acquire, if any. There can be no assurance that additional funds will be available when we need them on terms that are acceptable to us, or at all. If adequate funds are not available on a timely basis, we may be required to terminate or delay development for one or more of our product candidates.

The amount and timing of any expenditure needed will depend on numerous factors, some of which are outside our control, including:

- the type, number, scope, progress, expansion costs, results of and timing of our ongoing or future clinical trials or the need for additional clinical trials of Coversin for PNH or any other indications or product candidates which we are pursuing or may choose to pursue in the future;
- the costs of obtaining, maintaining and enforcing our patents and other intellectual property rights;
- the costs and timing of obtaining or maintaining manufacturing for Coversin for PNH or any other indications or product candidates, including commercial manufacturing if any product candidate is approved;
- the costs and timing of establishing sales marketing, and reimbursement capabilities and enhanced internal controls over financial reporting;
- the terms and timing of establishing and maintaining collaborations, license agreements and other partnerships;
- costs associated with any new product candidates that we may develop, in-license or acquire;
- the effect of competing technological and market developments; and
- the costs associated with being a public company.

We have not sold any products, and we do not expect to sell or derive revenue from any product sales for the foreseeable future. We may seek additional funding through future debt and equity financing, as well as potential additional collaborations or strategic partnerships with other companies or through non-dilutive financings. Additional funding may not be available to us on acceptable terms or at all. General market conditions may make it very difficult for us to seek financing from the capital markets. We may be required to relinquish rights to our technologies or product candidates, or grant licenses on terms that are not favorable to us, in order to raise additional funds through alliance, joint venture or licensing arrangements. In addition, the terms of any financing may adversely affect the holdings or the rights of our shareholders and the issuance of additional shares by us, or the possibility of such issuance, may cause the market price of our shares to decline.

If we are unable to obtain funding on a timely basis, we will be unable to complete ongoing and planned clinical trials for Coversin and we may be required to significantly curtail some or all of our activities. We also could be required to seek funds through arrangements with collaborative partners or otherwise that may require us to relinquish rights to our product candidates or some of our technologies or otherwise agree to terms unfavorable to us.

Future sales and issuances of the ADSs or rights to purchase ADSs and any equity financing that we pursue, could result in significant dilution of the percentage ownership of our shareholders and could cause our ADS price to fall.

To the extent we raise additional capital by issuing equity securities, our shareholders may experience substantial dilution. In any financing transaction, we may sell ordinary shares or ADSs, convertible securities or other equity securities. If we sell ordinary shares or ADSs, convertible securities or other equity securities, our shareholders' investment in our ordinary shares or ADSs will be diluted. These sales may also result in material dilution to our existing shareholders, and new investors could gain rights superior to our existing shareholders.

Risks Related to the Clinical Development and Regulatory Approval of Our Product Candidates

Our business depends on the success of Coversin, which is still under development. If we are unable to obtain regulatory approval for or successfully commercialize Coversin, our business will be materially harmed.

Coversin has been the sole focus of our product development. Successful continued development and ultimate regulatory approval of Coversin for at least one autoimmune disease including PNH or aHUS and others, is critical to the future success of our business. We have invested, and will continue to invest, a significant portion of our time and financial resources in the development of Coversin. We will need to raise sufficient funds for, and successfully enroll and complete, our ongoing clinical development program for Coversin in PNH and for our planned clinical development program for Coversin in aHUS and other indications. The future regulatory and commercial success of this product candidate is subject to a number of risks, including the following:

- we may not have sufficient financial and other resources to complete the necessary clinical trials for Coversin;
- we may not be able to obtain adequate evidence of efficacy and safety for Coversin;
- we do not know the degree to which Coversin will be accepted as a therapy, even if approved;
- in our clinical programs, we may experience difficulty in enrollment, variability in patients, adjustments to clinical trial procedures and the need for additional clinical trial sites, which could delay our clinical trial progress;
- our reliance on a sole manufacturer to supply the drug product formulation of Coversin that is being used in our clinical trials;
- the results of our clinical trials may not meet the level of statistical or clinical significance required by the FDA, EMA or comparable foreign regulatory bodies for marketing approval;
- patients in our clinical trials may die or suffer other adverse effects for reasons that may or may not be related to Coversin, which could delay or prevent further clinical development;
- the standards implemented by clinical or regulatory agencies may change at any time;
- the FDA, EMA or foreign clinical or regulatory agencies may require efficacy endpoints for a clinical trial for the treatment of PNH, aHUS, and in conditions such as antibody mediated transplant rejection that differ from the endpoints of our planned current or future trials, which may require us to conduct additional clinical trials;
- the mechanism of action of Coversin is complex and we do not know the degree to which it will translate into a medical benefit in certain indications;
- our intellectual property rights may not be patentable, valid or enforceable; and
- we may not be able to obtain, maintain or enforce our patents and other intellectual property rights.

Of the large number of drugs in development in the pharmaceutical industry, only a small percentage results in the submission of a new drug application, or NDA, to the FDA, or a marketing authorisation application, or MAA, to the EMA and even fewer are approved for commercialization. Furthermore, even if we do receive regulatory approval to market Coversin, any such approval may be subject to limitations on the indicated uses or patient populations for which we may market the product. Accordingly, even if we are able to obtain the requisite financing to continue to fund our development programs, we cannot assure you that Coversin will be successfully developed or commercialized. If we or any of our future development partners are unable to develop, or obtain regulatory approval for, or, if approved, successfully commercialize Coversin, we may not be able to generate sufficient revenue to continue our business.

If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

We may not be able to initiate or continue clinical trials required by the FDA, EMA or other foreign regulatory agencies for Coversin if we are unable to locate and enroll a sufficient number of eligible patients to participate in these clinical trials. We will be required to identify and enroll a sufficient number of patients with PNH, aHUS, and other rare and orphan autoimmune and inflammatory diseases for each of our ongoing and planned clinical trials of Coversin in these indications. Each of these is a rare disease or indication with relatively small patient populations, which could result in slow enrollment of clinical trial participants.

Patient enrollment is affected by other factors, including:

- severity of the disease under investigation;
- design of the clinical trial protocol;
- size and nature of the patient population;
- eligibility criteria for the trial in question;
- perceived risks and benefits of the product candidate under trial;
- proximity and availability of clinical trial sites for prospective patients;
- availability of competing therapies and clinical trials;
- clinicians' and patients' perceptions as to the potential advantages of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians; and
- our ability to monitor patients adequately during and after treatment.

Further, there are only a limited number of specialist physicians that treat patients with these diseases. We also may encounter difficulties in identifying and enrolling such patients with a stage of disease appropriate for our ongoing or future clinical trials. In addition, the process of finding and diagnosing patients may prove costly. Our inability to enroll a sufficient number of patients for any of our clinical trials would result in significant delays or may require us to abandon one or more clinical trials.

If clinical trials or regulatory approval processes for Coversin are prolonged, delayed or suspended, we may be unable to commercialize Coversin on a timely basis.

We cannot predict whether we will encounter problems with any of our completed, ongoing or planned clinical trials that will cause us or any regulatory authority to delay or suspend those clinical trials or delay the completion of our ongoing and planned clinical trials and negatively impact our ability to obtain regulatory approval for, and to market and sell, a particular product candidate:

- conditions imposed on us by the FDA, EMA or another foreign regulatory authority regarding the scope or design of our clinical trials;
- insufficient supply of our product candidates or other materials necessary to conduct and complete our clinical trials;
- slow enrollment and retention rate of subjects in our clinical trials; and
- serious and unexpected drug-related side effects related to the product candidate being tested.

Commercialization may be delayed by the imposition of additional conditions on our clinical trials by the FDA, EMA or any other applicable foreign regulatory authority or the requirement of additional supportive studies by the FDA, EMA or such foreign regulatory authority.

We do not know whether our clinical trials will begin as planned, will need to be restructured, or will be completed on schedule, if at all. For example, we plan on commencing a Phase III clinical trial for Coversin in PNH in the first quarter of 2018 and a Phase II clinical trial for Coversin in aHUS in the fourth quarter of 2017. Delays in our clinical trials will result in increased development costs for our product candidates, and our financial resources may be insufficient to fund any incremental costs. In addition, if our clinical trials are delayed, our competitors may be able to bring products to market before we do and the commercial viability of our product candidates could be limited.

The efficacy of Coversin may not be known until advanced stages of testing, after we have incurred significant product development costs which may not be recoverable.

Coversin may fail to show the desired safety and efficacy at any phase in the clinical development program. Good efficacy in animal models of the target indication are no guarantee of success in human clinical trials. Often there is no adequate animal model of a human disease, such as PNH. As a result, the first definitive proof of efficacy may not occur until clinical trials in humans. In our ongoing Phase II PNH trial, while all four patients that completed the trial saw declines in LDH levels, two of the four patients did not meet the primary endpoint which was assessed at day 28 and a fifth patient, that withdrew from the trial, also did not meet the primary endpoint. If Coversin does not demonstrate adequate safety and efficacy, its development may be delayed or terminated, which could have a material adverse effect on our financial condition and results of operation.

Results of earlier preclinical studies or clinical trials may not be predictive of advancement to the next phase of development.

Completion of preclinical studies or clinical trials does not guarantee that we will initiate additional studies or trials for our product candidates, that if further studies or trials are initiated what the scope and phase of the trial will be or that they will be completed, or that if these further studies or trials are completed, that the design or results will provide a sufficient basis to apply for or receive regulatory approvals or to commercialize products. Results of clinical trials could be inconclusive, requiring additional or repeat trials. Data obtained from preclinical studies and clinical trials are subject to varying interpretations that could delay, limit or prevent regulatory approval. If the design or results achieved in our clinical trials are insufficient to proceed to further trials or to regulatory approval of our product candidates, we could be materially adversely affected. Failure of a clinical trial to achieve its pre-specified primary endpoint, generally increases the likelihood that additional studies or trials will be required if we determine to continue development of the product candidate, reduces the likelihood of timely development of and regulatory approval to market the product candidate, and may decrease the chances for successfully achieving the primary endpoint in scientifically similar indications.

The route of administration or dose for Coversin may be inadequate.

Unsatisfactory drug availability due to problems relating to the route of administration or the target tissue availability of the drug is another potential cause of lack of efficacy of Coversin if and when it is commercialized. Complement component C5, the target of Coversin is predominantly found in blood. For PNH and aHUS, Coversin is being administered subcutaneously. The completed single dose Phase I study shows that Coversin is able to enter the systemic circulation by absorption from subcutaneous sites in healthy volunteers. However, if subcutaneous administration proves to be unfeasible, then we may need to research additional routes of administration, which could delay commercialization of Coversin and result in significant additional costs to us.

Long-term animal toxicity studies of Coversin could result in adverse results.

While we have conducted toxicity studies in certain animals without any evidence of toxicity, we are currently undertaking long-term animal toxicity studies of Coversin. Such tests may show that Coversin is toxic in certain animals, is not as effective as we expected, or other adverse results. If animal toxicity tests do not yield favorable results, we may be required to abandon our development of Coversin, which could have a material adverse effect on our financial condition and results of operation.

Chronic dosing of patients with Coversin could lead to an immune response that causes adverse reactions or impairs the activity of the drug.

There is a risk that chronic dosing of patients with Coversin may lead to an immune response that causes adverse reactions or impairs the activity of the drug. Patients may develop an allergic reaction to the drug and/or develop antibodies directed at the drug. Impaired drug activity could be caused by neutralization of the drug's inhibitory activity or by an increased rate of clearance of the drug from circulation.

One potential toxic side effect of Coversin that has occurred in patients receiving Soliris® (eculizumab), a humanized antibody against complement component C5, may include the inhibition of the terminal complement system, which can result in an increased incidence of meningitis. As a result, we expect that patients receiving Coversin would also receive meningitis immunization and prophylactic antibiotics as indicated.

Coversin has a secondary binding site that sequesters LTB4. LTB4 synthesis from eicosanoid fatty acids can be induced by a variety of triggers including complement. LTB4 is a pro-inflammatory mediator which attracts and activates white blood cells at the area of inflammation. LTB4 inhibition may lead to positive anti-inflammatory benefits, but another potential cause of undesired side effects is that the reduction of these neutrophil attractant properties may include increased risk of infection, among others.

Any immune response that causes adverse reactions or impairs the activity of the drug could cause a delay in or termination of our development of Coversin, which would have a material adverse effect on our financial condition and results of operation.

If Coversin is not convenient for patients to use, then potential sales may decrease materially.

Coversin may be required to be kept refrigerated prior to use and will likely require self-injection. If the drug product is not stable at temperatures of between four and eight degrees Celsius, then the drug product may need to be defrosted before use, which patients could view as inconvenient, causing sales to decrease. In addition, if Coversin shows a lack of long-term stability at low storage temperatures, this may negatively impact our ability to manage the commercial supply chain, which could result in us having to refund customers or replace products that are unstable, which could materially increase our costs and have a material adverse effect on our financial condition and results of operation.

Because Coversin has not yet received regulatory approval, it is difficult to predict the time and cost of development and our ability to successfully complete clinical development and obtain the necessary regulatory approvals for commercialization.

Coversin has not yet received regulatory approval for the treatment of PNH, aHUS or other potential indications, and unexpected problems may arise that could cause us to delay, suspend or terminate our development efforts. To date, a total of eight patients have been enrolled in Phase II PNH clinical trials of Coversin, with one patient withdrawing early from one of the trials. Larger scale trials will be required to obtain regulatory approval and the efficacy or non-efficacy of Coversin will ultimately be determined by the applicable regulatory agencies. The long-term safety consequences of inhibition of C5 with Coversin is not known. Regulatory approval of product candidates such as Coversin can be more expensive and take longer than approval for candidates for the treatment of more well understood diseases with previously approved products.

We have obtained orphan drug status for Coversin in PNH and GBS, both in the United States and the EU, but we may be unable to maintain the benefits associated with orphan drug status, including market exclusivity.

In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages, and user-fee waivers. After the FDA grants orphan drug designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA. Although we have received orphan drug designation for Coversin in PNH and GBS and intend to seek orphan product designation for Coversin in further indications, we may never receive such additional designations.

If a product that has orphan drug designation subsequently receives the first FDA approval for a particular active ingredient for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications, including a BLA, to market the same biologic for the same indication for seven years, except in limited circumstances such as a showing of clinical superiority to the product with orphan product exclusivity or if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. Even if we were to obtain orphan drug designation for Coversin for a particular indication, we may not be the first to obtain marketing approval for any particular orphan indication due to the uncertainties associated with developing pharmaceutical products. If we do obtain exclusive marketing rights in the United States, they may be limited if we seek approval for an indication broader than the orphan designated indication and may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of the relevant patients. Further, exclusivity may not effectively protect the product from competition because different drugs with different active moieties can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve a drug with the same active moiety for the same condition if the FDA concludes that the later drug is safer, more effective, or makes a major contribution to patient care. Furthermore, the FDA can waive orphan exclusivity if we are unable to manufacture sufficient supply of our product.

In the EU, where a marketing authorization in respect of an orphan medicinal product is granted, the Agency and the Member States shall not, for a period of 10 years, accept another application for a marketing authorization, or grant a marketing authorization or accept an application to extend an existing marketing authorization, for the same therapeutic indication, in respect of a similar medicinal product. A marketing authorization may be granted, for the same therapeutic indication, to a similar medicinal product if: (i) the holder of the marketing authorization for the original orphan medicinal product has given his consent to the second applicant, or; (ii) the holder of the marketing authorization for the original orphan medicinal product is unable to supply sufficient quantities of the medicinal product, or; (iii) the second applicant can establish in the application that the second medicinal product, although, similar to the orphan medicinal product already authorized, is safer, more effective or otherwise clinically superior.

The receipt of orphan drug designation status does not change the regulatory requirements or process for obtaining marketing approval and designation does not mean that marketing approval will be received.

We may seek a breakthrough therapy designation from the FDA for Coversin. Such designation or a similar designation from other national or international regulatory agencies, may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that Coversin or any other product candidates will receive marketing approval.

We may seek a breakthrough therapy designation for Coversin. A breakthrough therapy is defined as a product that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. Designation as a breakthrough therapy is within the discretion of the FDA. Receipt of a breakthrough therapy designation for Coversin may not result in a faster development process, review or approval compared to products considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if Coversin qualifies as a breakthrough therapy, the FDA may later decide that it no longer meets the conditions for qualification.

Even if we obtain FDA approval of Coversin, we or our partners may never obtain approval or commercialize our product candidates outside of the United States and, conversely, even if we obtain regulatory approval of Coversin in the EU, we or our partners may never obtain approval or commercialize our product candidates outside the EU.

In order to market any products in a country, we must establish and comply with numerous and varying regulatory requirements of other countries regarding clinical trial design, 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 other countries could result in significant delays, difficulties and costs for us and may require additional preclinical studies or clinical trials which would be costly and time consuming and could delay or prevent introduction of Coversin in those countries. We rely on contract research organizations for experience in obtaining regulatory approval in international markets. If we or our partners fail to comply with regulatory requirements or to obtain and maintain required approvals, our target market will be reduced and our ability to realize the full market potential of Coversin will be harmed.

If we or our partners market products in a manner that violates fraud and abuse and other healthcare laws, or if we or they violate government price reporting laws, we or our partners may be subject to administrative civil and/or criminal penalties.

In addition to FDA restrictions on marketing of pharmaceutical products, several other types of state and federal healthcare laws, including those commonly referred to as “fraud and abuse” laws have been applied in recent years to restrict certain marketing practices in the pharmaceutical industry. These laws include, among others, false claims and anti-kickback statutes. At such time, if ever, as we or any of our partners market any of our future approved products, it is possible that some of the business activities of us and/or our partners could be subject to challenge under one or more of these laws.

Federal false claims, false statements and civil monetary penalties laws prohibit any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government or to get a false claim paid. The federal healthcare program anti-kickback statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce, or in return for, purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid or other federally financed healthcare programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other. Although there are several statutory exceptions and regulatory safe harbors protecting certain common activities from prosecution, they are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor.

In addition, we and/or our partners may be subject to data privacy and security regulation, including the Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their respective implementing regulations, which impose specified requirements relating to the privacy, security and transmission of individually identifiable health information.

Most states also have statutes or regulations similar to these federal laws, which may apply to items such as pharmaceutical products and services reimbursed by private insurers. We and/or our partners may be subject to administrative, civil and criminal sanctions for violations of any of these federal and state laws.

Our employees, principal investigators, consultants, commercial partners or vendors may engage in misconduct or other improper activities, including non-compliance with regulatory standards.

We are also exposed to the risk of employees, independent contractors, principal investigators, consultants, commercial partners or vendors engaging in fraud or other misconduct. Misconduct by employees, independent contractors, principal investigators, consultants, commercial partners and vendors could include intentional failures to comply with EU regulations, to provide accurate information to the EMA or EU Member States authorities or to comply with manufacturing or quality standards we have or will have established. In particular, 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 such as promotion of products by medical practitioners. Of general application are the European Anti-Fraud Office Regulation 883/2013, and the UK Bribery Act 2010. Under the latter, a commercial organisation can be guilty of the offence if the bribery is carried out by an employee, agent, subsidiary, or another third-party, and the location of the third-party is irrelevant to the prosecution. The advertising of medicinal products in the EU is regulated by Title VIII of European Directive 2001/83/EC. The corresponding UK implementing legislation is Part 14 of the Human Medicines Regulations 2012 (S.I. 2012/1916 as amended). Such laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programmes and other business arrangements. Misconduct could also involve the improper use of information obtained in the course of clinical studies, which could result in regulatory sanctions and serious and irreparable harm to our reputation. This could also apply with respect to data privacy. In the EU, the collection and use of Personal Data is governed by EU Directive 95/46/EEC. In the UK this was implemented by the Data Protection Act 1998. However, the current legislation is in the process of being replaced by the General Data Protection Regulation (EU) 2016/679, or GDPR, on the protection of natural persons with regard to the processing of personal data and on the free movement of such data. The GDPR entered into force on May 24, 2016 and repealed Directive 95/46/EC. The GDPR will apply directly in all member states (including the UK) from May 25, 2018. It is not always possible to identify and deter misconduct by employees or other parties. The precautions we take to detect and prevent this activity may not protect us from legal or regulatory action resulting from a failure to comply with applicable laws or regulations. Misconduct by our employees, principal investigators, consultants, commercial partners or vendors could result in significant financial penalties, criminal sanctions and thus have a material adverse effect on our business, including through the imposition of significant fines or other sanctions, and our reputation.

Risks Related to our Intellectual Property

Our success depends on our ability to protect our intellectual property and our proprietary technologies.

Our commercial success depends in part on our ability to obtain and maintain patent protection and trade secret protection for our product candidates, proprietary technologies, and their uses as well as our ability to operate without infringing upon the proprietary rights of others. We can provide no assurance that our patent applications or those of our licensors will result in additional patents being issued or that issued patents will afford sufficient protection against competitors with similar technologies, nor can there be any assurance that the patents issued will not be infringed, designed around or invalidated by third parties. Even issued patents may later be found unenforceable or may be modified or revoked in proceedings instituted by third parties before various patent offices or in courts. The degree of future protection for our proprietary rights is uncertain. Only limited protection may be available and may not adequately protect our rights or permit us to gain or keep any competitive advantage. Composition-of-matter patents on the biological or chemical active pharmaceutical ingredients are generally considered to offer the strongest protection of intellectual property and provide the broadest scope of patent protection for pharmaceutical products, as such patents provide protection without regard to any method of use or any method of manufacturing. While we have issued composition-of-matter patents in the United States and other countries for Coversin, we cannot be certain that the claims in our issued composition-of-matter patents will not be found invalid or unenforceable if challenged. We cannot be certain that the claims in our patent applications covering composition-of-matter or formulations of our product candidates will be considered patentable by the United States Patent and Trademark Office, or USPTO, and courts in the United States or by the patent offices and courts in foreign countries, nor can we be certain that the claims in our issued composition-of-matter patents will not be found invalid or unenforceable if challenged. Even if our patent applications covering formulations of our product candidates issue as patents, the formulation patents protect a specific formulation of a product and may not be enforced against competitors making and marketing a product that has the same active pharmaceutical ingredient in a different formulation. Method-of-use patents protect the use of a product for the specified method or for treatment of a particular indication. This type of patents may not be enforced against competitors making and marketing a product that has the same active pharmaceutical ingredient but is used for a method not included in the patent. Moreover, even if competitors do not actively promote their product for our targeted indications, physicians may prescribe these products “off-label.” Although off-label prescriptions may infringe or contribute to the infringement of method-of-use patents, the practice is common and such infringement is difficult to prevent or prosecute.

Our issued patents for Coversin and its uses are expected to expire between 2024 and 2031 (excluding any patent term adjustment or potential patent term extension). Our pending patent applications cover formulations, combination products and use of Coversin to treat various indications and, if issued, are expected to expire at various times that range from 2024 to 2037 (excluding any potential patent term adjustment or extension).

The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our future development partners will be successful in protecting our product candidates by obtaining and defending patents. These risks and uncertainties include the following:

- the USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case;

- patent applications may not result in any patents being issued;

- patents that may be issued or in-licensed may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable or otherwise may not provide any competitive advantage;

- our competitors, many of whom have substantially greater resources and many of whom have made significant investments in competing technologies, may seek or may have already obtained patents that will limit, interfere with or eliminate our ability to make, use, and sell our potential product candidates;

- there may be significant pressure on the U.S. government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns; and

- countries other than the United States may have patent laws less favorable to patentees than those upheld by U.S. courts, allowing foreign competitors a better opportunity to create, develop and market competing product candidates.

In addition, we rely on the protection of our trade secrets and proprietary know-how. Although we have taken steps to protect our trade secrets and unpatented know-how, including entering into confidentiality agreements with third parties, and confidential information and inventions agreements with employees, consultants and advisors, we cannot provide any assurances that all such agreements have been duly executed, and third parties may still obtain this information or may come upon this or similar information independently. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating its trade secrets. If any of these events occurs or if we otherwise lose protection for our trade secrets or proprietary know-how, our business may be harmed.

Others may claim an ownership interest in our intellectual property which could expose it to litigation and have a significant adverse effect on its prospects.

A third party may claim an ownership interest in one or more of our patents or other intellectual property. A third party could bring legal actions against us and seek monetary damages and/or enjoin clinical testing, manufacturing and marketing of the affected product or products. We cannot guarantee that a third-party will not assert a claim or an interest in any of such patents or intellectual property. If we become involved in any litigation, it could consume a substantial portion of our resources, and cause a significant diversion of effort by our technical and management personnel. If any of these actions are successful, in addition to any potential liability for damages, we could be required to obtain a license to continue to manufacture or market the affected product, in which case we may be required to pay substantial royalties or grant cross-licenses to our patents. We cannot, however, assure you that any such license will be available on acceptable terms, if at all. Ultimately, we could be prevented from commercializing a product, or be forced to cease some aspect of our business operations as a result of claims of patent infringement or violation of other IP rights, Further, the outcome of IP litigation is subject to uncertainties that cannot be adequately quantified in advance, including the demeanor and credibility of witnesses and the identity of the adverse party. This is especially true in IP cases that may turn on the testimony of experts as to technical facts upon which experts may reasonably disagree.

Risks Related to our Business Operations

Pending securities class action lawsuits against us and SEC requests for information could lead to adverse outcomes.

In May 2017, putative class actions asserting violations of Sections 10(b) and 20(a) of the Exchange Act, based primarily on our press releases or statements issued between March 30, 2017 and May 11, 2017 concerning the Phase II PNH trial of Coversin and the Edison Report about us and actions taken by us after the report was issued were commenced in the U.S. District Court for the Southern District of New York against us, our former Chief Executive Officer and our Chief Financial Officer. We intend to engage in a vigorous defense of the lawsuits. In certain circumstances, we are obliged to indemnify our current and former officers who are named as defendants in these lawsuits. In addition, we voluntarily reported to the SEC our special committee review of the involvement of our personnel in the Edison Report. In response, the SEC requested certain documents from us with respect to the matters we reported. We are cooperating with the SEC's requests for information. However, we are unable to predict the outcome of any of these matters at this time. Any conclusion of these matters in a manner adverse to us could have a material adverse effect on our financial condition and results of operations. For example, we may be required to pay substantial damages, incur payments of fines and penalties, incur substantial costs not covered by our directors' and officers' liability insurance, suffer a significant adverse impact on our reputation, and management's attention and resources may be diverted from other priorities, including the execution of business plans and strategies that are important to our ability to grow our business, any of which could have a material adverse effect on our business.

We currently have no marketing, sales or distribution infrastructure with respect to Coversin. If we are unable to develop our sales, marketing and distribution capability on our own or through collaborations with marketing partners, we will not be successful in commercializing our product candidates.

We currently have no marketing, sales or distribution capabilities and have limited sales or marketing experience within our organization. If our product candidate Coversin is approved, we intend either to establish a sales and marketing organization with technical expertise and supporting distribution capabilities to commercialize Coversin, 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 Coversin. In addition, we may not be able to hire a sales force in the United States or other target market 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 or third parties' internal sales, marketing and distribution capabilities would adversely impact the commercialization of Coversin and other future product candidates.

With respect to our existing and future product candidates, we may choose to collaborate with third parties that have direct sales forces and established distribution systems, either to augment or to serve as an alternative to our own sales force and distribution systems. Any future product revenue may be lower than if it directly marketed or sold any approved products. In addition, any revenue we receive will depend in whole or in part upon the efforts of these third parties, 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 any approved products. If we are not successful in commercializing any approved products, our future product revenue will suffer and we may incur significant additional losses.

We only have a limited number of employees to manage and operate our business.

As of September 30, 2017, we had sixteen full-time employees and one full-time equivalent consultants. Our focus on the development of Coversin requires us to optimize cash utilization and to manage and operate our business in a highly efficient manner. We cannot assure you that we will be able to hire and/or retain adequate staffing levels to develop Coversin or run our operations and/or to accomplish all of the objectives that we otherwise would seek to accomplish.

We depend heavily on our executive officers, directors, and principal consultants and the loss of their services would materially harm our business.

Our success depends, and will likely continue to depend, upon our ability to hire, retain the services of our current executive officers, directors, principal consultants and others. In addition, we have established relationships with universities and research institutions which have historically provided, and continue to provide, us with access to research laboratories, clinical trials, facilities and patients. The loss of the services of any of these individuals or institutions could have a material adverse effect on our business.

Our industry is highly competitive, and our product candidates may become obsolete.

We are engaged in a rapidly evolving field. Competition from other pharmaceutical companies, biotechnology companies and research and academic institutions is intense and likely to increase. Many of those companies and institutions have substantially greater financial, technical and human resources than us. Those companies and institutions also have substantially greater experience in developing products, conducting clinical trials, obtaining regulatory approval and in manufacturing and marketing pharmaceutical products. Our competitors may succeed in obtaining regulatory approval for their products more rapidly than we do. Competitors have developed or are in the process of developing technologies that are, or in the future may be, the basis for competitive products, such as Alexion Pharmaceuticals' Soliris® (eculizumab). Our competitors may succeed in developing products that are more effective and/or cost competitive than those we are developing, or that would render our product candidates less competitive or even obsolete. In addition, one or more of our competitors may achieve product commercialization or patent protection earlier than us, which could materially adversely affect our business.

If the FDA or other applicable regulatory authorities approve generic products that compete with any of our or any of our partners' product candidates, the sales of our product candidates would be adversely affected.

Once an NDA or marketing authorization application outside the United States is approved, the product covered thereby becomes a "listed drug" that can, in turn, be cited by potential competitors in support of approval of an abbreviated new drug application in the United States. Agency regulations and other applicable regulations and policies provide incentives to manufacturers to create modified, non-infringing versions of a drug to facilitate the approval of an abbreviated new drug application or other application for generic substitutes in the United States and in nearly every pharmaceutical market around the world. These generic equivalents, which must meet the same quality standards as branded pharmaceuticals, would be significantly less costly than us to bring to market, and companies that produce generic equivalents are generally able to offer their products at lower prices. Thus, after the introduction of a generic competitor, a significant percentage of the sales of any branded product is typically lost to the generic product. Accordingly, competition from generic equivalents to our or any of our partners' future products, if any, could materially adversely impact our future revenue, profitability and financial condition.

If physicians and patients do not accept our future products or if the market for indications for which any product candidate is approved is smaller than expected, we may be unable to generate significant revenue, if any.

Even if any of our product candidates obtain regulatory approval, they may not gain market acceptance among physicians, patients, and third-party payers. Physicians may decide not to recommend its treatments for a variety of reasons including:

- timing of market introduction of competitive products;
- demonstration of clinical safety and efficacy compared to other products;
- cost-effectiveness;

- limited or no coverage by third-party payers;
- convenience and ease of administration;
- prevalence and severity of adverse side effects;
- restrictions in the label of the drug;
- other potential advantages of alternative treatment methods; and
- ineffective marketing and distribution support of any future products.

If any of our product candidates are approved, but fail to achieve market acceptance or such market is smaller than anticipated, we may not be able to generate significant revenue and our business would suffer.

The uncertainty associated with pharmaceutical reimbursement and related matters may adversely affect our business.

Market acceptance and sales of any one or more of our product candidates will depend on reimbursement policies and may be affected by future healthcare reform measures in the United States and in foreign jurisdictions. Government authorities and third-party payers, such as private health insurers and health maintenance organizations, decide which drugs they will cover and establish payment levels. We cannot be certain that reimbursement will be available for any of our product candidates. Also, we cannot be certain that reimbursement policies will not reduce the demand for, or the price paid for, any future products. The insurance coverage and reimbursement status of newly-approved products for orphan diseases is particularly uncertain, and failure to obtain or maintain adequate coverage and reimbursement for Coversin or any other product candidates could limit our ability to generate revenue.

The United States and several foreign jurisdictions are considering, or have already enacted, a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell any future products profitably. There is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access to healthcare. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. We expect to experience pricing pressures in connection with the sale of any products that we develop due to the trend toward managed healthcare, increasing influence of health maintenance organizations and additional legislative proposals.

In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, PPACA, became law in the United States. Since its enactment, there have been judicial and Congressional challenges to certain aspects of the PPACA. Congress and President Trump have expressed their intentions to repeal or repeal and replace the PPACA. President Trump issued an Executive Order and both chambers of Congress passed bills, all with the goal of fulfilling their intensions. However, to date, the Executive Order has had limited effect and the Congressional activities have not resulted in the passage of a law. If a law is enacted, many if not all of the provisions of the PPACA may no longer apply to prescription drugs. While we are unable to predict what changes may ultimately be enacted, to the extent that future changes affect how any future products are paid for and reimbursed by government and private payers our business could be adversely impacted.

If any product liability lawsuits are successfully brought against us or any of our collaborative partners, we may incur substantial liabilities and may be required to limit commercialization of our product candidates.

We face an inherent risk of product liability lawsuits related to the testing of our product candidates in seriously ill patients and will face an even greater risk if product candidates are approved by regulatory authorities and introduced commercially. Product liability claims may be brought against us or our partners by participants enrolled in our clinical trials, patients, health care providers or others using, administering or selling any of our future approved products. If we cannot successfully defend ourselves against any such claims, we may incur substantial liabilities, which may result in:

- decreased demand for any of our future approved products;
- injury to our reputation;
- withdrawal of clinical trial participants;
- termination of clinical trial sites or entire trial programs;
- significant litigation costs;
- substantial monetary awards to or costly settlements with patients or other claimants;
- product recalls or a change in the indications for which they may be used;
- loss of revenue;
- diversion of management and scientific resources from our business operations; and
- the inability to commercialize our product candidates.

If any of our product candidates are approved for commercial sale, we will be highly dependent upon consumer perceptions of us and the safety and quality of our products. We could be adversely affected if we are subject to negative publicity associated with illness or other adverse effects resulting from patients' use or misuse of our products or any similar products distributed by other companies.

Although we currently carry clinical trial insurance, the amount of such insurance coverage may not be adequate. In addition, we will need to obtain more comprehensive insurance and increase our insurance coverage when we begin the commercialization of our product candidates. Insurance coverage is becoming increasingly expensive. As a result, we may be unable to maintain or obtain sufficient insurance at a reasonable cost to protect us against losses that could have a material adverse effect on our business.

We enter into various contracts in the normal course of our business in which we indemnify the other party to the contract. In the event we have to perform under these indemnification provisions, it could have a material adverse effect on our business, financial condition and results of operations.

In the normal course of business, we periodically enter into academic, commercial, service, collaboration, licensing, consulting and other agreements that contain indemnification provisions. With respect to our academic and other research agreements, we typically indemnify the institution and related parties from losses arising from claims relating to the products, processes or services made, used, sold or performed pursuant to the agreements for which we have secured licenses, and from claims arising from our or our sublicensees' exercise of rights under the agreement. With respect to our commercial agreements, we indemnify our vendors from any third-party product liability claims that could result from the production, use or consumption of the product, as well as for alleged infringements of any patent or other intellectual property right by a third party.

Should our obligation under an indemnification provision exceed applicable insurance coverage or if we were denied insurance coverage, our business, financial condition and results of operations could be adversely affected. Similarly, if we are relying on a collaborator to indemnify us and the collaborator is denied insurance coverage or the indemnification obligation exceeds the applicable insurance coverage and does not have other assets available to indemnify us, our business, financial condition and results of operations could be adversely affected.

Our business and operations would suffer in the event of computer system failures.

Despite the implementation of security measures, our internal computer systems, and those of our partners and other third parties on which we rely, are vulnerable to damage from computer viruses, unauthorized access, natural disasters, fire, terrorism, war and telecommunication and electrical failures. In addition, our systems safeguard important confidential personal data regarding our subjects. If a disruption event were to occur and cause interruptions in our operations, it could result in a material disruption of our drug development programs. For example, the loss of clinical trial data from completed, ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development of Coversin and other product candidates could be delayed.

If we fail to develop and commercialize other product candidates, we may be unable to grow our business.

Although the development and commercialization of Coversin is our primary focus, as part of our longer-term growth strategy, we plan to evaluate the development and commercialization of other therapies related to immune-mediated, inflammatory, orphan and other diseases. We may from time to time evaluate internal opportunities from our current product candidates, and also may choose to in-license or acquire other product candidates as well as commercial products to treat patients suffering from immune-mediated or orphan or other disorders with high unmet medical needs and limited treatment options. These other product candidates will require additional, time-consuming development efforts prior to commercial sale, including preclinical studies, clinical trials and approval by the FDA, EMA and/or applicable foreign regulatory authorities. All product candidates are prone to the risks of failure that are inherent in pharmaceutical product development, including the possibility that the product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities. In addition, we cannot assure you that any such products that are approved will be manufactured or produced economically, successfully commercialized or widely accepted in the marketplace or be more effective than other commercially available alternatives.

Risks Related to Our Reliance on Third Parties

If the third parties on which we rely for our clinical trials and results do not perform our clinical trial activities in accordance with good clinical practices and related regulatory requirements, we may be unable to obtain regulatory approval for or commercialize our product candidates.

We use and heavily rely on third-party service providers to conduct and/or oversee the clinical trials of our product candidates and expect to continue to do so for the foreseeable future. Nonetheless, we are responsible for confirming that each of our clinical trials is conducted in accordance with the FDAs and/or EMA's requirements and its general investigational plan and protocol.

The FDA and EMA require us and our third-party service providers to comply with regulations and standards, commonly referred to as good clinical practices, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the trial participants are adequately protected. Our reliance on third parties that we do not control does not relieve us of these responsibilities and requirements. Third parties may not complete activities on schedule or conduct our clinical trials in accordance with regulatory requirements or the respective trial plans and protocols. In addition, third parties may not be able to repeat their past successes in clinical trials. The third parties' failure to carry out their obligations could delay or prevent the development, approval and commercialization of our product candidates or result in enforcement action against us.

Use of third parties to manufacture our product candidates may increase the risk that we will not have sufficient quantities of our product candidates, products, or necessary quantities at an acceptable cost.

We do not own or operate manufacturing facilities for the production of clinical or commercial quantities of our product candidates, and we lack the resources and the capabilities to do so. As a result, we currently rely on third parties for supply of the active pharmaceutical ingredients, or API, in our product candidates. Our strategy is to outsource all manufacturing of our product candidates and products to third parties.

We currently engage a third-party manufacturer to provide clinical material of the API, lyophilization, release testing and fill and finish services for the final drug product formulation of Coversin that is being used in our clinical trials. Although we believe that there are several potential alternative manufacturers who could manufacture Coversin, we may incur added costs and delays in identifying and qualifying any such replacement. In addition, we have not yet concluded a commercial supply contract with any commercial manufacturer. There is no assurance that we will be able to timely secure needed supply arrangements on satisfactory terms, or at all. Our failure to secure these arrangements as needed could have a material adverse effect on our ability to complete the development of our product candidates or, to commercialize them. We may be unable to conclude agreements for commercial supply with third-party manufacturers, or may be unable to do so on acceptable terms. There may be difficulties in scaling up to commercial quantities and formulation of Coversin and the costs of manufacturing could be prohibitive.

Even if we are able to establish and maintain arrangements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- reliance on third-parties for manufacturing process development, regulatory compliance and quality assurance;
- limitations on supply availability resulting from capacity and scheduling constraints of third-parties;
- the possible breach of manufacturing agreements by third-parties because of factors beyond our control; and
- the possible termination or non-renewal of the manufacturing agreements by the third-party, at a time that is costly or inconvenient to us.

If we do not maintain our key manufacturing relationships, we may fail to find replacement manufacturers or develop our own manufacturing capabilities, which could delay or impair our ability to obtain regulatory approval for our products. If we do find replacement manufacturers, we may not be able to enter into agreements with them on terms and conditions favorable to us and there could be a substantial delay before new facilities could be qualified and registered with the FDA and other foreign regulatory authorities.

The FDA, EMA and other foreign regulatory authorities require manufacturers to register manufacturing facilities. The FDA and corresponding foreign regulators also inspect these facilities to confirm compliance with current good manufacturing practices, or cGMPs. Contract manufacturers may face manufacturing or quality control problems causing drug substance production and shipment delays or a situation where the contractor may not be able to maintain compliance with the applicable cGMP requirements. Any failure to comply with cGMP requirements or other FDA, EMA and comparable foreign regulatory requirements could adversely affect our clinical research activities and our ability to develop our product candidates and market our products following approval.

If our third-party manufacturer of Coversin is unable to increase the scale of its production of Coversin, and/or increase the product yield of its manufacturing, then our costs to manufacture the product may increase and commercialization may be delayed.

In order to produce sufficient quantities of Coversin to meet the demand for clinical trials and subsequent commercialization, our third party manufacturer of Coversin will be required to increase its production and optimize its manufacturing processes while maintaining the quality of the product. The transition to larger scale production could prove difficult. In addition, if our third party manufacturer is not able to optimize its manufacturing process to increase the product yield for Coversin, or if it is unable to produce increased amounts of Coversin while maintaining the quality of the product, then we may not be able to meet the demands of clinical trials or market demands, which could decrease our ability to generate profits and have a material adverse impact on our business and results of operation.

Risks Related to our Ordinary Shares and ADSs

Ownership of our ADSs and/or ordinary shares involves a high degree of risk.

Investing in and owning our ADSs and ordinary shares involve a high degree of risk. Shareholders should read carefully the risk factors provided within this section, as well as our public documents filed with the SEC, including the financial statements therein.

If we are deemed or become a passive foreign investment company, or PFIC, for U.S. federal income tax purposes in 2017 or in any prior or subsequent years, there may be negative tax consequences for U.S. taxpayers that are holders of our ADSs.

We will be treated as a passive foreign investment company, or PFIC, for U.S. federal income tax purposes in any taxable year in which either (i) at least 75% of our gross income is "passive income" or (ii) on average at least 50% of our assets by value produce passive income or are held for the production of passive income. Passive income for this purpose generally includes, among other things, certain dividends, interest, royalties, rents and gains from commodities and securities transactions and from the sale or exchange of property that gives rise to passive income. Passive income also includes amounts derived by reason of the temporary investment of funds, including those raised in a public offering. In determining whether a non-U.S. corporation is a PFIC, a proportionate share of the income and assets of each corporation in which it owns, directly or indirectly, at least a 25% interest (by value) is taken into account.

We believe we are not a PFIC for 2016 and although we have not determined whether we will be a PFIC in 2017, or in any subsequent year, our operating results for any such years may cause us to be a PFIC. If we are deemed a PFIC for any taxable year, and a U.S. Holder does not make an election to treat us as a "qualified electing fund," or QEF, or make a "mark-to-market" election, then "excess distributions" to a U.S. shareholder, and any gain realized on the sale or other disposition of our ADSs will be subject to special rules. Under these rules: (i) the excess distribution or gain would be allocated ratably over the U.S. Holder's holding period for ADSs; (ii) the amount allocated to the current taxable year and any period prior to the first day of the first taxable year in which we were a PFIC would be taxed as ordinary income; and (iii) the amount allocated to each of the other taxable years would be subject to tax at the highest rate of tax in effect for the applicable class of taxpayer for that year, and an interest charge for the deemed deferral benefit would be imposed with respect to the resulting tax attributable to each such other taxable year. In addition, if the U.S. Internal Revenue Service determines that we are a PFIC for a year with respect to which we have determined that we were not a PFIC, it may be too late for a U.S. shareholder to make a timely QEF or mark-to-market election. U.S. Holders who hold our ADSs during a period when we are a PFIC will be subject to the foregoing rules, even if we cease to be a PFIC in subsequent years, subject to exceptions for U.S. shareholders who made a timely QEF or mark-to-market election. A U.S. shareholder can make a QEF election by completing the relevant portions of and filing IRS Form 8621 in accordance with the instructions thereto. A QEF election generally may not be revoked without the consent of the IRS. If an investor provides reasonable notice to us that it has determined to make a QEF election, we shall provide annual financial information to such investor as may be reasonably required for purposes of filing United States federal income tax returns in connection with such QEF election.

A limited public market exists for our securities and we cannot assure you that our securities will continue to be listed on The NASDAQ Capital Market or any other securities exchange or that an active trading market will ever develop for any of our securities.

Our ADSs were approved for listing and began trading on The NASDAQ Capital Market under the symbol "CLTX" on January 31, 2014 and commenced trading under the symbol "AKTX" commencing on September 21, 2015. An active trading market for our shares has not fully developed and, even if it does, it may not be sustained. In addition, we cannot assure you that we will be successful in meeting the continuing listing standards of The NASDAQ Capital Market and cannot assure you that our ADSs will be listed on a national securities exchange. If an active market for our ADS does not develop or is not sustained, it may be difficult for investors to sell their shares without depressing the market price for the shares or at all. Further, an inactive market may also impair our ability to raise capital and may impair our ability to enter into strategic partnerships or acquire companies or products by using our ADSs or ordinary shares as consideration.

The market price of our ADSs may be volatile and may fluctuate in a way that is disproportionate to our operating performance.

Our stock price may experience substantial volatility as a result of a number of factors. The market prices for securities of biotechnology companies in general have been highly volatile and may continue to be so in the future. The following factors, in addition to other risk factors described in this section, may have a significant impact on the market price of our ADSs:

- sales or potential sales of substantial amounts of our ordinary shares or ADSs;
- delay or failure in initiating, enrolling, or completing pre-clinical or clinical trials or unsatisfactory results of these trials or events reported in any of our current or future clinical trials;
- announcements about us or about our competitors, including clinical trial results, regulatory approvals or new product introductions;
- developments concerning our licensors or product manufacturers;
- litigation and other developments relating to our patents or other proprietary rights or those of our competitors;
- developments relating to the putative shareholder class action and SEC requests for information;
- conditions in the pharmaceutical or biotechnology industries;
- governmental regulation and legislation;
- variations in our anticipated or actual operating results;
- change in securities analysts' estimates of our performance, or our failure to meet analysts' expectations;
- whether, to what extent and under what conditions the FDA or EMA will permit us to continue developing our product candidates, if at all, and if development is continued, any reports of safety issues or other adverse events observed in any potential future studies of these product candidates;
- adverse publicity;
- our ability to enter into new collaborative arrangements with respect to our product candidates;
- the terms and timing of any future collaborative, licensing or other arrangements that we may establish;
- our ability to raise additional capital to carry through with our clinical development plans and current and future operations and the terms of any related financing arrangements;
- the timing of achievement of, or failure to achieve, our and any potential future collaborators' clinical, regulatory and other milestones, such as the commencement of clinical development, the completion of a clinical trial or the receipt of regulatory approval;
- announcement of FDA or EMA approval or non-approval of our product candidates or delays in or adverse events during the FDA or EMA review process;
- actions taken by regulatory agencies with respect to our product candidates or products, our clinical trials or our sales and marketing activities, including regulatory actions requiring or leading to restrictions, limitations and/or warnings in the label of an approved product candidate;
- uncontemplated problems in the supply of the raw materials used to produce our product candidates;

- the commercial success of any product approved by the FDA, EMA or any other foreign counterpart;
- introductions or announcements of technological innovations or new products by us, our potential future collaborators, or our competitors, and the timing of these introductions or announcements;
- market conditions for equity investments in general, or the biotechnology or pharmaceutical industries in particular;
- we may have limited or very low trading volume that may increase the volatility of the market price of our ADSs;
- regulatory developments in the United States and foreign countries;
- changes in the structure or reimbursement policies of health care payment systems;
- any intellectual property infringement lawsuit involving us;
- actual or anticipated fluctuations in our results of operations;
- changes in financial estimates or recommendations by securities analysts;
- hedging activity that may develop regarding our ADSs;
- regional or worldwide recession;
- sales of large blocks of our ordinary shares or ADSs;
- sales of our ordinary shares or ADSs by our executive officers, directors and significant shareholders;
- managerial costs and expenses;
- changes in accounting principles; and
- the loss of any of our key scientific or management personnel.

The stock markets in general, and the markets for biotechnology stocks in particular, have experienced significant volatility that has often been unrelated to the operating performance of particular companies. The financial markets continue to face significant uncertainty, resulting in a decline in investor confidence and concerns about the proper functioning of the securities markets, which decline in general investor confidence has resulted in depressed stock prices for many companies notwithstanding the lack of a fundamental change in their underlying business models or prospects. These broad market fluctuations may adversely affect the trading price of our ADSs.

In the past, class action litigation has often been instituted against companies whose securities have experienced periods of volatility in market price. Any such litigation brought against us, in addition to the ongoing putative class action against us, could result in substantial costs, which could hurt our financial condition and results of operations and divert management’s attention and resources, which could result in delays of our clinical trials or commercialization efforts.

Insiders have control over us which could delay or prevent a change in corporate control or result in the entrenchment of management and/or the board of directors.

As of September 30, 2017, our directors and executive officers, together with their affiliates and related persons, beneficially own, in the aggregate, approximately 62.1% of our outstanding ordinary shares. RPC, which is controlled by our chairman Dr. Ray Prudo, beneficially owns approximately 61.3% of our outstanding ordinary shares. Accordingly, these shareholders, if acting together, or Dr. Prudo, individually, may have the ability to impact the outcome of matters submitted to our shareholders for approval, including the election and removal of directors and any merger, consolidation, or sale of all or substantially all of our assets. In addition, these persons may have the ability to influence the management and affairs of our company. Accordingly, this concentration of ownership may harm the market price of our ADSs by:

- delaying, deferring, or preventing a change in control;
- entrenching our management and/or the board of directors;
- impeding a merger, consolidation, takeover, or other business combination involving us; or
- discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of us.

Future sales and issuances of our ordinary shares or ADSs or rights to purchase ordinary shares or ADSs pursuant to our equity incentive plans could result in additional dilution of the percentage ownership of our shareholders and could cause our share price to fall.

We expect that significant additional capital will be needed in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our shareholders may experience substantial dilution. We may sell ordinary shares (which may be represented by ADSs), convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell ordinary shares, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. Such sales may also result in material dilution to our existing shareholders, and new investors could gain rights superior to our existing shareholders.

Sales of a substantial number of our ADSs by our existing shareholders in the public market could cause our stock price to fall.

Sales of a substantial number of our ADSs in the public market or the perception that these sales might occur, could significantly reduce the market price of our ADSs and impair our ability to raise adequate capital through the sale of additional equity securities.

The vote by the United Kingdom to leave the European Union could adversely affect our business, financial condition, results of operations and prospects.

On March 29, 2017, the Prime Minister of the United Kingdom submitted formal notice to the European Union in order to trigger Article 50 of the Treaty on European Union. This is the formal mechanism which begins the two-year process of negotiating the UK's exit from the EU, and to determine the future terms of the UK's relationship with the EU, including the terms of trade between the UK and the EU, and potentially other countries. The effects of the UK exiting the EU (commonly referred to as Brexit) will depend on any agreements the UK makes to retain access to EU markets. In addition, Brexit could lead to legal uncertainty and potentially divergent national laws and regulations as the UK determines which EU laws to replace or replicate. Brexit could adversely affect economic or market conditions in the UK, Europe or globally and could contribute to instability in global financial markets, in particular until there is more certainty as to the outcome of the aforementioned decisions and negotiations. Exports from the United Kingdom may incur increased duties and tariffs following Brexit, or Brexit could result in the regulatory compliance and patent costs associated with our business compliance costs increasing significantly so as to adversely affect our financial condition, results of operations and prospects. Our regulatory compliance costs may increase as a result of Brexit. Following an exit by the UK from the EU, we may be required to register any current EU-wide patents separately with the UK Intellectual Property Office, which could require significant additional expense. Further, our regulatory compliance costs may increase as a result of Brexit, as on an exit from the EU, the UK may cease compliance with the EU and the EMA's legislative regime for medicines, their research, development and commercialisation. Any changes to such regulatory regimes could require us to comply with separate regimes in the UK and the EU, or to develop new policies and procedures or reorganise our operations, any of which could increase our compliance costs. Brexit has also led to a decrease in the value of pounds sterling against the U.S. dollar, as well as general volatility in currency exchange markets. The challenges faced by the UK following Brexit could result in an overall decline in trade and economic growth and/or an increase in economic volatility and therefore may affect the attractiveness of the UK as a leading centre for business and commerce. Any of the aforementioned possible effects of Brexit, and others that the we cannot anticipate, may materially adversely affect our business, financial condition, results of operations and prospects.

Provisions in our Articles of Association and under English law could make an acquisition of our company more difficult and may prevent attempts by our shareholders to replace or remove our organization management.

Provisions in our Articles of Association may delay or prevent an acquisition or a change in management. These provisions include a staggered board and prohibition on actions by written consent of our shareholders. Although we believe these provisions collectively will provide for an opportunity to receive higher bids by requiring potential acquirors to negotiate with our board of directors, they would apply even if the offer may be considered beneficial by some shareholders. In addition, these provisions may frustrate or prevent any attempts by our shareholders to replace or remove then current management by making it more difficult for shareholders to replace members of the board of directors, which is responsible for appointing the members of management.

We do not anticipate paying cash dividends, and accordingly, shareholders must rely on the appreciation in our ADSs for any return on their investment.

We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Therefore, the success of an investment in our ADSs will depend upon any future appreciation in their value. There is no guarantee that our ADSs will appreciate in value or even maintain the price at which our shareholders have purchased their shares.

We were and are required to evaluate our internal control over financial reporting under Section 404 of the Sarbanes-Oxley Act of 2002, and any adverse results from such evaluation could result in a loss of investor confidence in our financial reports and have an adverse effect on the price of our ADSs.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, we are required to furnish an annual report by our management on our internal control over financial reporting. Such reports contain, among other matters, an assessment of the effectiveness of our internal control over financial reporting as of the end of our fiscal year, including a statement as to whether or not our internal control over financial reporting is effective. These assessments must include disclosure of any material weaknesses in our internal control over financial reporting identified by management. If we are unable to assert that our internal control over financial reporting is effective, we could lose investor confidence in the accuracy and completeness of our financial reports, which could have an adverse effect on the price of our stock ADSs.

Our independent registered public accounting firm is not required to formally attest to the effectiveness of our internal control over financial reporting until the later of the year following our first annual report required to be filed with the SEC, or the date we are no longer an “emerging growth company.” At such time, our independent registered public accounting firm may issue a report that is adverse in the event it is not satisfied with the level at which our controls are documented, designed or operating. Our remediation efforts may not enable us to avoid a material weakness in the future. We will remain an “emerging growth company” for up to five years following the date of the first sale of our common equity securities pursuant to an effective registration statement, although if the market value of our ADSs that is held by non-affiliates exceeds $700 million as of any June 30 before that time, we would cease to be an “emerging growth company” as of the following December 31. Furthermore, as a result of the extended time period afforded us as an “emerging growth company,” the effectiveness of our internal control over financial reporting may not be as transparent to our investors as they may otherwise expect of a public reporting company, which could further impact investor confidence in the accuracy and completeness of our financial reports.

We incur significant costs and demands upon management as a result of complying with the laws and regulations affecting public companies, which could harm our operating results.

As a public company, we incur significant legal, accounting and other expenses, including costs associated with public company reporting requirements. We also incur costs associated with current corporate governance requirements, including requirements under Section 404 and other provisions of the Sarbanes-Oxley Act of 2002, as well as rules implemented by the SEC and The NASDAQ Stock Market. The expenses incurred by public companies for reporting and corporate governance purposes have increased dramatically in recent years.

We are an "emerging growth company" and a "foreign private issuer" and as a result of this and other reduced disclosure requirements applicable to emerging growth companies and foreign private issuers, our ADSs may be less attractive to investors.

We are an "emerging growth company," as defined in the JOBS Act, and we intend to take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not "emerging growth companies" including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. In addition, Section 107 of the JOBS Act also provides that an "emerging growth company" can take advantage of the extended transition period provided in Section 7(a)(2)(B) of Securities Act of 1933, as amended, or the Securities Act, for complying with new or revised accounting standards. In other words, an "emerging growth company" can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We chose to "opt out" of the extended transition period related to the exemption from new or revised accounting standards, and as a result, we will comply with new or revised accounting standards on the relevant dates on which adoption of such standards is required for non-emerging growth companies. This election is irrevocable. We cannot predict if investors will find our ordinary shares or ADSs less attractive because of our reduced disclosure requirements. If some investors find our ordinary shares or ADSs less attractive as a result, there may be a less active trading market for our ADSs and our stock price may be more volatile. We may take advantage of these reporting exemptions until we are no longer an "emerging growth company." We will remain an "emerging growth company" for up to five years after the first sale of our common equity securities pursuant to an effective registration statement under the Securities Act, although if the market value of our ADSs that is held by non-affiliates exceeds $700 million as of any June 30 before that time, we would cease to be an "emerging growth company" as of the following December 31.

Furthermore, on July 1, 2016 we became a foreign private issuer having previously lost this status at the end of 2014. As a foreign private issuer, we are not subject to the same requirements that are imposed upon U.S. domestic issuers by the SEC. Under the Exchange Act, we are subject to reporting obligations that, in certain respects, are less detailed and less frequent than those of U.S. domestic reporting companies. For example, we will not be required to issue proxy statements that comply with the requirements applicable to U.S. domestic reporting companies. We will also have four months after the end of each fiscal year to file our annual reports with the SEC and will not be required to file current reports as frequently or promptly as U.S. domestic reporting companies. Furthermore, our officers, directors, and principal shareholders will be exempt from the requirements to report transactions in our equity securities and from the short-swing profit liability provisions contained in Section 16 of the Exchange Act. These exemptions and leniencies, along with other corporate governance exemptions resulting from our ability to rely on home country rules, will reduce the frequency and scope of information and protections to which you may otherwise have been eligible in relation to a U.S. domestic reporting companies. If we were to lose our foreign private issuer status, the regulatory and compliance costs to us under U.S. securities laws as a U.S. domestic issuer will be significantly more than costs we incur as a foreign private issuer.

U.S. investors may not be able to enforce their civil liabilities against our company or certain of our directors, controlling persons and officers.

It may be difficult for U.S. investors to bring and/or effectively enforce suits against our company outside of the United States. We are a public limited company incorporated in England and Wales under the Companies Act 2006, as amended, or the Companies Act. A majority our directors are not residents of the United States, and all or substantial portions of their assets are located outside of the United States. As a result, it may be difficult for U.S. holders of our ordinary shares or ADSs to effect service of process on these persons within the United States or to make effective recovery in the United States by enforcing any judgments rendered against them. In addition, if a judgment is obtained in the U.S. courts based on civil liability provisions of the U.S. federal securities laws against us or our directors or officers, it may, depending on the jurisdiction, be difficult to enforce the judgment in the non-U.S. courts against us and any of our non-U.S. resident executive officers or directors. Accordingly, U.S. shareholders may be forced to bring legal proceedings against us and our respective directors and officers under English law and in the English courts in order to enforce any claims that they may have against us or our directors and officers. The enforceability of a U.S. judgment in the United Kingdom will depend on the particular facts of the case as well as the laws and treaties in effect at the time. The United States and the United Kingdom do not currently have a treaty providing for reciprocal recognition and enforcement of judgments (other than arbitration awards) in civil and commercial matters. Nevertheless, it may be difficult for U.S. shareholders to bring an original action in the English courts to enforce liabilities based on the U.S. federal securities laws against us and any of our non-U.S. resident executive officers or directors.

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, and by our Articles of Association. These rights differ in certain respects from the rights of shareholders in typical U.S. corporations.

Holders of ADSs must act through the depositary to exercise their rights as shareholders of our company.

Holders of our ADSs do not have the same rights of our shareholders and may only exercise the voting rights with respect to the underlying ordinary shares in accordance with the provisions of the deposit agreement for the ADSs. Under our Articles of Association, the minimum notice period required to convene an Annual General Meeting is no less than 21 clear days' notice and 14 clear days' notice for a general meeting (unless, in the case of an annual general meeting all members entitled to attend and vote at the meeting, or in the case of a general meeting, a majority of the members entitled to attend and vote who hold not less than 95% of the voting shares (excluding treasury shares), agree to shorter notice). When a general meeting is convened, holders of our ADSs may not receive sufficient notice of a shareholders' meeting to permit them to withdraw their ordinary shares to allow them to cast their vote with respect to any specific matter. In addition, the depositary and its agents may not be able to send voting instructions to holders of our ADSs or carry out their voting instructions in a timely manner. We will make all reasonable efforts to cause the depositary to extend voting rights to holders of our ADSs in a timely manner, but we cannot assure them that they will receive the voting materials in time to ensure that they can instruct the depositary to vote their ADSs. Furthermore, the depositary and its agents will not be responsible 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 their right to vote and they may lack recourse if their ADSs are not voted as they requested. In addition, in the capacity as an ADS holder, they will not be able to call a shareholders' meeting.

The depositary for our ADSs will give us a discretionary proxy to vote our ordinary shares underlying ADSs if a holder of our ADSs does not vote at shareholders' meetings, except in limited circumstances, which could adversely affect their interests.

Under the deposit agreement for the ADSs, the depositary will give us a discretionary proxy to vote our ordinary shares underlying ADSs at shareholders' meetings if a holder of our ADSs does not vote, unless:

- we have failed to timely provide the depositary with our notice of meeting and related voting materials;
- we have instructed the depositary that we do not wish a discretionary proxy to be given;

- we have informed the depositary that there is substantial opposition as to a matter to be voted on at the meeting; or

- a matter to be voted on at the meeting would have a material adverse impact on shareholders.

The effect of this discretionary proxy is that a holder of our ADSs cannot prevent our ordinary shares underlying such ADSs from being voted, absent the situations described above, and it may make it more difficult for shareholders to influence the management of our company. Holders of our ordinary shares are not subject to this discretionary proxy.

Holders of our ADSs may be subject to limitations on transfers of 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.

The rights of holders of our ADSs to participate in any future rights offerings may be limited, which may cause dilution to their holdings and they may not receive cash dividends if it is impractical to make them available to them.

We may from time to time distribute rights to our shareholders, including rights to acquire our securities. However, we cannot make rights available to holders of our ADSs in the United States unless we register the rights and the securities to which the rights relate under the Securities Act or an exemption from the registration requirements is available. Also, under the deposit agreement, the depositary will not make rights available to holders of our ADSs unless either both the rights and any related securities are registered under the Securities Act, or the distribution of them to ADS holders is exempted from registration under the Securities Act. We are under no obligation to file a registration statement with respect to any such rights or securities or to endeavor to cause such a registration statement to be declared effective. Moreover, we may not be able to establish an exemption from registration under the Securities Act. Accordingly, holders of our ADSs may be unable to participate in our rights offerings and may experience dilution in their holdings.

In addition, the depositary 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 ordinary shares their ADSs represent. However, the depositary may, at its discretion, decide that it is inequitable or impractical to make a distribution available to any holders of ADSs. For example, the depositary may determine that it is not practicable to distribute certain property through the mail, or that the value of certain distributions may be less than the cost of mailing them. In these cases, the depositary may decide not to distribute such property and holders of our ADSs will not receive any such distribution.

GOVERNMENT REGULATION

Government Regulation and Product Approval

Government authorities in the U.S., at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, marketing and export and import of products such as those that we are developing. A new drug must be approved by the FDA, generally through the new drug application, or NDA, process and a new biologic must be approved by the FDA through the biologics license application, or BLA, process before it may be legally marketed in the U.S. The animal and other non-clinical data and the results of human clinical trials performed under an Investigational New Drug application, or IND, and under similar foreign applications will become part of the NDA or BLA.

U.S. Drug Development Process

In the U.S., the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and in the case of biologics, also under the Public Health Service Act, or PHSA, and implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local, and foreign statutes and regulations require 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 administrative or judicial sanctions. These sanctions could include the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, warning letters, requesting 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. Any agency or judicial enforcement action could have a material adverse effect on us. The process required by the FDA before a drug or biologic may be marketed in the U.S. generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies according to Good Laboratory Practices or other applicable regulations;
- submission to the FDA of an IND which must become effective before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials according to Good Clinical Practices to establish the safety and efficacy of the proposed drug for its intended use;
- submission to the FDA of an NDA or BLA;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with current good manufacturing practice, or cGMP, 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 or BLA.

Once a pharmaceutical candidate is identified for development, it enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information and analytical data, to the FDA as part of the IND. The sponsor will also include a protocol detailing, among other things, the objectives of the first phase of the clinical trials, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated, if the first phase lends itself to an efficacy evaluation. Some preclinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, 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. Clinical holds also may be imposed by the FDA at any time before or during studies due to safety concerns or non-compliance.

All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with good clinical practice regulations. They must be conducted under protocols detailing the objectives of the trial, dosing procedures, subject selection and exclusion criteria and the safety and effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND, and progress reports detailing the results of the clinical trials must be submitted at least annually. In addition, timely safety reports must be submitted to the FDA and the investigators for serious and unexpected adverse events. An institutional review board, or IRB, responsible for the research conducted at each institution participating in the clinical trial must review and approve each protocol before a clinical trial commences at that institution and must also approve the information regarding the trial and the consent form that must be provided to each trial subject or his or her legal representative, monitor the study until completed and otherwise comply with IRB regulations.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- ***Phase I:*** The product candidate is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion. In the case of some products for severe or life-threatening diseases, such as cancer, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing may be conducted in patients.

- ***Phase II***: This phase involves studies in 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 III***: Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical study sites. These studies are intended to establish the overall risk-benefit ratio of the product candidate and provide, if appropriate, an adequate basis for product labeling.

The FDA or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the research subjects or patients 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. Phase I, Phase II, and Phase III testing may not be completed successfully within any specified period, if at all.

During the development of a new drug, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to submission of an IND, at the end of Phase II, and before an NDA or BLA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice, and for the sponsor and FDA to reach agreement on the next phase of development. Sponsors typically use the end of Phase II meeting to discuss their Phase II clinical results and present their plans for the pivotal Phase III clinical trial that they believe will support approval of the new drug.

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

U.S. Review and Approval Processes

The results of product development, preclinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling, and other relevant information are submitted to the FDA as part of an NDA or BLA requesting approval to market the product. The submission of an NDA or BLA is subject to the payment of user fees; a waiver of such fees may be obtained under certain limited circumstances. The FDA initially reviews all NDAs and BLAs submitted to ensure that they are sufficiently complete for substantive review before it accepts them for filing. The FDA may request additional information rather than accept a NDA or BLA for filing. In this event, the NDA or BLA must be resubmitted with the additional information. The resubmitted application also is 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. FDA may refer the NDA or BLA to an advisory committee for review, evaluation and recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. The approval process is lengthy and often difficult, and the FDA may refuse to approve an NDA or BLA if the applicable regulatory criteria are not satisfied or may require additional clinical or other data and information. Even if such data and information are submitted, the FDA may ultimately decide that the NDA or BLA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data. The FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP-compliant to assure and preserve the product's identity, strength, quality and purity. The FDA reviews a BLA to determine, among other things whether the product is safe, pure and potent and the facility in which it is manufactured, processed, packed or held meets standards designed to assure the product's continued safety, purity and potency. Before approving an NDA or BLA, the FDA will inspect the facility or facilities where the product is manufactured. The FDA may issue a complete response letter, which may require additional clinical or other data or impose other conditions that must be met in order to secure final approval of the NDA or BLA, or an approval letter following satisfactory completion of all aspects of the review process.

NDAs or BLAs may receive either standard or priority review. Under current FDA review goals, standard review of an NDA for a new molecular entity (NME) or original BLA will be 10 months from the date that the NDA or BLA is filed. A drug representing a significant improvement in treatment, prevention or diagnosis of disease may receive a priority review of six months. Priority review does not change the standards for approval, but may expedite the approval process.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. In addition, the FDA may require a sponsor to conduct Phase IV testing which involves clinical trials designed to further assess a drug's safety and effectiveness after NDA or BLA approval, and may require testing and surveillance programs to monitor the safety of approved products which have been commercialized.

The Food and Drug Administration Safety and Innovation Act, or FDASIA, which was enacted in 2012, made permanent the Pediatric Research Equity Act, or PREA, which requires a sponsor to conduct pediatric studies for most drugs and biologics with a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, original NDAs, BLAs and supplements thereto, must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor or FDA may request a deferral of pediatric studies for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug or biologic is ready for approval for use in adults before pediatric studies are complete or that additional safety or effectiveness data needs to be collected before pediatric studies can begin. After April 2013, the FDA must send a non-compliance letter to any sponsor that fails to submit a required pediatric assessment within specified deadlines or fails to submit a timely request for approval of a pediatric formulation, if required.

Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of FDA approval of our drugs, some 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. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as partial compensation for effective patent term lost due to time spent during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND, and the submission date of an NDA or BLA, plus the time between the submission date of an NDA or BLA and the approval of that application, except that the period is reduced by any time during which the applicant failed to exercise due diligence. Only one patent applicable to an approved drug may be extended, and the extension must be applied for prior to expiration of the patent. The United States Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration.

Pediatric exclusivity is another type of marketing exclusivity available in the U.S. The FDASIA made permanent the Best Pharmaceuticals for Children Act, or BPCA, which provides, under certain circumstances, for an additional six months of marketing exclusivity if a sponsor conducts clinical trials in children in response to a written request from the FDA, or a Written Request. If the Written Request does not include studies in neonates, the FDA is required to include its rationale for not requesting those studies. The FDA may request studies on approved or unapproved indications in separate Written Requests. The issuance of a Written Request does not require the sponsor to undertake the described studies.

Biologics Price Competition and Innovation Act of 2009

The Biologics Price Competition and Innovation Act of 2009, or BPCIA, amended the PHSA to create an abbreviated approval pathway for two types of "generic" biologics — biosimilars and interchangeable biologic products, and provides for a twelve-year exclusivity period for the first approved biological product, or reference product, against which a biosimilar or interchangeable application is evaluated; however if pediatric studies are performed and accepted by the FDA, the twelve-year exclusivity period will be extended for an additional six months A biosimilar product is defined as one that is highly similar to a reference product notwithstanding minor differences in clinically inactive components and for which there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity and potency of the product. An interchangeable product is a biosimilar product that may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product.

The biosimilar applicant must demonstrate that the product is biosimilar based on data from (1) analytical studies showing that the biosimilar product is highly similar to the reference product; (2) animal studies (including toxicity); and (3) one or more clinical studies to demonstrate safety, purity and potency in one or more appropriate conditions of use for which the reference product is approved. In addition, the applicant must show that the biosimilar and reference products have the same mechanism of action for the conditions of use on the label, route of administration, dosage and strength, and the production facility must meet standards designed to assure product safety, purity and potency.

An application for a biosimilar product may not be submitted until four years after the date on which the reference product was first approved. The first approved interchangeable biologic product will be granted an exclusivity period of up to one year after it is first commercially marketed, but the exclusivity period may be shortened under certain circumstances.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the U.S., or more than 200,000 individuals in the U.S. and for which there is no reasonable expectation that the cost of developing and making available in the U.S. a drug for this type of disease or condition will be recovered from sales in the U.S. for that drug. Orphan drug designation must be requested before submitting an NDA or BLA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not itself convey any advantage in or shorten the duration of the regulatory review and approval process. If a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication, except in very limited circumstances, for seven years. Orphan drug exclusivity, however, also could block the approval of one of our product candidates for seven years if a competitor obtains approval of the same drug, for the same designated orphan indication or if our product candidate is determined to be contained within the competitor's product for the same indication or disease.

The FDA also administers a clinical research grants program, whereby researchers may compete for funding to conduct clinical trials to support the approval of drugs, biologics, medical devices, and medical foods for rare diseases and conditions. A product does not have to be designated as an orphan drug to be eligible for the grant program. An application for an orphan grant should propose one discrete clinical study to facilitate FDA approval of the product for a rare disease or condition. The study may address an unapproved new product or an unapproved new use for a product already on the market.

Fast Track Designation and Accelerated Approval

The FDA is required to facilitate the development, and expedite the review, of drugs that it finds are intended for the treatment of a serious or life-threatening disease or condition for which there is no effective treatment and which demonstrate the potential to address unmet medical needs for the condition. Under the fast track program, the sponsor of a new product candidate may request that the FDA designate the product candidate for a specific indication as a fast track drug concurrent with, or after, the filing of the IND for the product candidate. The FDA must determine if the product candidate qualifies for fast track designation within 60 days of receipt of the sponsor's request.

Under the fast track program, the FDA may designate a drug for fast-track status if it is intended to treat a serious or life-threatening illness and nonclinical or clinical data demonstrate the potential to address an unmet medical need. Similarly, the agency may designate a drug for accelerated approval if it treats a serious condition and generally provides meaningful therapeutic benefit to patients over existing treatments based upon a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments.

In clinical trials, a surrogate endpoint is a measurement of laboratory or clinical signs of a disease or condition that substitutes for a direct measurement of how a patient feels, functions, or survives. Surrogate endpoints can often be measured more easily or more rapidly than other clinical endpoints. A product candidate approved on this basis is generally subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, will allow the FDA to withdraw the drug from the market on an expedited basis. All promotional materials for product candidates approved under accelerated regulations are subject to prior review by the FDA.

In addition to other benefits such as the ability to use surrogate endpoints and engage in more frequent interactions with the FDA, the FDA may initiate review of sections of a fast track drug's NDA or BLA before the application is complete. This rolling review is available if the applicant provides, and the FDA approves, a schedule for the submission of the remaining information and the applicant pays applicable user fees. However, the FDA's time period goal for reviewing an application does not begin until the last section of the application is submitted. Additionally, the fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Post-Approval Requirements

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory standards is not maintained or if problems are identified after the product reaches the market. Later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market. 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 FDA review and approval. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws and regulations. We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products. Future inspections by the FDA and other regulatory agencies may identify compliance issues at the facilities of our contract manufacturers that may disrupt production or distribution, or require substantial resources to correct.

Any drug products manufactured or distributed by us pursuant to FDA approvals are subject to continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of adverse experiences with the drug, providing the FDA with updated safety and efficacy information, drug sampling and distribution requirements, complying with certain electronic records and signature requirements, and complying with FDA promotion and advertising requirements. The FDA strictly regulates labeling, advertising, promotion and other types of information that may be disseminated about 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.

From time to time, legislation is drafted, introduced and passed in Congress that could significantly change the statutory provisions governing the development, approval, manufacturing and marketing of products regulated by the FDA. It is impossible to predict whether further legislative changes will be enacted, or FDA regulations, guidance or interpretations changed or what the impact of such changes, if any, may be.

Regulation and Marketing Authorization in the European Union

The process governing approval of medicinal products in the European Union follows essentially the same lines as in the United States and, likewise, generally involves satisfactorily completing each of the following:

- preclinical laboratory tests, animal studies and formulation studies all performed in accordance with the applicable E.U. Good Laboratory Practice regulations;
- submission to the relevant national authorities of a clinical trial application, or CTA, which must be approved before human clinical trials may begin;
- performance of adequate and well-controlled clinical trials to establish the safety and efficacy of the product for each proposed indication
- submission to the relevant competent authorities of a MAA, which includes the data supporting safety and efficacy as well as detailed information on the manufacture and composition of the product in clinical development and proposed labelling;
- satisfactory completion of an inspection by the relevant national authorities of the manufacturing facility or facilities, including those of third parties, at which the product is produced to assess compliance with strictly enforced current cGMP;
- potential audits of the non-clinical and clinical trial sites that generated the data in support of the MAA; and
- review and approval by the relevant competent authority of the MAA before any commercial marketing, sale or shipment of the product.

Preclinical Studies

Preclinical tests include laboratory evaluations of product chemistry, formulation and stability, as well as studies to evaluate toxicity in animal studies, in order to assess the potential safety and efficacy of the product. The conduct of the preclinical tests and formulation of the compounds for testing must comply with the relevant E.U. regulations and requirements. The results of the preclinical tests, together with relevant manufacturing information and analytical data, are submitted as part of the CTA.

Clinical Trial Approval

Requirements for the conduct of clinical trials in the European Union including Good Clinical Practice, or GCP, are implemented in the Clinical Trials Directive 2001/20/EC and the GCP Directive 2005/28/EC. Pursuant to Directive 2001/20/EC and Directive 2005/28/EC, as amended, a system for the approval of clinical trials in the European Union has been implemented through national legislation of the member states. Under this system, approval must be obtained from the competent national authority of an E.U. member state in which a study is planned to be conducted, or in multiple member states if the clinical trial is to be conducted in a number of member states. To this end, a CTA is submitted, which must be supported by an investigational medicinal product dossier, or IMPD, and further supporting information prescribed by Directive 2001/20/EC and Directive 2005/28/EC and other applicable guidance documents. Furthermore, a clinical trial may only be started after a competent ethics committee has issued a favorable opinion on the clinical trial application in that country.

In April 2014, a new Clinical Trials Regulation, (EU) No 536/2014 was adopted which will replace the current Clinical Trials Directive 2001/20/EC. To ensure that the rules for clinical trials are identical throughout the European Union, the new E.U. clinical trials legislation was passed as a "regulation" that is directly applicable in all E.U. member states. All clinical trials performed in the European Union are required to be conducted in accordance with the Clinical Trials Directive 2001/20/EC until the new Clinical Trials Regulation (EU) No 536/2014 becomes applicable, which is scheduled to be in 2018.

The new Regulation (EU) No 536/2014 aims to harmonize, simplify and streamline the approval of clinical trials in the European Union. The main characteristics of the Regulation include:

- A streamlined application procedure via a single entry point, the E.U. portal.
- A single set of documents to be prepared and submitted for the application as well as simplified reporting procedures that will spare sponsors from submitting broadly identical information separately to various bodies and different member states.
- A harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts. Part I is assessed jointly by all member states concerned. Part II is assessed separately by each member state concerned.
- Strictly defined deadlines for the assessment of clinical trial application.
- The involvement of the ethics committees in the assessment procedure in accordance with the national law of the member state concerned but within the overall timelines defined by the Regulation (EU) No 536/2014.

Marketing Authorization

Authorization to market a product in the member states of the European Union proceeds under one of four procedures: a centralized authorization procedure, a mutual recognition procedure, a decentralized procedure or a national procedure.

Centralized Authorization Procedure

The centralized procedure enables applicants to obtain a marketing authorization that is valid in all E.U. member states based on a single application. Certain medicinal products, including products developed by means of biotechnological processes, must undergo the centralized authorization procedure for marketing authorization, which, if granted by the European Commission, is automatically valid in all 28 E.U. member states. The EMA and the European Commission administer this centralized authorization procedure pursuant to Regulation (EC) No 726/2004.

Pursuant to Regulation (EC) No 726/2004, this procedure is mandatory for:

- medicinal products developed by means of one of the following biotechnological processes:
  - recombinant DNA technology;

- controlled expression of genes coding for biologically active proteins in prokaryotes and eukaryotes including transformed mammalian cells; and
- hybridoma and monoclonal antibody methods;

- advanced therapy medicinal products as defined in Article 2 of Regulation (EC) No. 1394/2007 on advanced therapy medicinal products;
- medicinal products for human use containing a new active substance that, on the date of effectiveness of this regulation, was not authorized in the European Union, and for which the therapeutic indication is the treatment of any of the following diseases:
  - acquired immune deficiency syndrome;
  - cancer;
  - neurodegenerative disorder;
  - diabetes;
  - auto-immune diseases and other immune dysfunctions; and
  - viral diseases; and
- medicinal products that are designated as orphan medicinal products pursuant to Regulation (EC) No 141/2000.

The centralized authorization procedure is optional for other medicinal products if they contain a new active substance or if the applicant shows that the medicinal product concerned constitutes a significant therapeutic, scientific or technical innovation or that the granting of authorization is in the interest of patients in the European Union.

Administrative Procedure

Under the centralized authorization procedure, the EMA's Committee for Human Medicinal Products, or CHMP, serves as the scientific committee that renders opinions about the safety, efficacy and quality of medicinal products for human use on behalf of the EMA. The CHMP is composed of experts nominated by each member state's national authority for medicinal products, with expert appointed to act as Rapporteur for the co-ordination of the evaluation with the possible assistance of a further member of the Committee acting as a Co-Rapporteur. After approval, the Rapporteur(s) continue to monitor the product throughout its life cycle. The CHMP has 210 days to adopt an opinion as to whether a marketing authorization should be granted. The process usually takes longer in case additional information is requested, which triggers clock-stops in the procedural timelines. The process is complex and involves extensive consultation with the regulatory authorities of member states and a number of experts. When an application is submitted for a marketing authorization in respect of a drug that is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation, the applicant may pursuant to Article 14(9) Regulation (EC) No 726/2004 request an accelerated assessment procedure. If the CHMP accepts such request, the time-limit of 210 days will be reduced to 150 days but it is possible that the CHMP can revert to the standard time-limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment. Once the procedure is completed, a European Public Assessment Report, or EPAR, is produced. If the opinion is negative, information is given as to the grounds on which this conclusion was reached. After the adoption of the CHMP opinion, a decision on the MAA must be adopted by the European Commission, after consulting the E.U. member states, which in total can take more than 60 days.

Conditional Approval

In specific circumstances, E.U. legislation (Article 14(7) Regulation (EC) No 726/2004 and Regulation (EC) No 507/2006 on Conditional Marketing Authorisations for Medicinal Products for Human Use) enables applicants to obtain a conditional marketing authorization prior to obtaining the comprehensive clinical data required for an application for a full marketing authorization. Such conditional approvals may be granted for product candidates (including medicines designated as orphan medicinal products) if (1) the risk-benefit balance of the product candidate is positive, (2) it is likely that the applicant will be in a position to provide the required comprehensive clinical trial data, (3) the product fulfills unmet medical needs and (4) the benefit to public health of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required. A conditional marketing authorization may contain specific obligations to be fulfilled by the marketing authorization holder, including obligations with respect to the completion of ongoing or new studies, and with respect to the collection of pharmacovigilance data. Conditional marketing authorizations are valid for one year, and may be renewed annually, if the risk-benefit balance remains positive, and after an assessment of the need for additional or modified conditions and/or specific obligations. The timelines for the centralized procedure described above also apply with respect to the review by the CHMP of applications for a conditional marketing authorization.

Marketing Authorization under Exceptional Circumstances

Under Article 14(8) Regulation (EC) No 726/2004, products for which the applicant can demonstrate that comprehensive data (in line with the requirements laid down in Annex I of Directive 2001/83/EC, as amended) cannot be provided (due to specific reasons foreseen in the legislation) might be eligible for marketing authorization under exceptional circumstances. This type of authorization is reviewed annually to reassess the risk-benefit balance. The fulfillment of any specific procedures/obligations imposed as part of the marketing authorization under exceptional circumstances is aimed at the provision of information on the safe and effective use of the product and will normally not lead to the completion of a full dossier/approval.

Market Authorizations Granted by Authorities of E.U. Member States

In general, if the centralized procedure is not followed, there are three alternative procedures as prescribed in Directive 2001/83/EC:

- The decentralized procedure allows applicants to file identical applications to several E.U. member states and receive simultaneous national approvals based on the recognition by E.U. member states of an assessment by a reference member state.

- The national procedure is only available for products intended to be authorized in a single E.U. member state.

- A mutual recognition procedure similar to the decentralized procedure is available when a marketing authorization has already been obtained in at least one E.U. member state.

A marketing authorization may be granted only to an applicant established in the European Union.

Pediatric Studies

Prior to obtaining a marketing authorization in the European Union, applicants have to demonstrate compliance with all measures included in an EMA-approved Paediatric Investigation Plan, or PIP, covering all subsets of the paediatric population, unless the EMA has granted a product-specific waiver, a class waiver, or a deferral for one or more of the measures included in the PIP. The respective requirements for all marketing authorization procedures are set forth in Regulation (EC) No 1901/2006, which is referred to as the Pediatric Regulation. This requirement also applies when a company wants to add a new indication, pharmaceutical form or route of administration for a medicine that is already authorized. The Pediatric Committee of the EMA, or PDCO, may grant deferrals for some medicines, allowing a company to delay development of the medicine in children until there is enough information to demonstrate its effectiveness and safety in adults. The PDCO may also grant waivers when development of a medicine in children is not needed or is not appropriate, such as for diseases that only affect the elderly population.

Before a marketing authorization application can be filed, or an existing marketing authorization can be amended, the EMA determines that companies actually comply with the agreed studies and measures listed in each relevant PIP.

Periods of Authorization and Renewals

A marketing authorization is valid for five years in principle and the marketing authorization may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the competent authority of the authorizing member state. To this end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. Once renewed, the marketing authorization is valid for an unlimited period, unless the European Commission or the competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal. Any authorization which is not followed by the actual placing of the drug on the E.U. market (in case of centralized procedure) or on the market of the authorizing member state within three years after authorization ceases to be valid (the so-called sunset clause).

Orphan Drug Designation and Exclusivity

Pursuant to Regulation (EC) No 141/2000 and Regulation (EC) No. 847/2000, the European Commission can grant such orphan medicinal product designation to products for which the sponsor can establish that it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 people in the European Union, or a life threatening, seriously debilitating or serious and chronic condition in the European Union and that without incentives it is unlikely that sales of the drug in the European Union would generate a sufficient return to justify the necessary investment. In addition, the sponsor must establish that there is no other satisfactory method approved in the European Union of diagnosing, preventing or treating the condition, or if such a method exists, the proposed orphan drug will be of significant benefit to patients.

Orphan drug designation is not a marketing authorization. It is a designation that provides a number of benefits, including fee reductions, regulatory assistance, and the possibility to apply for a centralized E.U. marketing authorization, as well as ten years of market exclusivity following a marketing authorization. During this market exclusivity period, neither the EMA, the European Commission nor the member states can accept an application or grant a marketing authorization for a “similar medicinal product.” A “similar medicinal product” is defined as a medicinal product containing a similar active substance or substances as those contained in an authorized orphan medicinal product and that is intended for the same therapeutic indication. The market exclusivity period for the authorized therapeutic indication may be reduced to six years if, at the end of the fifth year, it is established that the orphan designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. In addition, a competing similar medicinal product may in limited circumstances be authorized prior to the expiration of the market exclusivity period, including if it is shown to be safer, more effective or otherwise clinically superior to the already approved orphan drug. Furthermore, a product can lose orphan designation, and the related benefits, prior to us obtaining a marketing authorization if it is demonstrated that the orphan designation criteria are no longer met.

Regulatory Data Protection

E.U. legislation also provides for a system of regulatory data and market exclusivity. According to Article 14(11) of Regulation (EC) No 726/2004, as amended, and Article 10(1) of Directive 2001/83/EC, as amended, upon receiving marketing authorization, new chemical entities approved on the basis of complete independent data package benefit from eight years of data exclusivity and an additional two years of market exclusivity. Data exclusivity prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic (abbreviated) application. During the additional two-year period of market exclusivity, a generic marketing authorization can be submitted, and the innovator's data may be referenced, but no generic medicinal product can be marketed until the expiration of the market exclusivity. The overall ten-year period will be extended to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorization holder, or MAH, 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. Even if a compound is considered to be a new chemical entity and the innovator is able to gain the period of data exclusivity, another company nevertheless could also market another version of the drug if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical test, preclinical tests and clinical trials. However, products designated as orphan medicinal products enjoy, upon receiving marketing authorization, a period of ten years of orphan market exclusivity—see also *Orphan Drug Designation and Exclusivity*. Depending upon the timing and duration of the E.U. marketing authorization process, products may be eligible for up to five years' supplementary protection certificates, or SPCs, pursuant to Regulation (EC) No 469/2009. Such SPCs extend the rights under the basic patent for the drug.

Regulatory Requirements After a Marketing Authorization has been Obtained

If we obtain authorization for a medicinal product in the European Union, we will be required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products:

Pharmacovigilance and other requirements

We will, for example, have to comply with the E.U.'s stringent pharmacovigilance or safety reporting rules, pursuant to which post-authorization studies and additional monitoring obligations can be imposed. Other requirements relate, for example, to the manufacturing of products and APIs in accordance with good manufacturing practice standards. E.U. regulators may conduct inspections to verify our compliance with applicable requirements, and we will have to continue to expend time, money and effort to remain compliant. Non-compliance with E.U. requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties in the European Union. Similarly, failure to comply with the E.U.'s requirements regarding the protection of individual personal data can also lead to significant penalties and sanctions. Individual E.U. member states may also impose various sanctions and penalties in case we do not comply with locally applicable requirements.

Manufacturing

The manufacturing of authorized drugs, for which a separate manufacturer's license is mandatory, must be conducted in strict compliance with the EMA's Good Manufacturing Practices, or GMP, requirements and comparable requirements of other regulatory bodies in the European Union, which mandate the methods, facilities and controls used in manufacturing, processing and packing of drugs to assure their safety and identity. The EMA enforces its current GMP requirements through mandatory registration of facilities and inspections of those facilities. The EMA may have a coordinating role for these inspections while the responsibility for carrying them out rests with the member states competent authority under whose responsibility the manufacturer falls. Failure to comply with these requirements could interrupt supply and result in delays, unanticipated costs and lost revenues, and could subject the applicant to potential legal or regulatory action, including but not limited to warning letters, suspension of manufacturing, seizure of product, injunctive action or possible civil and criminal penalties.

Marketing and Promotion

The marketing and promotion of authorized drugs, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs and/or the general public, are strictly regulated in the European Union under Directive 2001/83/EC. The applicable regulations aim to ensure that information provided by holders of marketing authorizations regarding their products is truthful, balanced and accurately reflects the safety and efficacy claims authorized by the EMA or by the competent authority of the authorizing member state. Failure to comply with these requirements can result in adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties.

Patent Term Extension

In order to compensate the patentee for delays in obtaining a marketing authorization for a patented product, a supplementary certificate, or SPC, may be granted extending the exclusivity period for that specific product by up to five years. Applications for SPCs must be made to the relevant patent office in each E.U. member state and the granted certificates are valid only in the member state of grant. An application has to be made by the patent owner within six months of the first marketing authorization being granted in the European Union (assuming the patent in question has not expired, lapsed or been revoked) or within six months of the grant of the patent (if the marketing authorization is granted first). In the context of SPCs, the term "product" means the active ingredient or combination of active ingredients for a medicinal product and the term "patent" means a patent protecting such a product or a new manufacturing process or application for it. The duration of an SPC is calculated as the difference between the patent's filing date and the date of the first marketing authorization, minus five years, subject to a maximum term of five years.

A six month pediatric extension of an SPC may be obtained where the patentee has carried out an agreed pediatric investigation plan, the authorized product information includes information on the results of the studies and the product is authorized in all member states of the European Union. The six month paediatric extension of SPCs is not available for orphan medicinal products, as such products benefit from a separate two year paediatric extension of orphan status and exclusivity. The six month paediatric extension of SPCs is, however, available for medicinal products which were originally designated as orphan medicinal products but were subsequently (voluntarily) removed from the EU's Community Register of Orphan Medicinal Products.

Foreign Regulation

In addition to regulations in the United States and European Union, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our products. Whether or not we obtain FDA or EMA approval for a product, we must obtain approval by the comparable regulatory authorities of foreign countries before we may commence clinical trials or market products in those countries or areas. The approval process and requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from place to place, and the time may be longer or shorter than that required for FDA or EMA approval.

Pharmaceutical Pricing and Reimbursement

Sales of pharmaceutical products depend in significant part on the extent of coverage and reimbursement from government programs, including Medicare and Medicaid in the U.S., and other third party payers. Third party payers are sensitive to the cost of drugs and are increasingly seeking to implement cost containment measures to control, restrict access to, or influence the purchase of drugs, biologicals, and other health care products and services. Governments may regulate reimbursement, pricing, and coverage of products in order to control costs or to affect levels of use of certain products. Payers may restrict coverage of some products due to cost concerns, by various means such as using payer formularies under which only selected drugs are covered, variable co-payments that make drugs that are not preferred by the payer more expensive in terms of higher out-of-pocket expenses for patients, and by employing utilization management controls, such as requirements for prior authorization before a prescription can be billed or prior clinical failure on another type of treatment before a new product can be prescribed. Payers may especially impose these obstacles to coverage for higher-priced drugs in order to limit the payer's cost for treatment of the disease. Consequently, any future products may be subject to payer-driven restrictions, rendering patients responsible for a higher percentage of the total cost of drugs in the outpatient setting. This could lower the demand for any future products if the increased patient out-of-pocket cost-sharing obligations are more than they can afford.

Medicare is a U.S. federal government insurance program that covers individuals aged 65 years or older, as well as individuals of any age with certain disabilities, and individuals with End-Stage Renal Disease. The primary Medicare programs that may affect reimbursement for Akari are Medicare Part B, which covers physician services and outpatient care, and Medicare Part D, which provides a voluntary outpatient prescription drug benefit. Medicare Part B provides limited coverage of certain outpatient drugs and biologicals that are reasonable and necessary for diagnosis or treatment of an illness or injury. Under Medicare Part B, reimbursement for most drugs is based on a fixed percentage above the applicable product's average sales price, or ASP. Manufacturers calculate ASP based on a statutory formula and must report ASP information on a quarterly basis to the Centers for Medicare and Medicaid Services (CMS), the federal agency that administers Medicare and the Medicaid Drug Rebate Program. The current reimbursement rate for drugs and biologicals in both the hospital outpatient department setting and the physician office setting is ASP + 6%. The rate for the physician clinic setting is set by statute, but CMS has the authority to adjust the rate for the hospital outpatient setting on an annual basis. This reimbursement rate may decrease in the future. In both settings, the amount of reimbursement is updated quarterly based on the manufacturer's submission of new ASP information.

Medicare Part D is a prescription drug benefit available to all Medicare beneficiaries. It is a voluntary benefit that is implemented through private plans under contractual arrangements with the federal government. Similar to pharmaceutical coverage through private health insurance, Part D plans negotiate discounts from drug manufacturers. Medicare Part D coverage is available through private plans, and the list of prescription drugs covered by Part D plans varies by plan. However, individual plans are required by statute to cover certain therapeutic categories and classes of drugs or biologicals and to have at least two drugs in each unique therapeutic
category or class, with certain exceptions.

Medicare Part A covers inpatient hospital benefits. Hospitals typically receive a single payment for an inpatient stay depending on the Medicare Severity Diagnosis Related Group (MS-DRG) to which the inpatient stay is assigned. The MS-DRG for a hospital inpatient stay varies based on the patient's condition. Hospitals generally do not receive separate payment for drugs and biologicals administered to patients during an inpatient hospital stay. As a result, hospitals may not have a financial incentive to utilize any future products for inpatients.

Beginning April 1, 2013, the Budget Control Act of 2011, Pub. L. No. 112-25, as amended by the American Taxpayer Relief Act of 2012, Pub. L. 112-240, required Medicare payments for all items and services, including drugs and biologicals, to be reduced by 2% under sequestration (i.e., automatic spending reductions). Subsequent legislation extended the 2% reduction, on average, to 2025. This 2% reduction in Medicare payments affects all Parts of the Medicare program and could impact any future sales of any future products.

Medicaid is a government health insurance program for low-income children, families, pregnant women, and people with disabilities. It is jointly funded by the federal and state governments, and it is administered by individual states within parameters established by the federal government. Coverage and reimbursement for drugs and biologics thus varies by state. Drugs and biologics may be covered under the medical or pharmacy benefit. State Medicaid programs may impose utilization management controls, such as prior authorization, step therapy, or quantity limits on drugs and biologics. Medicaid also includes the Medicaid Drug Rebate Program, under which we would be required to pay a rebate to each state Medicaid program for quantities of any future products that are dispensed to Medicaid beneficiaries and paid for by a state Medicaid program as a condition of having federal funds being made available to the states for any future products under Medicaid and Medicare Part B. Those rebates are based on pricing data that would be reported by us on a monthly and quarterly basis to CMS. These data include the average manufacturer price and the best price for each product we sell. As further described below under "U.S. Healthcare Reform and Other U.S. Healthcare Laws," the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, the PPACA, made significant changes to the Medicaid Drug Rebate Program that could negatively impact our results of operations.

Federal law requires that any company that participates in the Medicaid Drug Rebate Program also participate in the Public Health Service's 340B drug discounted pricing program in order for federal funds to be available for the manufacturer's drugs under Medicaid and Medicare Part B. The 340B pricing program requires participating manufacturers to agree to charge statutorily-defined covered entities no more than the 340B "ceiling price" for the manufacturer's covered outpatient drugs. These 340B covered entities include a variety of community health clinics and other entities that receive health services grants from the Public Health Service as well as hospitals that serve a disproportionate share of low-income patients. The 340B ceiling price is calculated using a statutory formula, which is based on the average manufacturer price and rebate amount for the covered outpatient drug as calculated under the Medicaid Drug Rebate Program. Changes to the definition of average manufacturer price and the Medicaid rebate amount under PPACA and CMS's issuance of final regulations implementing those changes also could affect the 340B ceiling price calculation for any future products and could negatively impact our results of operations. As described below under "U.S. Healthcare Reform and Other U.S. Healthcare Laws," PPACA expanded the 340B program to include additional types of covered entities but exempts "orphan drugs" designated under section 526 of the FDCA from the ceiling price requirements for these newly-eligible entities.

In order to be eligible to have products paid for with federal funds under the Medicaid and Medicare Part B programs and purchased by certain federal agencies and grantees, manufacturers must participate in the Department of Veterans Affairs Federal Supply Schedule, or FSS, pricing program, established by Section 603 of the Veterans Health Care Act of 1992, or VHCA. Under this program, we would be obligated to make our innovator "covered drugs" available for procurement on an FSS contract and charge a price to four federal agencies, Department of Veterans Affairs, Department of Defense, Public Health Service and Coast Guard that is no higher than the statutory Federal Ceiling Price, or FCP. The FCP is based on the non-federal average manufacturer price, or Non-FAMP, which we would calculate and report to the Department of Veterans Affairs on a quarterly and annual basis. Under the Tricare Retail Pharmacy program, established by Section 703 of the National Defense Authorization Act for FY 2008 and related regulations, participating manufacturers pay quarterly rebates on utilization of innovator products that are dispensed through the Tricare Retail Pharmacy network to Tricare beneficiaries. The rebates are calculated as the difference between Annual Non-FAMP and FCP. The FCP is based on a weighted average non-federal average manufacturer price (Non-FAMP) which manufacturers are required to report on a quarterly and annual basis to the VA. If a company misstates Non-FAMPs or FCPs it must restate these figures.

Pursuant to the VHCA, knowing provision of false information in connection with a Non-FAMP filing can subject a manufacturer to penalties of one hundred seventy-eight thousand dollars for each item of false information.

Payers also are increasingly considering new metrics as the basis for reimbursement rates, such as ASP, average manufacturer price, and actual acquisition cost. The existing data for reimbursement based on these metrics is relatively limited, although certain states have begun to survey acquisition cost data for the purpose of setting Medicaid reimbursement rates. CMS surveys and publishes retail community pharmacy acquisition cost information in the form of National Average Drug Acquisition Cost files to provide state Medicaid agencies with a basis of comparison for their own reimbursement and pricing methodologies and rates. It may be difficult to project the impact of these evolving reimbursement mechanics on the willingness of payers to cover any future products.

FSS contracts are federal procurement contracts that include standard government terms and conditions, separate pricing for each product, and extensive disclosure and certification requirements. All items on FSS contracts are subject to a standard FSS contract clause that requires FSS contract price reductions under certain circumstances where pricing is reduced to an agreed "tracking customer." Further, in addition to the "Big Four" agencies, all other federal agencies and some non-federal entities are authorized to access FSS contracts. FSS contractors are permitted to charge FSS purchasers other than the Big Four agencies "negotiated pricing" for covered drugs that is not capped by the FCP; instead, such pricing is negotiated based on a mandatory disclosure of the contractor's commercial "most favored customer" pricing.

In addition, pursuant to regulations issued by the DoD TRICARE Management Activity, now the Defense Health Agency, to implement Section 703 of the National Defense Authorization Act for Fiscal Year 2008, participating manufacturers have each of their covered drugs is listed on a Section 703 Agreement under which they have agreed to pay rebates on covered drug prescriptions dispensed to TRICARE beneficiaries by TRICARE network retail pharmacies. Companies are required to list their innovator products on Section 703 Agreements in order for those products to be eligible for DoD formulary inclusion. The formula for determining the rebate is established in the regulations and our Section 703 Agreement and is based on the difference between the annual Non-FAMP and the FCP (as described above, these price points are required to be calculated by us under the VHCA).

In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. Moreover, the requirements governing drug pricing and reimbursement vary widely from country to country. For example, in the EU the sole legal instrument at the EU level governing the pricing and reimbursement of medicinal products is Council Directive 89/105/EEC, or the Price Transparency Directive. The aim of the Price Transparency Directive is to ensure that pricing and reimbursement mechanisms established in EU member states are transparent and objective, do not hinder the free movement and trade of medicinal products in the EU and do not hinder, prevent or distort competition on the market. The Price Transparency Directive does not, however, provide any guidance concerning the specific criteria on the basis of which pricing and reimbursement decisions are to be made in individual EU member states. Neither does it have any direct consequence for pricing or levels of reimbursement in individual EU member states. The national authorities of the individual EU member states are free to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices and/or reimbursement of medicinal products for human use. Some individual EU member states adopt policies according to which a specific price or level of reimbursement is approved for the medicinal product. Other EU member states adopt a system of reference pricing, basing the price or reimbursement level in their territory either, on the pricing and reimbursement levels in other countries, or on the pricing and reimbursement levels of medicinal products intended for the same therapeutic indication. Furthermore, some EU member states impose direct or indirect controls on the profitability of the company placing the medicinal product on the market.

Health Technology Assessment, or HTA, of medicinal products is becoming an increasingly common part of the pricing and reimbursement procedures in some EU member states. These countries include the United Kingdom, France, Germany and Sweden. The HTA process in the EU member states is governed by the national laws of these countries. HTA is the procedure according to which the assessment of the public health impact, therapeutic impact and the economic and societal impact of the use of a given medicinal product in the national healthcare systems of the individual country is conducted. HTA generally focuses on the clinical efficacy and effectiveness, safety, cost, and cost-effectiveness of individual medicinal products as well as their potential implications for the national healthcare system. Those elements of medicinal products are compared with other treatment options available on the market.

The outcome of HTA may influence the pricing and reimbursement status for specific medicinal products within individual EU member states. The extent to which pricing and reimbursement decisions are influenced by the HTA of a specific medicinal product vary between the EU member states.

In 2011, Directive 2011/24/EU was adopted at the EU level. This Directive concerns the application of patients' rights in cross-border healthcare. The Directive is intended to establish rules for facilitating access to safe and high-quality cross-border healthcare in the EU. Pursuant to Directive 2011/24/EU, a voluntary network of national authorities or bodies responsible for HTA in the individual EU Member States was established. The purpose of the network is to facilitate and support the exchange of scientific information concerning HTAs. In October 2016, the European Commission initiated a public consultation on strengthening EU cooperation on HTA. The consultation was closed in January 2017 and the report was published on 15 May 2017. The Commission's focus on HTA could lead to harmonization of the criteria taken into account in the conduct of FSS contract with the VA, under which we must make our innovator "covered drugs" available to the "Big Four" federal HTA between EU member states in pricing and reimbursement decisions and negatively impact price in at least some EU member states.

U.S. Healthcare Reform and Other U.S. Healthcare Laws

In addition to FDA restrictions on marketing of pharmaceutical products, several other types of state and federal healthcare laws, including those commonly referred to as "fraud and abuse" laws have been applied in recent years to restrict certain marketing practices in the pharmaceutical industry. These laws may impact, among other things, our proposed sales, marketing and education programs. In addition, we may be subject to patient privacy regulation by both the U.S. federal government and the states in which we conduct our business. The laws that may affect our ability to operate include the following:

- The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully soliciting, offering, receiving, or paying any remuneration, directly or indirectly, in cash or in kind, to induce or reward purchasing, ordering or arranging for or recommending the purchase or order of any item or service for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid. Liability may be established without a person or entity having actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it. This statute has been interpreted to apply broadly to arrangements between pharmaceutical manufacturers on the one hand and prescribers, patients, purchasers and formulary managers on the other. In addition, PPACA amended the Social Security Act to provide that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. A conviction for violation of the Anti-kickback Statute requires mandatory exclusion from participation in federal health care programs. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution, the exemptions and safe harbors are drawn narrowly, and those activities may be subject to scrutiny or penalty if they do not qualify for an exemption or safe harbor.

- The federal civil False Claims Act, or FCA, prohibits, among other things, knowingly presenting, or causing to be presented claims for payment of government funds that are false or fraudulent, or knowingly making, using or causing to be made or used a false record or statement material to such a false or fraudulent claim, or knowingly concealing or knowingly and improperly avoiding, decreasing, or concealing an obligation to pay money to the federal government. This statute also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery. FCA liability is potentially significant in the healthcare industry because the statute provides for treble damages and mandatory penalties of $5,500 to $11,000 per false claim or statement ($10,781 to $21,563 per false claim or statement for penalties assessed after August 1, 2016 for violations occurring after November 2, 2015, and $10,957 to $21,916 per false claim or statement for penalties assessed after February 3, 2017 for violations occurring after November 2, 2015). Government enforcement agencies and private whistleblowers have investigated pharmaceutical companies for or asserted liability under the FCA for a variety of alleged promotional and marketing activities, such as providing free product to customers with the expectation that the customers would bill federal programs for the product; providing consulting fees and other benefits to physicians to induce them to prescribe products; engaging in promotion for "off-label" uses; and submitting inflated best price information to the Medicaid Rebate Program.

- The federal False Statements Statute prohibits knowingly and willfully falsifying, concealing, or covering up a material fact or making any materially false, fictitious or fraudulent statement or representation, or making or using any false writing or document knowing the same to contain any materially false, fictitious or fraudulent statement or entry, in connection with the delivery of or payment for healthcare benefits, items, or services.

- The federal Civil Monetary Penalties Law authorizes the imposition of substantial civil monetary penalties against an entity, such as a pharmaceutical manufacturer, that engages in activities including, among others (1) knowingly presenting, or causing to be presented, a claim for services not provided as claimed or that is otherwise false or fraudulent in any way; (2) arranging for or contracting with an individual or entity that is excluded from participation in federal healthcare programs to provide items or services reimbursable by a federal healthcare program; (3) violations of the federal Anti-Kickback Statute; or (4) failing to report and return a known overpayment.

- The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for 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 federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

- The majority of states also have statutes similar to the federal anti-kickback law and false claims laws that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, that apply regardless of whether the payer is a government entity or a private commercial entity.

- The federal Open Payments (Physician Payments Sunshine Act) program requires manufacturers of products for which payment is available under Medicare, Medicaid or the State Children's Health Insurance Program, to track and report annually to the federal government (for disclosure to the public) certain payments and other transfers of value made to physicians and teaching hospitals as well as disclosure of payments and other transfers of value provided to physicians and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members and applicable group purchasing organizations . In addition, several U.S. states and localities have enacted legislation requiring pharmaceutical companies to establish marketing compliance programs, file periodic reports with the state, and/or make periodic public disclosures on sales, marketing, pricing, clinical trials, and other activities. Other state laws prohibit certain marketing-related activities including the provision of gifts, meals or other items to certain healthcare providers. Many of these laws and regulations contain ambiguous requirements that government officials have not yet clarified. Given the lack of clarity in the laws and their implementation, our reporting actions could be subject to the penalty provisions of the pertinent federal and state laws and regulations.

Sanctions under these federal and state healthcare laws may include civil monetary penalties, exclusion of a manufacturer's products from reimbursement under government programs, monetary damages, criminal fines, disgorgement, additional reporting obligations and oversight if the manufacture becomes subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, and individual imprisonment.

Federal and state authorities are continuing to devote significant attention and resources to enforcement of fraud and abuse laws within the pharmaceutical industry, and private individuals have been active in alleging violations of the law and bringing suits on behalf of the government under the FCA. For example, federal enforcement agencies recently have investigated certain pharmaceutical companies' product and patient assistance programs, including manufacturer reimbursement support services, relationships with specialty pharmacies, and grants to independent charitable foundations.

The PPACA, was adopted in the U.S. in March 2010. This law substantially changes the way healthcare is financed by both governmental and private insurers in the U.S., and significantly impacts the pharmaceutical industry. PPACA contains a number of provisions that are expected to impact our business and operations. Changes that may affect our business include those governing enrollment in federal healthcare programs, reimbursement changes, rules regarding prescription drug benefits under the health insurance exchanges, expansion of the 340B program, expansion of state Medicaid programs, and fraud and abuse and enforcement. These changes will impact existing government healthcare programs and will result in the development of new programs, including Medicare payment for performance initiatives and improvements to the physician quality reporting system and feedback program.

PPACA contains several provisions that have or could potentially impact our business. PPACA made significant changes to the Medicaid Drug Rebate Program. Effective March 23, 2010, rebate liability expanded from fee-for-service Medicaid utilization to include the utilization of Medicaid managed care organizations as well. With regard to the amount of the rebates owed, PPACA increased the minimum Medicaid rebate from 15.1% to 23.1% of the average manufacturer price for most innovator products; changed the calculation of the rebate for certain innovator products that qualify as line extensions of existing drugs; and capped the total rebate amount for innovator drugs at 100% of the average manufacturer price. In addition, PPACA and subsequent legislation changed the definition of average manufacturer price. In early 2016, CMS issued final regulations to implement the changes to the Medicaid Drug Rebate Program under PPACA, which became effective on April 1, 2016. Finally, PPACA requires pharmaceutical manufacturers of branded prescription drugs to pay a branded prescription drug fee to the federal government. Each individual pharmaceutical manufacturer pays a prorated share of the branded prescription drug fee of $4,000 in 2017 (and set to increase in ensuing years), based on the dollar value of its branded prescription drug sales to certain federal programs identified in the law. Sales of "orphan drugs" are excluded from this fee. "Orphan drugs" are specifically defined for purposes of the fee. For each indication approved by the FDA for the drug, such indication must have been designated as orphan by the FDA under section 526 of the FDCA, an orphan drug tax credit under section 45C of the Internal Revenue Code must have been claimed with respect to such indication, and such tax credit must not have been disallowed by the Internal Revenue Service. Finally, the FDA must not have approved the drug for any indication other than an orphan indication for which a section 45C orphan drug tax credit was claimed (and not disallowed).

Additional provisions of PPACA may negatively affect manufacturer's revenues in the future. For example, as part of PPACA's provisions closing a coverage gap that currently exists in the Medicare Part D prescription drug program (commonly known as the "donut hole"), manufacturers of branded prescription drugs are required to provide a 50% discount on branded prescription drugs dispensed to beneficiaries within this donut hole.

PPACA also expanded the Public Health Service's 340B drug pricing discount program. The 340B pricing program requires participating manufacturers to agree to charge statutorily-defined covered entities no more than the 340B "ceiling price" for the manufacturer's covered outpatient drugs. PPACA expanded the 340B program to include additional types of covered entities: certain free-standing cancer hospitals, critical access hospitals, rural referral centers and sole community hospitals, each as defined by PPACA. PPACA exempts "orphan drugs" designated under section 526 of the FDCA, from the ceiling price requirements for these newly-eligible entities.

Finally, numerous federal and state laws, including state security breach notification laws, state health information privacy laws, and federal and state consumer protection laws govern the collection, use, and disclosure of personal information. In addition, most healthcare providers and research institutions with whom we collaborate are subject to privacy and security requirements under HIPAA, as amended by HITECH, and its implementing regulations. Although we are currently neither a "covered entity" nor a "business associate" under HIPAA, and these privacy and security requirements do not apply to us, the regulations may affect our interactions with healthcare providers, health plans, and research institutions from whom we obtain patient health information. Further, we could be subject to criminal penalties if we knowingly obtain individually identifiable health information from a HIPAA covered entity in a manner that is not authorized or permitted by HIPAA or for aiding and abetting the violation of HIPAA.

There is significant interest in the United States in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access, including increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices, particularly with respect to drugs that have been subject to relatively large price increases over relatively short time periods. There have been several recent U.S. Congressional inquiries and proposed bills designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. Legislative changes to PPACA also remain possible and appear likely in the 115th U.S. Congress and under the Trump Administration. Although multiple bills to repeal or repeal and replace portions of the PPACA have been introduced in 2017, none of these measure has successfully passed both houses of Congress. Congress may consider other legislation to repeal and replace elements of the PPACA or other health reform measures in the future.

Other Regulations

We are also subject to the U.S. Foreign Corrupt Practices Act (FCPA), the U.K. Bribery Act (U.K. Bribery Act), and other anticorruption laws and regulations pertaining to our financial relationships with foreign government officials. The FCPA prohibits U.S. companies and their representatives from paying, offering to pay, promising, or authorizing the payment of anything of value to any foreign government official, government staff member, political party, or political candidate to obtain or retain business or to otherwise seek favorable treatment. In many countries in which we operate, the healthcare professionals with whom we interact may be deemed to be foreign government officials for purposes of the FCPA. The U.K. Bribery Act, which applies to any company incorporated or doing business in the UK, prohibits giving, offering, or promising bribes in the public and private sectors, bribing a foreign public official or private person, and failing to have adequate procedures to prevent bribery amongst employees and other agents. Penalties under the Bribery Act include potentially unlimited fines for companies and criminal sanctions for corporate officers under certain circumstances. Liability in relation to breaches of the Bribery Act is strict. This means that it is not necessary to demonstrate elements of a corrupt state of mind. However, a defense of having in place adequate procedures designed to prevent bribery is available.

Recent years have seen a substantial increase in anti-bribery law enforcement activity by U.S. regulators, with more frequent and aggressive investigations and enforcement proceedings by both the DOJ and the SEC, increased enforcement activity by non-U.S. regulators, and increases in criminal and civil proceedings brought against companies and individuals. Increasing regulatory scrutiny of the promotional activities of pharmaceutical companies also has been observed in a number of EU member states. In Germany, a specific anti-corruption provision with regard to healthcare professionals was introduced in the Criminal Code in 2017.

Similar strict restrictions are imposed on the promotion and marketing of drug products in the EU, where a large portion of our non-U.S. business is conducted, and other territories. Laws in the EU, including in the individual EU member states, require promotional materials and advertising for drug products to comply with the product's Summary of Product Characteristics, or SmPC, which is approved by the competent authorities. Promotion of a medicinal product which does not comply with the SmPC is considered to constitute off-label promotion. The off-label promotion of medicinal products is prohibited in the EU and in other territories. The promotion of medicinal products that are not subject to a marketing authorization is also prohibited in the EU. Laws in the EU, including in the individual EU member states, also prohibit the direct-to-consumer advertising of prescription-only medicinal products. Violations of the rules governing the promotion of medicinal products in the EU and in other territories could be penalized by administrative measures, fines and imprisonment. Furthermore, illegal advertising can be challenged by competitors, and as a result, can be prohibited by court and the responsible company can be obligated to pay damages to the competitor.

Interactions between pharmaceutical companies and physicians are also governed by strict laws, regulations, industry self-regulation codes of conduct and physicians' codes of professional conduct in the individual EU member states. The provision of any inducements to physicians to prescribe, recommend, endorse, order, purchase, supply, use or administer a medicinal product is prohibited. A number of EU member states have introduced additional rules requiring pharmaceutical companies to publicly disclose their interactions with physicians and to obtain approval from employers, professional organizations and/or competent authorities before entering into agreements with physicians. These rules have been supplemented by provisions of related industry codes, including the EFPIA Disclosure Code on Disclosure of Transfers of Value from Pharmaceutical Companies to Healthcare Professionals and Healthcare Organizations and related codes developed at national level in individual EU member states. Additional countries may consider or implement similar laws and regulations. Violations of these rules could lead to reputational risk, public reprimands, and/or the imposition of fines or imprisonment. Our present and future business has been and will continue to be subject to various other laws and regulations. Laws, regulations and recommendations relating to safe working conditions, laboratory practices, the experimental use of animals, and the purchase, storage, movement, import and export and use and disposal of hazardous or potentially hazardous substances, including radioactive compounds, used in connection with our research work are or may be applicable to our activities. We cannot predict the impact of government regulation, which may result from future legislation or administrative action, on our business.

DESCRIPTION OF SHARE CAPITAL AND ARTICLES OF ASSOCIATION

The following summarizes the material rights of holders of ordinary shares, as set out in our Articles of Association. The following summary is qualified in its entirety by reference to the Companies Act and to our Articles of Association, which is filed as an exhibit to our Form 6-K filed with the SEC on July 18, 2017, which is incorporated by reference in this Report on Form 6-K.

We were originally established as a private limited company under the laws of England and Wales on October 7, 2004 under the name Freshname No. 333 Limited. On January 19, 2005, we changed our name to Morria Biopharmaceuticals Limited and on February 3, 2005, we completed a reverse merger with Morria Biopharmaceuticals Inc., or Morria, a Delaware corporation, in which Morria became our wholly-owned subsidiary and we re-registered as a non-traded public limited company under the laws of England and Wales. Morria was dedicated to the discovery and development of novel, first-in-class, non-steroidal, synthetic anti-inflammatory drugs. On March 22, 2011, we incorporated an Israeli subsidiary, Morria Biopharma Ltd. On June 25, 2013, we changed our name to Celsus Therapeutics PLC and on October 13, 2013 Morria was renamed Celsus Therapeutics Inc. On September 25, 2015, we further changed our name to "Akari Therapeutics, PLC". As such our affairs are governed by our Articles of Association and the English law.

In the following summary, a "shareholder" is the person registered in our register of members as the holder of the relevant securities. For those ordinary shares that have been deposited in our ADS facility pursuant to our deposit agreement with Deutsche Bank Trust Company Americas, Deutsche Bank Trust Company Americas or its nominee is deemed the shareholder.

Share Capital

Our board of directors is generally authorized to issue up to 10,000,000,000 ordinary shares of £0.01 each until June 28, 2022, without seeking shareholder approval, subject to certain limitations. As of September 30, 2017, there were 1,177,693,393 ordinary shares outstanding, outstanding options and warrants to purchase 96,827,088 ordinary shares and 45,180,422 ordinary shares available for future issuance under our 2014 Equity Incentive Plan. All of our existing issued ordinary shares are fully paid. Accordingly, no further capital may be required by us from the holders of such shares.

The rights and restrictions to which the ordinary shares will be subject are prescribed in our Articles of Association. Our Articles of Association permit our board of directors, with shareholder approval, to determine the terms of any preferred shares that we may issue. Our board of directors is authorized, having obtained the consent of the shareholders, to provide from time to time for the issuance of other classes or series of shares and to establish the characteristics of each class or series, including the number of shares, designations, relative voting rights, dividend rights, liquidation and other rights, redemption, repurchase or exchange rights and any other preferences and relative, participating, optional or other rights and limitations not inconsistent with applicable law.

English law does not recognize fractional shares held of record. Accordingly, our Articles of Association do not provide for the issuance of fractional ordinary shares, and our official English share register will not reflect any fractional shares.

We are not permitted under English law to hold our own ordinary shares unless they are repurchased by us and held in treasury.

During the last three years, we have issued an aggregate of 1,122,057,110 ordinary shares and options to purchase an aggregate of 126,578,625 ordinary shares.

Issuance of Options and Warrants

Our Articles of Association provide that, subject to any shareholder approval requirement under any laws, regulations or the rules of any stock exchange to which we are subject, our board of directors is authorized, from time to time, in its discretion, to grant such persons, for such periods and upon such terms as it deems advisable, options to purchase such number of shares of any class or classes or of any series of any class as our board of directors may deem advisable, and to cause warrants or other appropriate instruments evidencing such options to be issued. The Companies Act provides that directors may issue options or warrants without shareholder approval once authorized to do so by the Articles of Association or an ordinary resolution of shareholders. Our board of directors may issue shares upon exercise of options or warrants without shareholder approval or authorization, up to the relevant authorized share capital limit.

Dividends

Our Articles of Association provide that our board of directors may, subject to the applicable provisions of the Companies Act, from time to time, declare such dividend as may appear to the board of directors to be justified by the distributable profits of the company. Subject to the rights of the holders of shares with preferential or other special rights that may be authorized in the future, holders of ordinary shares are entitled to receive dividends according to their rights and interest in our distributable profits. Dividends, to the extent declared, are distributed according to the proportion of the nominal value paid up on account of the shares held at the date so appointed by the Company, without regard to the premium paid in excess of the nominal value, if any. A company may only distribute a dividend out of the company's distributable profits, as defined under the Companies Act.

Any dividend unclaimed after a period of twelve years from the date of declaration of such dividend shall be forfeited and shall revert to us. In addition, the payment by the board of directors of any unclaimed dividend, interest or other sum payable on or in respect of an ordinary share into a separate account shall not constitute us as a trustee in respect thereof.

Rights in a Liquidation

In the event of our liquidation, subject to applicable law, after satisfaction of liabilities to creditors, our assets will be distributed to the holders of ordinary shares in proportion to their respective holdings. This liquidation right may be affected by the grant of preferential dividends or distribution rights to the holders of a class of shares with preferential rights that may be authorized in the future.

Voting Rights

Holders of ordinary shares have one vote for each ordinary share held on all matters submitted to a vote of shareholders. These voting rights may be affected by the grant of any special voting rights to the holders of a class of shares with preferential rights that may be authorized in the future.

The ordinary shares do not have cumulative voting rights in the election of directors. As a result, holders of ordinary shares that represent more than 50% of the voting power at the general meeting of shareholders, in person or by proxy, have the power to elect all the directors whose positions are being filled at that meeting to the exclusion of the remaining shareholders. At every annual general meeting, one third of the directors who are subject to retirement by rotation, or as near to it as may be, will retire from office. In any two year period, a majority of the directors must stand for re-election or replacement. In the event that this majority has not been met and the number of directors eligible for retirement by rotation under the provision of our Articles of Association are not met, any further directors to retire are those who have been in office the longest since their last appointment or re-appointment, but as between persons who became or were last re-appointed directors on the same day, those to retire are determined by the Board of Directors at the recommendation of the Chairman. A retiring director is eligible for re-appointment, subject to the terms of our Articles of Association.

The actions necessary to change the rights of holders of the ordinary shares are as follows: the rights of the shareholders would need to be altered by way of a special resolution requiring 75% vote of the shareholders who are present and voting in person or by proxy. In order to change the rights of a separate class of shares, it will require such a vote by shareholders of that class of shares.

Preemptive Rights

There are no rights of pre-emption under our Articles of Association in respect of transfers of issued ordinary shares. In certain circumstances, our shareholders have preemptive rights with respect to new issuances of equity securities. However our board of directors is generally authorized to allot equity securities for cash without triggering shareholder preemptive rights, provided that this power shall (i) be limited to the allotment of equity securities up to an aggregate nominal amount of £100,000,000; and (ii) expire (unless previously revoked or varied by us), on June 28, 2022.

Transfer of Shares

Fully paid ordinary shares are issued in registered form and may be transferred pursuant to our Articles of Association, unless such transfer is restricted or prohibited by another instrument and subject to applicable securities laws. The Articles of Association state that the directors of the Company may refuse to authorize a transfer of shares if the shares in question have not been paid in full and are therefore only partly paid.

Limitation on Owning Securities

Our Articles of Association do not restrict in any way the ownership or voting of ordinary shares by non-residents. If the company serves a demand on a person under section 793 to the Companies Act 2006, that person will be required to disclose any interest he has in the shares of the company.

Fiduciary Duties of Office Holders

The Companies Act imposes a duty of care and a duty of loyalty on all office holders of a company. The duty of care requires an office holder to act with the standard of skills with which a reasonable office holder in the same position would have acted under the same circumstances. The duty of care includes a duty to use reasonable means to obtain:

- information regarding the business advisability of a given action brought for his or her approval or performed by him or her by virtue of his or her position; and
- all other information of importance pertaining to the aforesaid actions.

The duty of loyalty requires an office holder to act in good faith and for the benefit of the company and includes a duty to:

- refrain from any act involving a conflict of interest between the fulfillment of his or her role in the company and the fulfillment of any other role or his or her personal affairs;
- refrain from any activity that is competitive with the business of the company;
- refrain from exploiting any business opportunity of the company with the aim of obtaining a personal gain for himself or herself or others; and
- disclose to the company all information and provide it with all documents relating to the company's affairs which the office holder has obtained due to his position in the company.

Under equity, directors have owed fiduciary duties to their companies. Chapter 2 of Part 10 of the Companies Act 2006 (2006 Act) codifies certain of those duties. The relevant statutory duties under the 2006 Act are:

- to act within powers;
- to promote the success of the company;
- to exercise independent judgment;
- to avoid conflicts of interest;

- not to accept benefits from third parties; and

- to declare an interest in a proposed transaction or arrangement.

In addition, the general principles of fiduciary duties as set out in common law continue in place in respect of Directors. The general four principles of fiduciary duties are:

- *No conflict*: A must not place himself in a position where his own interests conflict with those of B or where there is a real possibility that this will happen. This is also known as conflict of duty or conflict of interest.

- *No-profit*: A must not profit from his position at the expense of B. This is also known as misuse of property held in a fiduciary capacity.

- *Undivided loyalty*: A fiduciary owes undivided loyalty to his beneficiary. Rather confusingly, this is sometimes called conflict of duty. A must not place himself in a position where his duty to another customer conflicts with his duty to B.

- *Confidentiality*: A must use or disclose information obtained in confidence from B for the benefit only of B.

In the corporate realm, these have been refined as follows:

- *Duty to act in good faith in the best interests of the company:* A director had to act at all times in good faith in what he considered was the best interests of the company.

- *Duty to act within the powers conferred by the company's memorandum and articles of association and to exercise powers for proper purposes:* A director could not cause the company to undertake activities outside that permitted by the company's constitutional documents, or exercise his powers for any "improper purpose".

- *Duty to avoid conflicting interests and duties:* A director was obliged to avoid placing himself in a position where there was a conflict, or possible conflict, between the duties which he owed to the company and either his personal interests or other duties which he owed to a third party.

- *Duty not to make unauthorized profits:* A director was under a duty to account for any personal profit made by virtue of his directorship unless the prof it was authorized by shareholder resolution or was in accordance with the company's articles. The duty to account was strict, and did not depend on fraud or lack of good faith, or on the company suffering any loss.

Standard of Care

A director had to take such actions as would be taken by "a reasonably diligent person," having both:

- the general knowledge, skill and experience that may reasonably be expected of a person carrying out the same functions as are carried out by that director in relation to the company; and

- the general knowledge, skill and experience that that director has.

Disclosure of Personal Interests of an Officer Holder

The Companies Act requires that an office holder disclose to the Company any direct or indirect personal interest that he or she may have, and all related material information and documents known to him or her, in connection with any existing or proposed transaction by the company. The disclosure is required to be made promptly and in any event, no later than the board of directors meeting in which the transaction is first discussed.

Section 177 of the Companies Act requires any transaction in which a director has an interest to be declared, and not only those that are extraordinary transactions.

Disclosure of Conflicts of Interests

Except as provided in our Articles of Association, a director may not vote at a meeting of the board or of a committee of the board on any resolution concerning a matter:

- in which he has (either alone or together with any person connected with him, as provided in the Companies Act) a material interest, other than an interest in shares or debentures or other securities of or in the company; and
- subject to the Companies Act, which conflicts or may conflict with the interests of the Company.

A director is not counted in the quorum at a meeting in relation to any resolution on which he is debarred from voting.

Notwithstanding the foregoing, a director is entitled to vote and be counted in the quorum in respect of any resolution concerning any of the following matters:

- the giving of any security, guarantee or indemnity to a third party in respect of a debt or obligation of Celsus or any of our subsidiaries for which he himself has assumed responsibility in whole or in part under a guarantee or indemnity or by the giving of security;
- any proposal concerning an offer of shares or debentures or other securities of or by Celsus or any of our subsidiaries for subscription or purchase in which offer he is or is to be interested as a participant as the holder of such shares, debentures or other securities or in its underwriting or sub-underwriting;
- any contract, arrangement, transaction or other proposal concerning any other company in which he holds an interest not representing one per cent. or more of any class of the equity share capital (calculated exclusive of any shares of that class held as treasury shares) of such company, or of any third company through which his interest is derived, or of the voting rights available to members of the relevant company, any such interest being deemed for the purpose of this regulation to be a material interest in all circumstances;
- any contract, arrangement, transaction or other proposal concerning the adoption, modification or operation of a superannuation fund or retirement, death or disability benefits scheme under which he may benefit and which has been approved by or is subject to and conditional upon approval by Her Majesty's Revenue & Customs;
- any contract, arrangement, transaction or proposal concerning the adoption, modification or operation of any scheme for enabling employees, including full time executive directors of Celsus or any of our subsidiaries to acquire shares of Celsus or any arrangement for the benefit of employees of Celsus or any of our subsidiaries, which does not award him any privilege or benefit not awarded to the employees to whom such scheme relates; or
- any contract, arrangement, transaction or proposal concerning insurance which Celsus proposes to maintain or purchase for the benefit of directors or for the benefit of persons including directors.

Article 26 of the Articles of Association states, that the board may authorize any matter which may otherwise involve a director breaching his duties under certain sections of the Companies Act 2006 to avoid conflicts of interest.

Any director (including the director which has the conflict) may propose that such conflicted director be authorized in relation to any matter which is the subject of such a conflict. The director with the conflict will not count towards the quorum at the meeting at which the conflict is considered and may not vote on any resolution authorizing the conflict. Where the board gives authority in relation to such a conflicts, the board may impose such terms on the relevant director as it deems appropriate.

Directors' and Officers' Compensation

The Companies Act requires that a resolution approving provisions to appoint a director for a fixed period of more than two years, must not be passed unless a memorandum setting out the proposed contract incorporating the provision is made available to members: in the case of a resolution at a meeting, by being made available for inspection by members of the company both (i) at the company's registered office for not less than 15 days ending with the date of the meeting, and (ii) at the meeting itself.

Directors' Borrowing Powers

Our board of directors may, from time to time, in its discretion, cause us to borrow or secure the payment of any sum or sums of money for the purposes of our company.

Retirement of Directors

We do not have any age limitations for our directors, nor do we have mandatory retirement as a result of reaching a certain age.

Share Qualification of Directors

No shareholding qualification is required by a director.

Redemption Provisions.

We may, subject to applicable law and to our Articles of Association, issue redeemable preference shares and redeem the same.

Capital Calls.

Under our Articles of Association and the Companies Act, the liability of our shareholders is limited to the nominal value (i.e. par). The board of directors has the authority to make calls upon the shareholders in respect of any money unpaid on their shares and each shareholder shall pay to us as required by such notice the amount called on his shares. If a call remains unpaid after it has become due and payable, and the fourteen days' notice provided by the board of directors has not been complied with, any share in respect of which such notice was given may be forfeited by a resolution of the board.

No Sinking Fund

Our ordinary shares do not have sinking fund provisions.

Modification of Rights

Subject to the provisions of the Companies Act, if at any time our capital is divided into different classes of shares, the rights attached to any class may be varied or abrogated with the consent in writing of the holders of at least three-fourths in nominal value of that class or with the sanction of a special resolution passed at a separate meeting of the holders of that class, but not otherwise. The quorum at any such meeting is two or more persons holding, or representing by proxy, at least one-third in nominal value of the issued shares in question.

Transfer Restrictions

Upon the listing of our shares on a Regulated Market (as defined by the Financial Services and Markets Act 2000, the AIM market of the London Stock Exchange, the New York Stock Exchange, the NYSE American, NASDAQ and similar securities exchanges), the Board may decide that up to 100% of each shareholders' free shares (i.e. unrestricted shares under the applicable rules and regulations) shall be restricted to sale or transfer according to the following provisions, such shares as restricted by the Board being Restricted Shares: (i) during the first six months commencing on the date of the listing, no transfer of Restricted Shares is permitted; (ii) as of the seventh and eighth month following the date of the listing, such a shareholder may transfer shares that constitute up to 12.5% of his Restricted Shares per month; and (iii) as of the ninth month following the date of the listing, the remaining Restricted Shares are no longer considered restricted.

Shareholders' Meetings and Resolutions

Pursuant to our Articles of Association, the quorum required for an ordinary meeting of shareholders consists of at least two shareholders present in person or by proxy, who hold shares conferring in the aggregate more than 15% of our voting power. If at any time the Company has only one shareholder, such shareholder, in person, by proxy or, if a corporation, by its representative, shall constitute a quorum. A meeting adjourned for lack of a quorum generally is adjourned to the same day in the following week at the same time and place or any time and place as the chairman of the board may designate. Furthermore, the board of the company may call a general meeting whenever they think fit. If the Board, in its absolute discretion, considers that it is impractical or unreasonable for any reason to hold a general meeting on the date or at the time or place specified in the notice calling the general meeting, it may postpone the general meeting to another date, time and/or place.

Under the Companies Act, each shareholder of record must be provided at least 14 calendar days prior to the notice of any general shareholders' meeting and 21 days prior to the notice of an annual general meeting. Subject to the provisions of the Companies Act, our annual general meeting will be held at such time and place or places as our board may determine. Our board may call a general meeting whenever it thinks fit, and must do so when required under the Companies Act. General meetings must also be convened on such requisition, or in default may be convened by such requisitionists or by court order, as provided by the Companies Act.

Voting at any general meeting of shareholders is by a show of hands, unless a poll is demanded. A poll may be demanded by:

- the chairman of the meeting;
- at least five shareholders entitled to vote at the meeting;
- any shareholder or shareholders representing in the aggregate not less than one-tenth of the total voting rights of all shareholders entitled to vote at the meeting; or
- any shareholder or shareholders holding shares conferring a right to vote at the meeting on which there have been paid up sums in the aggregate equal to not less than one-tenth of the total sum paid up on all the shares conferring that right.

In a vote by a show of hands, every shareholder who is present in person or by proxy at a general meeting has one vote. In a vote on a poll, every shareholder who is present in person or by proxy shall have one vote for every share of which they are registered as the holder (provided that no shareholder shall have more than one vote on a show of hands notwithstanding that he may have appointed more than one proxy to vote on his behalf). The quorum for a shareholders' meeting is a minimum of two persons holding at least 15% of the share capital, present in person or by proxy. To the extent the Articles of Association provide for a vote by a show of hands in which each shareholder has one vote, this differs from U.S. law, under which each shareholder typically is entitled to one vote per share at all meetings.

Holders of ADSs are also entitled to vote by supplying their voting instructions to Deutsche Bank Trust Company Americas who will vote the ordinary shares represented by their ADSs in accordance with their instructions. The ability of Deutsche Bank Trust Company Americas to carry out voting instructions may be limited by practical and legal limitations, the terms of our Articles of Association, and the terms of the ordinary shares on deposit. We cannot assure the holders of our ADSs that they will receive voting materials in time to enable them to return voting instructions to Deutsche Bank Trust Company Americas a timely manner.

Unless otherwise required by law or the Articles of Association, voting in a general meeting is by ordinary resolution. An ordinary resolution is approved by a majority vote of the shareholders present at a meeting at which there is a quorum. Examples of matters that can be approved by an ordinary resolution include:

- the election of directors;
- the approval of financial statements;
- the declaration of final dividends;
- the appointment of auditors;
- the increase of authorized share capital; or
- the grant of authority to issue shares.

A special resolution or an extraordinary resolution requires the affirmative vote of not less than three-fourths of the eligible votes. Examples of matters that must be approved by a special resolution include modifications to the rights of any class of shares, certain changes to the Articles of Association, or our winding-up.

Limitation on Owning Securities

Our Articles of Association do not restrict in any way the ownership or voting of ordinary shares by non-residents. Furthermore, there is no longer an obligation of a shareholder of a UK company which is a non-listed (in the UK or EU) company to voluntarily disclose his shareholding unless, required to do so by the company. If the company serves a demand on a person under section 793 to the Companies Act 2006, that person will be required to disclose any interest he has in the shares of the company.

Change in Control

We can issue additional shares with any rights or restrictions attached to them as long as not restricted by any rights attached to existing shares. These rights or restrictions can be decided by the directors so long as there is no conflict with any resolution passed by the shareholders. The ability of the directors to issue shares with rights or restrictions that are different than those attached to the currently outstanding ordinary shares could have the effect of delaying, deferring or preventing change of control of our company.

In addition, as discussed above under “- A. Directors and Senior Management”, our board of directors is divided into three classes for purposes of election. One class is elected at each annual meeting of stockholders to serve for a three-year term. Because this would prevent shareholders from replacing the entire board at a single meeting, this provision could also have the effect of delaying, deferring or preventing a change in control of our company.

We may in the future be subject to the UK Takeover Code which is not binding on our company at the present time. Nevertheless, the UK Takeover Code could apply to our company under certain circumstances in the future and if that were to occur, each shareholder who is to acquire more than 29.9% of our issued and outstanding shares could, in most circumstances, be required to make an offer for all the shares in our company under the terms of the UK Takeover Code.

Differences In Corporate Law Between England And The State Of Delaware

As a public limited company incorporated under the laws of England and Wales, the rights of our shareholders are governed by applicable English law, including the Companies Act, and not by the law of any U.S. state. As a result, our directors and shareholders are subject to different responsibilities, rights and privileges than are applicable to directors and shareholders of U.S. corporations. We have set below a summary of the differences between the provisions of the Companies Act applicable to us and the Delaware General Corporation Law relating to shareholders' rights and protections. This summary is not intended to be a complete discussion of the respective rights and it is qualified in its entirety by reference to English law, Delaware law and our Articles of Association. Before investing, you should consult your legal advisor regarding the impact of English corporate law on your specific circumstances and reasons for investing. The summary below does not include a description of rights or obligations under the U.S. federal securities laws or NASDAQ listing requirements. You are also urged to carefully read the relevant provisions of the Delaware General Corporation Law and the Companies Act for a more complete understanding of the differences between Delaware and English law.

	Delaware	**England**
Number of Directors	Under Delaware law, a corporation must have at least one director and the number of directors shall be fixed by or in the manner provided in the bylaws, unless specified in the certificate of incorporation.	Under the Companies Act, a public limited company must have at least two directors and the number of directors may be fixed by or in the manner provided in a company's articles of association.
Removal of Directors	Under Delaware law, directors may be removed from office, with or without cause, by a majority shareholder vote, except (a) in the case of a corporation whose board is classified, shareholders may effect such removal only for cause, unless otherwise provided in the certificate of incorporation, and (b) in the case of a corporation having cumulative voting, if less than the entire board is to be removed, no director may be removed without cause if the votes cast against his or her removal would be sufficient to elect him or her if then cumulatively voted at an election of the entire board of directors, or, if there are classes of directors, at an election of the class of directors of which he or she is a part.	Under the Companies Act, shareholders may remove a director without cause by an ordinary resolution (which is passed by a simple majority of those voting in person or by proxy at a general meeting) irrespective of any provisions of any service contract the director has with the company, provided that 28 clear days' notice of the resolution is given to the company and certain other procedural requirements under the Companies Act are followed (such as allowing the director to make representations against his or her removal at the meeting and/or in writing).
Vacancies on the Board of Directors	Under Delaware law, vacancies and newly created directorships may be filled by a majority of the directors then in office (even though less than a quorum) or by a sole remaining director unless otherwise provided in the certificate of incorporation or bylaws of the corporation.	Under English law, the procedure by which directors (other than a company's initial directors) are appointed is generally set out in a company's articles of association, provided that where two or more persons are appointed as directors of a public limited company by resolution of the shareholders, resolutions appointing each director must be voted on individually unless a resolution of the shareholders that such resolutions do not have to be voted on individually is first agreed to by the meeting without any vote being given against it.

	Delaware	England
Annual General Meeting	Under Delaware law, the annual meeting of shareholders shall be held at such place, on such date and at such time as may be designated from time to time by the board of directors or as provided in the certificate of incorporation or by the bylaws.	Under the Companies Act, a public limited company must hold an annual general meeting each year. This meeting must be held within six months beginning with the day following the company's accounting reference date.
General Meeting	Under Delaware law, special meetings of the shareholders may be called by the board of directors or by such person or persons as may be authorized by the certificate of incorporation or by the bylaws.	Under the Companies Act, a general meeting of the shareholders of a public limited company may be called by the directors. Shareholders holding at least 5% of the paid-up capital (excluding any paid-up capital held as treasury shares) of the company carrying voting rights at general meetings can also require the directors to call a general meeting.
Notice of General Meetings	Under Delaware law, written notice of any meeting of the shareholders must be given to each shareholder entitled to vote at the meeting not less than ten nor more than 60 days before the date of the meeting and shall specify the place, date, hour and purpose or purposes of the meeting.	The Companies Act provides that a general meeting (other than an adjourned meeting) must be called by notice of: • in the case of an annual general meeting, at least 21 days; and • in any other case, at least 14 days. The company's articles of association may provide for a longer period of notice and, in addition, certain matters (such as the removal of directors or auditors) require special notice, which is 28 clear days' notice. The shareholders of a company may in all cases consent to a shorter notice period, the proportion of shareholders' consent required being 100% of those entitled to attend and vote in the case of an annual general meeting and, in the case of any other general meeting, a majority in number of the members having a right to attend and vote at the meeting, being a majority who together hold not less than 95% in nominal value of the shares giving a right to attend and vote at the meeting.

	Delaware	England
Quorum	The certificate of incorporation or bylaws may specify the number of shares, the holders of which shall be present or represented by proxy at any meeting in order to constitute a quorum, but in no event shall a quorum consist of less than $^{1}/3$ of the shares entitled to vote at the meeting. In the absence of such specification in the certificate of incorporation or bylaws, a majority of the shares entitled to vote, present in person or represented by proxy, shall constitute a quorum at a meeting of shareholders.	Subject to the provisions of a company's articles of association, the Companies Act provides that two shareholders present at a meeting (in person or by proxy) shall constitute a quorum.
Proxy	Under Delaware law, at any meeting of shareholders, a shareholder may designate another person to act for such shareholder by proxy, but no such proxy shall be voted or acted upon after three years from its date, unless the proxy provides for a longer period.	Under the Companies Act, at any meeting of shareholders, a shareholder may designate another person to attend, speak and vote at the meeting on their behalf by proxy (or, in the case of a shareholder which is a corporate body, by way of a corporate representative).
Issue of New Shares	Under Delaware law, if the company's certificate of incorporation so provides, the directors have the power to authorize additional stock. The directors may authorize capital stock to be issued for consideration consisting of cash, any tangible or intangible property or any benefit to the company or any combination thereof.	Under the Companies Act, the directors of a company must not exercise any power to allot shares or grant rights to subscribe for, or to convert any security into, shares unless they are authorized to do so by the company's articles of association or by an ordinary resolution of the shareholders. Any authorization given must state the maximum amount of shares that may be allotted under it and specify the date on which it will expire, which must be not more than five years from the date the authorization was given. The authority can be renewed by a further resolution of the shareholders.

	Delaware	England
Pre-emptive Rights	Under Delaware law, unless otherwise provided in a corporation's certificate of incorporation, a stockholder does not, by operation of law, possess pre-emptive rights to subscribe to additional issuances of the corporation's stock.	Under the Companies Act, "equity securities" (being (i) shares in the company other than shares that, with respect to dividends and capital, carry a right to participate only up to a specified amount in a distribution ("ordinary shares") or (ii) rights to subscribe for, or to convert securities into, ordinary shares) proposed to be allotted for cash must be offered first to the existing equity shareholders in the company in proportion to the respective nominal value of their holdings, unless an exception applies or a special resolution to the contrary has been passed by shareholders in a general meeting or the articles of association provide otherwise in each case in accordance with the provisions of the Companies Act.
Liability of Directors and Officers	Under Delaware law, a corporation's certificate of incorporation may include a provision eliminating or limiting the personal liability of a director to the corporation and its shareholders for monetary damages arising from a breach of fiduciary duty as a director. However, no provision can limit the liability of a director for: • any breach of the director's duty of loyalty to the corporation or its shareholders; • acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law; • willful or negligent payment of unlawful dividends or stock purchases or redemptions; or • any transaction from which the director derives an improper personal benefit.	Under the Companies Act, any provision (whether contained in a company's articles of association or any contract or otherwise) that purports to exempt a director of a company (to any extent) from any liability that would otherwise attach to him in connection with any negligence, default, breach of duty or breach of trust in relation to the company is void. Any provision by which a company directly or indirectly provides an indemnity (to any extent) for a director of the company or of an associated company against any liability attaching to him in connection with any negligence, default, breach of duty or breach of trust in relation to the company of which he or she is a director is also void except as permitted by the Companies Act, which provides exceptions for the company to: (i) purchase and maintain insurance against such liability; (ii) provide a "qualifying third party indemnity" (being an indemnity against liability incurred by the director to a person other than the company or an associated company. Such indemnity must not cover fines imposed in criminal proceedings, penalties imposed by regulatory bodies arising out of non-compliance with regulatory requirements, the defense costs of criminal proceedings where the director is found guilty, the defense costs of civil proceedings successfully brought against the director by the company or an associated company, and the costs of unsuccessful applications by the director for relief); and (iii) provide a "qualifying pension scheme indemnity" (being an indemnity against liability incurred in connection with the company's activities as trustee of an occupational pension plan).

	Delaware	England
Voting Rights	Delaware law provides that, unless otherwise provided in the certificate of incorporation, each shareholder of record is entitled to one vote for each share of capital stock held by such shareholder.	Under English law, unless a poll is demanded by the shareholders of a company or is required by the Chairman of the meeting or the company's articles of association, shareholders shall vote on all resolutions on a show of hands. Under the Companies Act, a poll may be demanded by: (i) not fewer than five shareholders having the right to vote on the resolution; (ii) any shareholder(s) representing at least 10% of the total voting rights of all the shareholders having the right to vote on the resolution (excluding any voting rights attached to treasury shares); or (iii) any shareholder (s) 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. A company's articles of association may provide more extensive rights for shareholders to call a poll. Under English law, an ordinary resolution is passed on a show of hands if it is approved by a simple majority (more than 50%) of the votes cast by shareholders present (in person or by proxy) and entitled to vote. If a poll is demanded, an ordinary resolution is passed if it is approved by holders representing a simple majority of the total voting rights of shareholders present (in person or by proxy) who (being entitled to vote) vote on the resolution. Special resolutions require the affirmative vote of not less than 75% of the votes cast by shareholders present (in person or by proxy) at the meeting.

	Delaware	England
Variation of Class Rights	Under Delaware law, the holders of the outstanding shares of a class shall be entitled to vote as a class upon a proposed amendment, whether or not entitled to vote thereon by the certificate of incorporation, if the amendment would increase or decrease the aggregate number of authorized shares of such class, increase or decrease the par value of the shares of such class, or alter or change the powers, preferences or special rights of the shares of such class so as to affect them adversely.	The Companies Act provides that rights attached to a class of shares may only be varied or abrogated in accordance with provision in the company's articles for the variation or abrogation of those rights or, where the company's articles contain no such provision, if the holders of shares of that class consent to the variation or abrogation. Consent for these purposes means: • consent in writing from the holders of at least 75% in nominal value of the issued shares of that class (excluding any shares held as treasury shares); or • a special resolution passed at a separate meeting of the holders of that class sanctioning the variation. The Companies Act provides that the quorum for a class meeting is not less than two persons holding or representing by proxy at least one-third of the nominal value of the issued shares of that class. Following a variation of class rights, shareholders who amount to not less than 15% of the shareholders of the class in question who did not approve the variation may apply to court to have the variation cancelled. Any application must be made within 21 days of the variation. The court may cancel the variation if it is satisfied having regard to all the circumstances of the case that the variation would unfairly prejudice the shareholders of the class represented by the applicant.

	Delaware	England
Shareholder Vote on Certain Transactions	Generally, under Delaware law, unless the certificate of incorporation provides for the vote of a larger portion of the stock, completion of a merger, consolidation, sale, lease or exchange of all or substantially all of a corporation's assets or dissolution requires: • the approval of the board of directors; and • approval by the vote of the holders of a majority of the outstanding stock or, if the certificate of incorporation provides for more or less than one vote per share, a majority of the votes of the outstanding stock of a corporation entitled to vote on the matter. Under Delaware law, a contract or transaction between the company and one or more of its directors or officers, or between the company and any other organization in which one or more of its directors or officers, are directors or officers, or have a financial interest, shall not be void solely for this reason, or solely because the director or officer participates in the meeting of the board which authorizes the contract or transaction, or solely because any such director's or officer's votes are counted for such purpose, if: • the material facts as to the director's or officer's relationship or interest and as to the contract or transaction are disclosed or are known to the board, and the board in good faith authorizes the contract or transaction by the affirmative votes of a majority of the disinterested directors, even though the disinterested directors be less than a quorum; • the material facts as to the director's or officer's relationship or interest and as to the contract or transaction are disclosed or are known to the shareholders entitled to vote thereon, and the contract or transaction is specifically approved in good faith by vote of the shareholders; or • the contract or transaction is fair as to the corporation as of the time it is authorized, approved or ratified, by the board of directors, a committee or the shareholders.	The Companies Act provides for schemes of arrangement, which are arrangements or compromises between a company and any class of shareholders or creditors and used in certain types of reconstructions, amalgamations, capital reorganizations or takeovers. These arrangements require: • the approval at a shareholders' or creditors' meeting convened by order of the court, of a majority in number of shareholders or creditors representing 75% in value of the capital held by, or debt owed to, the class of shareholders or creditors, or class thereof present and voting, either in person or by proxy; and • the approval of the court. Once approved, sanctioned and effective, all shareholders and creditors of the relevant class and the company are bound by the terms of the scheme. The Companies Act also contains certain provisions relating to transactions between a director and the company, including transactions involving the acquisition of substantial non-cash assets from a director or the sale of substantial noncash assets to a director, and loans between a company and a director or certain connected persons of directors. If such transactions meet certain thresholds set out within the Companies Act the approval of shareholders by ordinary resolution will be required.

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

	Delaware	England
Shareholder Suits	Under Delaware law, a shareholder may initiate a derivative action to enforce a right of a corporation if the corporation fails to enforce the right itself. The complaint must: • state that the plaintiff was a shareholder at the time of the transaction of which the plaintiff complains or that the plaintiff's shares thereafter devolved on the plaintiff by operation of law; and • allege with particularity the efforts made by the plaintiff to obtain the action the plaintiff desires from the directors and the reasons for the plaintiff's failure to obtain the action; or • state the reasons for not making the effort. Additionally, the plaintiff must remain a shareholder through the duration of the derivative suit.	Under English law, generally, the company, rather than its shareholders, is the proper claimant in an action in respect of a wrong done to the company or where there is an irregularity in the company's internal management. Notwithstanding this general position, the Companies Act provides that (i) a court may allow a shareholder to bring a derivative claim (that is, an action in respect of and on behalf of the company) in respect of a cause of action arising from a director's negligence, default, breach of duty or breach of trust, subject to complying with the procedural requirements under the Companies Act and (ii) a shareholder may bring a claim for a court order where the company's affairs have been or are being conducted in a manner that is unfairly prejudicial to some or all of its shareholders.

Other U.K. Law Considerations

Squeeze-Out

Under the Companies Act, if a takeover offer (as defined in Section 974 of the Companies Act) is made for the shares of a company and the offeror were to acquire, or unconditionally contract to acquire: (i) not less than 90% in value of the shares to which the takeover offer relates (the "Takeover Offer Shares"); and (ii) where those shares are voting shares, not less than 90% of the voting rights attached to the Takeover Offer Shares, the offeror could acquire compulsorily the remaining 10% within three months of the day after the last day on which its offer can be accepted. It would do so by sending a notice to outstanding shareholders telling them that it will acquire compulsorily their Takeover Offer Shares and then, six weeks later, it would execute a transfer of the outstanding Takeover Offer Shares in its favor and pay the consideration to the company, which would hold the consideration on trust for outstanding shareholders. The consideration offered to the shareholders whose Takeover Offer Shares are acquired compulsorily under the Companies Act must, in general, be the same as the consideration that was available under the takeover offer.

Sell-Out

The Companies Act also gives minority shareholders a right to be bought out in certain circumstances by an offeror who has made a takeover offer (as defined in Section 974 of the Companies Act). If a takeover offer related to all the shares of a company and, at any time before the end of the period within which the offer could be accepted, the offeror held or had agreed to acquire not less than 90% of the shares to which the offer relates, any holder of the shares to which the offer related who had not accepted the offer could by a written communication to the offeror require it to acquire those shares. The offeror is required to give any shareholder notice of his or her right to be bought out within one month of that right arising. The offeror may impose a time limit on the rights of the minority shareholders to be bought out, but that period cannot end less than three months after the end of the acceptance period. If a shareholder exercises his or her rights, the offeror is bound to acquire those shares on the terms of the offer or on such other terms as may be agreed.

Disclosure of Interest in Shares

Pursuant to Part 22 of the Companies Act, a company is empowered by notice in writing to require any person whom the company knows to be, or has reasonable cause to believe to be, interested in the company's shares or at any time during the three years immediately preceding the date on which the notice is issued to have been so interested, within a reasonable time to disclose to the company details of that person's interest and (so far as is within such person's knowledge) details of any other interest that subsists or subsisted in those shares. If a shareholder defaults in supplying the company with the required details in relation to the shares in question (the "Default Shares"), the shareholder shall not be entitled to vote or exercise any other right conferred by membership in relation to general meetings. Where the Default Shares represent 0.25% or more of the issued shares of the class in question, in certain circumstances the directors may direct that:

(i) any dividend or other money payable in respect of the Default Shares shall be retained by the company without any liability to pay interest on it when such dividend or other money is finally paid to the shareholder; and/or

(ii) no transfer by the relevant shareholder of shares (other than a transfer approved in accordance with the provisions of the company's articles of association) may be registered (unless such shareholder is not in default and the transfer does not relate to Default Shares).

Dividends

Under English law, before a company can lawfully make a distribution, it must ensure that it has sufficient distributable reserves. A company's distributable reserves are its accumulated, realized profits, so far as not previously utilized by distribution or capitalization, less its accumulated, realized losses, so far as not previously written off in a reduction or reorganization of capital duly made. In addition to having sufficient distributable reserves, a public company will not be permitted to make a distribution if, at the time, the amount of its net assets (that is, the aggregate of the company's assets less the aggregate of its liabilities) is less than the aggregate of its issued and paid-up share capital and undistributable reserves, or if the distribution would result in the amount of its net assets being less than that aggregate.

Purchase Of Own Shares

Under English law, a public limited company may purchase its own shares only out of the distributable profits of the company or the proceeds of a new issue of shares made for the purpose of financing the purchase, provided that it is not restricted from doing so by its articles. A public limited company may not purchase its own shares if as a result of the purchase there would no longer be any issued shares of the company other than redeemable shares or shares held as treasury shares. Shares must be fully paid in order to be repurchased.

Subject to the foregoing, because NASDAQ is not a "recognized investment exchange" under the Companies Act, a company may purchase its own fully paid shares only pursuant to a purchase contract authorized by ordinary resolution of the holders of its ordinary shares before the purchase takes place. Any authority will not be effective if any shareholder from whom the company proposes to purchase shares votes on the resolution and the resolution would not have been passed if such shareholder had not done so. The resolution authorizing the purchase must specify a date, not being later than five years after the passing of the resolution, on which the authority to purchase is to expire.

A share buy back by a company of its ordinary shares will give rise to U.K. stamp duty at the rate of 0.5% of the amount or value of the consideration payable by the company, and such stamp duty will be paid by the company. Our Articles of Association do not have conditions governing changes in our capital which are more stringent than those required by law.

Statutory Pre-Emption Rights

Under English law, a company must not allot equity securities to a person on any terms unless the following conditions are satisfied:

(i) it has made an offer to each person who holds ordinary shares in the company to allot to them on the same or more favorable terms a proportion of those securities that is as nearly as practicable equal to the proportion in nominal value held by them of the ordinary share capital of the company; and

(ii) the period during which any such offer may be accepted has expired or the company has received notice of the acceptance or refusal of every offer so made.

For these purposes "equity securities" means ordinary shares in the company or rights to subscribe for, or to convert securities into, ordinary shares in the company. "Ordinary shares" means shares other than shares that, with respect to dividends and capital, carry a right to participate only up to a specified amount in a distribution. The statutory pre-emption rights are subject to certain exceptions, including the issue of ordinary shares for non-cash consideration, an allotment of bonus shares and the allotment of equity securities pursuant to an employees' share scheme. The statutory pre-emption rights may also be disapplied with the approval of 75% of shareholders.

U.K. City Code On Takeovers And Mergers

Since our central place of management is not in the United Kingdom, we are currently not subject to the U.K. City Code on Takeovers and Mergers (the "Takeover Code"), which is issued and administered by the U.K. Panel on Takeovers and Mergers, or the Panel.

The Takeover Code provides a framework within which takeovers of companies subject to it are conducted. In particular, the Takeover Code contains certain rules in respect of mandatory offers. Under Rule 9 of the Takeover Code, if a person:

- acquires an interest in our shares which, when taken together with shares in which he or persons acting in concert with him are interested, carries 30% or more of the voting rights of our shares; or

- who, together with persons acting in concert with him, is interested in shares that in the aggregate carry not less than 30% and not more than 50% of the voting rights in us, acquires additional interests in shares that increase the percentage of shares carrying voting rights in which that person is interested, the acquirer and depending on the circumstances, its concert parties, would be required (except with the consent of the Panel) to make a cash offer for our outstanding shares at a price not less than the highest price paid for any interests in the shares by the acquirer or its concert parties during the previous 12 months.

TAXATION

The following summary contains a description of certain United Kingdom and United States federal income tax consequences of the acquisition, ownership and disposition of our ordinary shares or ADSs to a U.S. holder of our ordinary shares or ADSs. The summary is based upon the tax laws of the United Kingdom and the United States and the respective regulations thereunder as of the date hereof, which are subject to change.

For purposes of this description, a "U.S. Holder" includes any beneficial owner of our ordinary shares or ADSs that is, for U.S. federal income tax purposes:

- a citizen or individual resident of the United States;
- a corporation (or other entity treated as a corporation for U.S. federal income tax purposes) created or organized in or under the laws of the United States or organized under the laws of any state thereof, or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust if (1) a court within the United States is able to exercise primary supervision over its administration and one or more United States persons have the authority to control all of the substantial decisions of such trust; or (2) such trust has a valid election in effect to be treated as a United States person for U.S. federal income tax purposes.

A "Non-U.S. Holder" is any beneficial owner of our ordinary shares or ADSs that is not a U.S. Holder.

This section does not purport to be a comprehensive description of all of the tax considerations that may be relevant to any particular investor. This discussion assumes that you are familiar with the tax rules applicable to investments in securities generally, and with any special rules to which you may be subject. In particular, the discussion deals only with investors that will hold our ordinary shares or ADSs as capital assets, and does not address the tax treatment of investors that are subject to special rules, such as banks, financial institutions, insurance companies, dealers or traders in securities or currencies, persons that elect mark-to- market treatment, tax-exempt entities (including 401 pensions plans), real estate investment trusts, regulated investment companies, grantor trusts, individual retirement and other tax-deferred accounts, persons that received our ordinary or ADS shares as compensation for the performance of services, persons who own, directly, indirectly through non-U.S. entities or by attribution by application of the constructive ownership rules of section 958(b) of the United States Internal Revenue Code of 1986, or Code, 10% or more of our voting shares or ADS, persons that are residents of the U.K. for U.K. tax purposes or that conduct a business or have a permanent establishment in the U.K., persons that hold our ordinary shares or ADSs as a position in a straddle, hedging, conversion, integration, constructive sale or other risk reduction transaction, certain former citizens or long-term residents of the U.S., partnerships and their partners and persons whose functional currency is not the U.S. dollar. This discussion is based on laws, treaties, judicial decisions, and regulatory interpretations in effect on the date hereof, all of which are subject to change, as well as, in the United States, the Internal Revenue Code of 1986, as amended, or the Code, administrative pronouncements, judicial decisions, and final, temporary and proposed Treasury regulations, all as of the date hereof, any of which is subject to change, possibly with retroactive effect.

If a partnership holds ordinary shares or ADSs, the tax treatment of a partner will generally depend upon the status of the partner and upon the activities of the partnership.

We will not seek a ruling from the U.S. Internal Revenue Service, or IRS, with regard to the U.S. federal income tax treatment of an investment in our ordinary shares or ADSs, and we cannot assure you that the IRS will agree with the conclusions set forth below.

You are urged to consult with your own advisers regarding the tax consequences of the acquisition, ownership, and disposition of our ordinary shares or ADSs in the light of your particular circumstances, including the effect of any state, local, or other national laws.

United Kingdom tax considerations

Taxation of dividends

Under current U.K. tax law, no tax is required to be withheld in the United Kingdom at source from cash dividends paid to U.S. resident holders.

Taxation of Capital Gains

Subject to the comments in the following paragraph, a holder of our ordinary shares or ADSs who, for U.K. tax purposes, is not resident in the U.K. will not be liable for U.K. taxation on capital gains realized on the disposal of our ordinary shares or ADS unless at the time of the disposal:

- the holder carries on a trade, or in the case of an individual, a profession or vocation in the United Kingdom through, in the case of an individual, a branch or agency, or, in the case of a company, a permanent establishment, and

- our ordinary shares or ADSs are or have been used, held, or acquired for the purpose of such trade, profession, vocation, branch, agency or permanent establishment.

A holder of our ordinary shares or ADSs who (1) is an individual who has ceased to be resident for U.K. tax purposes in the United Kingdom, (2) was solely resident for U.K. tax purposes in the United Kingdom for at least four out of the seven U.K. tax years immediately preceding the year in which he or she ceased to be resident in the United Kingdom, (3) only remains non-resident in the United Kingdom for a period of five years or less and (4) disposes of his or her ordinary shares or ADSs during that period may also be liable, upon returning to the United Kingdom, for U.K. tax on capital gains, subject to any available exemption or relief, even though he or she was not resident in the United Kingdom at the time of the disposal.

Inheritance Tax

Our ordinary shares or ADSs are assets situated in the United Kingdom for the purposes of U.K. inheritance tax (the equivalent of U.S. estate and gift tax). Subject to the discussion of the U.K.-U.S. estate tax treaty in the next paragraph, U.K. inheritance tax may apply (subject to any available reliefs) if an individual who holds our ordinary shares or ADSs gifts them or dies even if he or she is neither domiciled in the United Kingdom nor deemed to be domiciled there under U.K. law. For inheritance tax purposes, a transfer of our ordinary shares or ADSs at less than full market value may be treated as a gift for these purposes. Special inheritance tax rules apply (1) to gifts if the donor retains some benefit, (2) to close companies and (3) to trustees of settlements.

However, as a result of the U.K.-U.S. estate tax treaty, our ordinary shares or ADSs held by an individual who is domiciled in the United States for the purposes of the U.K.-U.S. estate tax treaty and who is not a U.K. national will not be subject to U.K. inheritance tax on that individual’s death or on a gift of our ordinary shares or ADSs unless the ordinary shares or ADSs:

- are part of the business property of a permanent establishment in the United Kingdom, or

- pertain to a fixed base in the United Kingdom used for the performance of independent personal services.

The U.K.-U.S. estate tax treaty provides a credit mechanism if our ordinary shares or ADSs are subject to both U.K. inheritance tax and to U.S. estate and gift tax.

U.K. Stamp Duty and Stamp Duty Reserve Tax (SDRT)

U.K. legislation provides that SDRT is chargeable at 1.5% on the issuance of a depositary receipt for U.K. shares or securities, or the issuance of such shares or securities into a clearance system. HMRC currently accepts that these provisions contravene European Union law, and accordingly does not seek to enforce SDRT on issues of UK shares and securities to depositary receipt issuers and clearance services anywhere in the world. It is currently unclear whether HMRC might seek to reimpose such a charge if and when the United Kingdom leaves the European Union, which is expected to happen in March 2019. HMRC still contends that stamp duty/SDRT at 1.5% is payable on transfers (by sale or otherwise) of shares and securities to depository receipt systems or clearance services that are not an integral part of an issue of share capital.

Transfer of shares in registered form

A transfer of shares in registered form would attract ad valorem stamp duty generally at the rate of 0.5% of the purchase price of the shares. There is no charge to ad valorem stamp duty on gifts.

SDRT would generally be payable on an unconditional agreement to transfer shares in registered form at 0.5% of the amount or value of the consideration for the transfer, but is repayable if, within six years of the date of the agreement, an instrument transferring the shares is executed or, if the SDRT has not been paid, the liability to pay the tax (but not necessarily interest and penalties) would be cancelled.

United States federal income taxation considerations

Ownership of ADSs

For U.S. federal income tax purposes, a holder of ADSs generally will be treated as the owner of the ordinary shares represented by such ADSs. Gain or loss will generally not be recognized on account of exchanges of ordinary shares for ADSs, or of ADSs for ordinary shares. References to ordinary shares in the discussion below are deemed to include ADSs, unless context otherwise requires.

U.S. Taxation of Distributions

The gross amount of any distributions made by us to a U.S. Holder will generally be subject to U.S. federal income tax as dividend income to the extent paid or deemed paid out of our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. Such dividends will not be eligible for the dividends received deduction generally allowed to U.S. corporations with respect to dividends received from other U.S. corporations. To the extent that an amount received by a U.S. Holder exceeds its allocable share of our current and accumulated earnings and profits, such excess would, subject to the discussion below, be treated first as a tax-free return of capital which will reduce such U.S. Holder’s tax basis in his ordinary shares or ADSs and then, to the extent such distribution exceeds such U.S. Holder’s tax basis, it will be treated as capital gain. We have not maintained and do not plan to maintain calculations of earnings and profits under U.S. federal income tax principles. Accordingly, it is unlikely that U.S. Holders will be able to establish whether a distribution by us is in excess of our and accumulated earnings and profits (as computed under U.S. federal income tax principles). Thus, it is expected that any distribution will be reported as a dividend, even if that distribution would otherwise be treated as a non-taxable return of capital or as capital gain under the rules described above. The amount of any distribution of property other than cash will be the fair market value of that property on the date of distribution.

Subject to applicable holding period (which generally requires our ordinary shares to be held for at least 61 days without protection from the risk of loss during the 121-day period beginning 60 days before the ex-dividend date) and other limitations, the U.S. Dollar amount of dividends received on our ordinary shares or ADSs by certain non-corporate U.S. Holders are currently subject to taxation at a maximum rate of 20% if the dividends are "qualified dividends" and certain other requirements are met. Dividends paid on our ordinary shares or ADSs will be treated as qualified dividends if: (i) we are eligible for the benefits of the U.S.-U.K. Tax Treaty (as defined below) or the ordinary shares or ADSs are readily tradable on an established U.S. securities market and (ii) we were not, in the year prior to the year in which the dividend was paid, and are not, in the year in which the dividend is paid, a PFIC. Our ADSs are listed on The NASDAQ Capital Market, which is an established securities market in the United States, and we expect the ADSs to be readily tradable on The NASDAQ Capital Market. However, there can be no assurance that the ADSs will be considered readily tradable on an established securities market in the United States in later years. The Company, which is incorporated under the laws of England and Wales, believes that it qualifies as a resident of the United Kingdom for the purposes of, and is eligible for the benefits of, the Convention between the Government of the United States of America and the Government of the United Kingdom of Great Britain and Northern Ireland for the Avoidance of Double Taxation and the Prevention of Fiscal Evasion with Respect to Taxes on Income and Capital Gains, signed on July 24, 2001, or the U.S.-U.K. Tax Treaty, although there can be no assurance in this regard. Further, the IRS has determined that the U.S.-U.K. Tax Treaty is satisfactory for purposes of the qualified dividend rules and that it includes an exchange-of-information program. Based on the foregoing, we expect to be considered a qualified foreign corporation under the Code. Accordingly, dividends paid by us to non-corporate U.S. holders with respect to shares that meet the minimum holding period and other requirements are expected to be treated as "qualified dividend income." However, dividends paid by us will not qualify for the 20% maximum U.S. federal income tax rate if we are treated, for the tax year in which the dividends are paid or the preceding tax year, as a "passive foreign investment company" for U.S. federal income tax purposes, as discussed below. Although we currently believe that distributions on our ordinary shares or ADSs that are treated as dividends for U.S. federal income tax purposes should constitute qualified dividends, no assurance can be given that this will be the case. U.S. Holders should consult their tax advisors regarding the tax rate applicable to dividends received by them with respect to our ordinary shares or ADSs, as well as the potential treatment of any loss on a disposition of our ordinary shares or ADSs as long-term capital loss regardless of the U.S. Holders' actual holding period for our ordinary shares or ADSs.

The U.S. Treasury Department has announced its intention to issue rules regarding when and to what extent holders of ADSs will be permitted to rely on certifications from issuers to establish that dividends paid on shares to which such ADSs relate are treated as qualified dividends. Because such procedures have not yet been issued, it is not clear whether we will be able to comply with them.

For foreign tax credit computation purposes, dividends will generally constitute foreign source income, and with certain exceptions, will constitute "passive category income."

U.S. Taxation upon Sale or Other Disposition

Subject to the discussion under "Passive Foreign Investment Company Considerations" below, gain or loss realized by a U.S. Holder on the sale or other disposition of our ordinary shares or ADSs will be subject to U.S. federal income taxation as capital gain or loss in an amount equal to the difference between the U.S. Holder's adjusted tax basis in our ordinary shares or ADSs and the amount realized on the disposition. Such gain or loss generally will be treated as long-term capital gain or loss if our ordinary shares or ADSs have been held for more than one year at the time of the sale or disposition. Any such gain or loss realized will generally be treated as U.S. source gain or loss. In the case of a non-corporate U.S. Holder, long-term capital gains are currently eligible for federal income tax at preferential rates . The deductibility of capital losses is subject to significant limitations.

For a cash basis taxpayer, units of foreign currency paid or received are translated into U.S. dollars at the spot rate on the settlement date of the purchase or sale. In that case, no foreign currency exchange gain or loss will result from currency fluctuations between the trade date and the settlement date of such a purchase or sale. An accrual basis taxpayer, however, may elect the same treatment required of cash basis taxpayers with respect to purchases and sales of the ADSs that are traded on an established securities market, provided the election is applied consistently from year to year. Such election may not be changed without the consent of the IRS. For an accrual basis taxpayer who does not make such election, units of foreign currency paid or received are translated into U.S. dollars at the spot rate on the trade date of the purchase or sale. Such an accrual basis taxpayer may recognize exchange gain or loss based on currency fluctuations between the trade date and settlement date. Any foreign currency gain or loss a U.S. holder realizes will be U.S. source ordinary income or loss.

The maximum individual rate for long-term capital gain is currently 20%.

Medicare Tax

Individuals, estates and trusts are subject to a Medicare tax of 3.8% on "net investment income," which includes dividends, interest, and capital gain from the sale of investment securities, adjusted for certain deductions properly allocated to such investment income. The Medicare tax will apply to the lesser of such net investment income or the excess of the taxpayer's adjusted gross income (with certain modifications) over a specified amount. The specified amount is $250,000 for married individuals filing jointly, $125,000 for married individuals filing separately, and $200,000 for single individuals. U.S. Holders should consult with their own tax advisers regarding the application of the net investment income tax to them as a result of their investment in our ADSs or ordinary shares.

Passive foreign investment company rules

Based on the nature of our present business operations, assets and income, we believe that for the year 2016, we are not a PFIC. However, no assurance can be given that changes will not occur in our business operations, assets and income that might cause us to be treated as a PFIC at some future time.

We would be a PFIC for U.S. federal income tax purposes in any taxable year if 75% or more of our gross income would be passive income, or on average at least 50% of the gross value of our assets is held for the production of, or produces, passive income. In making the above determination, we are treated as earning our proportionate share of any income and owning our proportionate share of any asset of any company in which we are considered to own, directly or indirectly, 25% or more of the shares by value. If we were considered a PFIC at any time when a U.S. Holder held our ordinary shares or ADSs, we generally should continue to be treated as a PFIC with respect to that U.S. Holder, and the U.S. Holder generally will be subject to special rules with respect to (a) any gain realized on the disposition of our ordinary shares or ADSs and (b) any "excess distribution" by us to the U.S. Holder in respect of our ordinary shares or ADSs. Generally, a distribution during a taxable year to a U.S. Holder with respect to ordinary shares would be treated as an "excess distribution" to the extent that the distribution plus all other distributions received (or deemed to be received) by the U.S. Holder during the taxable year with respect to such ordinary shares, is greater than 125% of the average annual distributions received by the U.S. Holder with respect to such ordinary shares during the three preceding years (or during such shorter period as the U.S. Holder may have held the ordinary shares or ADSs). Under the PFIC rules: (i) the gain or excess distribution would be allocated ratably over the U.S. Holder's holding period for our ordinary shares or ADSs, (ii) the amount allocated to the taxable year in which the gain or excess distribution was realized or to any year before we became a PFIC would be taxable as ordinary income and (iii) the amount allocated to each other taxable year would be subject to tax at the highest tax rate in effect in that year and an interest charge generally applicable to underpayments of tax would be imposed in respect of the tax attributable to each such year. Because a U.S. Holder that is a direct (and in certain cases indirect) shareholder of a PFIC is deemed to own its proportionate share of interests in any lower-tier PFICs, U.S. Holders should be subject to the foregoing rules with respect to any of our subsidiaries characterized as PFICs, if we are deemed a PFIC.

In the event we were treated as a PFIC, the tax consequences under the default PFIC regime described above could be avoided by either a "mark-to-market" or "qualified electing fund" election. If our ordinary shares or ADSs are considered "marketable stock," a U.S. Holder may elect to "mark-to-market" its ADSs. A U.S. holder making a mark-to-market election (if the eligibility requirements for such an election were satisfied) generally would not be subject to the PFIC rules discussed above, except with respect to any portion of the holder's holding period that preceded the effective date of the election. Instead, such U.S. Holder would generally include in income any excess of the fair market value of the ordinary shares or ADSs at the close of each tax year over its adjusted basis in the ordinary shares or ADSs. If the fair market value of the ordinary shares of ADSs had depreciated below the U.S. Holders adjusted basis at the close of the tax year, the U.S. Holder may generally deduct the excess of the adjusted basis of the ordinary shares or ADSs over its fair market value at that time. However, such deductions generally would be limited to the net mark-to-market gains, if any, that the U.S. Holder included in income with respect to such ordinary shares or ADSs in prior years. Income recognized and deductions allowed under the mark-to-market provisions, as well as any gain or loss on the disposition of ordinary shares or ADSs with respect to which the mark-to-market election is made, is treated as ordinary income or loss (except that loss is treated as capital loss to the extent the loss exceeds the net mark-to-market gains, if any, that a U.S. Holder included in income with respect to such Ordinary Share or ADSs in prior years). Gain or loss from the disposition of ordinary shares or ADSs (as to which a "mark-to-market" election was made) in a year in which we are no longer a PFIC, will be capital gain or loss. Our ordinary shares or ADSs should be considered "marketable stock" if they traded at least 15 days during each calendar quarter of the relevant calendar year in more than de minimis quantities. Any such mark to market election would not be available for a lower-tier PFIC. Alternatively, a U.S. Holder making a valid and timely "qualified electing fund" or "QEF" election generally would not be subject to the default PFIC regime discussed above. Instead, for each PFIC year to which such an election applied, the electing U.S. Holder would be subject to U.S. federal income tax on the electing U.S. Holder's pro rata share of our net capital gain and ordinary earnings, regardless of whether such amounts were actually distributed to the electing U.S. Holder. Any gain on sale or other disposition of a U.S. Holder's ordinary shares or would be treated as capital, and the interest penalty will not be imposed. If an investor provides reasonable notice to us that it has determined to make a QEF election, we shall provide annual financial information to such investor as may be reasonably required for purposes of filing United States federal income tax returns in connection with such QEF election.

U.S. Holders are urged to consult their tax advisors about the PFIC rules, including the advisability, procedure and timing of making a mark-to-market election and the U.S. Holder's eligibility to file such an election (including whether our ordinary shares or ADSs are treated as "marketable stock" for such purpose). A U.S. Holder will be required to file Internal Revenue Service Form 8621 if such U.S. Holder owns our ordinary shares or ADSs in any year in which we are classified as a PFIC.

Information reporting and backup withholding

A U.S. Holder may be subject to information reporting to the IRS and possible backup withholding with respect to dividends paid on, or proceeds of the sale or other disposition of our ordinary shares or ADSs unless such U.S. Holder is a corporation or qualifies within certain other categories of exempt recipients or provides a taxpayer identification number and certifies as to no loss of exemption from backup withholding and otherwise complies with applicable requirements of the backup withholding rules. Amounts withheld under these rules may be credited against the U.S. Holder's U.S. federal income tax liability and a U.S. Holder may obtain a refund of any excess amounts withheld under the backup withholding rules by filing the appropriate IRS forms and furnishing any required information. A U.S. Holder who does not provide a correct taxpayer identification number may be subject to penalties imposed by the IRS.

A non-U.S. Holder generally will not be subject to information reporting or backup withholding with respect to dividends on our ordinary shares or ADSs, unless payment is made through a paying agent (or office) in the United States or through certain U.S.-related financial intermediaries. However, a Non-U.S. Holder generally may be subject to information reporting and backup withholding with respect to the payment within the United States of dividends on our ordinary shares or ADSs, unless such non-U.S. Holder provides a taxpayer identification number, certifies under penalties of perjury as to its foreign status, or otherwise establishes an exemption.

U.S. individuals (and, under proposed regulations, certain entities) that hold certain specified foreign financial assets, including stock in a foreign corporation, with values in excess of certain thresholds are required to file with their U.S. federal income tax return Form 8938, on which information about the assets, including their value, is provided. Taxpayers who fail to file the form when required are subject to penalties. An exemption from reporting applies to foreign assets held through certain financial institutions. Investors are encouraged to consult with their own tax advisors regarding the possible application of this disclosure requirement to their investment in our ordinary shares or ADSs.

Transfer of ADSs

No U.K. stamp duty will be payable on a written instrument transferring an ADS or on a written agreement to transfer an ADS provided that the instrument of transfer or the agreement to transfer is executed and remains at all times outside the United Kingdom. Where these conditions are not met, the transfer of, or agreement to transfer, an ADS could, depending on the circumstances, attract a charge to U.K. stamp duty at the rate of 0.5% of the value of the consideration given in connection with the transfer.

No SDRT will be payable in respect of an agreement to transfer an ADS.