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

For the month of: March 2023

Commission file number: 001-36288

AKARI THERAPEUTICS, PLC

(Translation of registrant's name into English)

75/76 Wimpole Street
London W1G 9RT
United Kingdom
(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 ☐

Akari Therapeutics Plc (the "Company") has updated certain business, risk factors, and other information which supplements information included in the Company's Annual Report on Form 20-F the fiscal year ended December 31, 2021, filed with the Securities and Exchange Commission (the "SEC") on May 16, 2022, as supplemented by the Company's subsequent filings with the SEC. The updated business, risk factors and other information is attached hereto as Exhibit 99.1 and incorporated by reference herein.

Exhibit 99.1 is hereby incorporated by reference into all effective registration statements filed by the Company under the Securities Act of 1933, as amended.

Exhibit No.	
99.1	Akari Therapeutics, Plc, Update

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/ Rachelle Jacques
Name: Rachelle Jacques
Title: President and Chief Executive Officer

Date: March 28, 2023

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 biotechnology company focused on developing advanced therapies for autoimmune and inflammatory diseases involving the complement (C5) and leukotriene (LTB4) pathways. Each of these pathways has scientifically well-supported causative roles in the diseases we are targeting. We believe that blocking early mediators of inflammation will prevent initiation and continual amplification of the processes that cause certain diseases. Our activities since inception have consisted of performing research and development activities and raising capital.

Our lead product candidate, nomacopan, is a recombinant small protein derived from a protein originally discovered in the saliva of the Ornithodoros moubata tick, which modulates the host immune system to allow the parasite to feed without alerting the host to its presence or provoking an immune response. Nomacopan is a second-generation complement inhibitor which 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 and specifically also inhibits leukotriene B4, or LTB4, activity, both elements that are often co-located as part of the immune/inflammatory response. The importance of nomacopan's dual inhibitory action is therefore twofold. First, it can prevent inflammatory and prothrombotic activities of two key pathways, and second, the pathways can be independently activated. Additionally, nomacopan's bio-physical properties allow it to be potentially used in a variety of formulations, including subcutaneous, intravenous, topical or inhaled routes of administration.

Nomacopan is a recombinant small protein (16,769 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.

Nomacopan has received orphan drug designation from the U.S. Food and Drug Administration, or the FDA, for use in HSCT-TMA and BP, and the European Medicines Agency, or the EMA, for PNH, GBS and BP (each as defined below). Orphan drug designation provides us with certain benefits and incentives, including a period of marketing exclusivity if marketing authorization 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 have received Fast Track designation from the FDA for the investigation of nomacopan for the treatment of pediatric HSCT-TMA and for the treatment of PNH in patients who have polymorphisms conferring Soliris® (eculizumab) resistance and the treatment of BP. 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 with Fast Track designation may also qualify for priority review to expedite the FDA review process, if relevant criteria are met.

Our clinical targets for nomacopan are auto-immune and inflammatory diseases where the inhibition of both C5 and LTB4 are implicated and we are currently focused on advancing nomacopan for the treatment of pediatric hematopoietic stem cell transplant-related thrombotic microangiopathy (HSCT-TMA). In November 2022, the FDA granted the Rare Pediatric Disease Designation to nomacopan for the treatment of pediatric HSCT-TMA. .Based on Type C guidance requested and received from the FDA, in February 2023, we announced that we are moving forward into design and planning for the pivotal Part B of the Phase 3 clinical trial of nomacopan for treatment of pediatric HSCT-TMA in pediatric patients between 2 years and <18 years of age. We also announced we have added a new pipeline program that will develop nomacopan as a potential treatment for adult HSCT-TMA, which will include a study that is supportive of the pediatric program. Study enrollment for the adult program is expected to begin in 2024. We additionally have a pre-clinical program of long-acting PAS-nomacopan in geographic atrophy (GA).

Recent Developments

September 2022 Financing

On September 12, 2022, we entered into a definitive agreement with healthcare-focused institutional investors and accredited investors alongside participation from certain existing investors, including the Akari Executive Chairman of the Board of Directors, Dr. Ray Prudo, providing for the issuance of an aggregate of 15,100,000 ADSs in a registered direct offering at $0.85 per ADS for aggregate gross proceeds of approximately $12.84 million, or the September 2022 Financing. The offering initially closed on September 14, 2022, and a second closing was held on September 16, 2022. In addition, we issued to the investors in the Private Placement that closed simultaneously with the September 2022 Financing (i) series A warrants exercisable to purchase up to 15,100,000 ADSs at an exercise price of $0.85 per ADS and (ii) series B warrants exercisable to purchase up to 15,100,000 ADSs at an exercise price of $0.85 per ADS. The series A warrants and series B warrants became exercisable immediately following the date of issuance and will expire two years following issuance, in the case of the series A warrants, and seven years following issuance, in the case of the series B warrants. We agreed to pay A.G.P./Alliance Global Partners a cash placement fee equal to 7% of the aggregate purchase price for the ADSs sold in the offering, expense reimbursement of up to $75,000 and a non-accountable expense allowance of $50,000. We paid an aggregate of $1,000,700 in placement agent fees and expenses.

Nasdaq Non-Compliance

On October 24, 2022, we were notified by Nasdaq that we were not in compliance with the minimum bid price requirements set forth in Nasdaq Listing Rule 5550(a)(2) for continued listing on the Nasdaq Capital Market, and in in accordance with the applicable Nasdaq rules, we were provided with a grace period, through April 24, 2023, to regain compliance with this rule. We can regain compliance, if at any time during this 180-day period, the closing bid price of our ADSs is at least $1.00 for a minimum of ten consecutive business days, in which case we will be provided with a written confirmation of compliance and this matter will be closed. In the event we do not regain compliance after the initial 180-day period, we may then be eligible for an additional time if we meet the continued listing requirement for market value of publicly held shares and all other initial listing standards for the Nasdaq Capital Market, with the exception of the bid price requirement, and will need to provide written notice of our intention to cure the deficiency during the second compliance period. If we cannot demonstrate compliance by the end of the second 180-day period, Nasdaq staff will notify us that our ADSs are subject to delisting. In addition, as a result of the expected accounting classification of the warrants issued in connection with our September 2022 registered direct offering as liabilities, we believe our shareholders' equity will fall below the $2,500,000 shareholders' equity requirement set forth in Nasdaq Listing Rule 5505(b)(1) for continued listing on the Nasdaq Capital Market as of December 31, 2022 and we expect that once we file our Annual Report on Form 20-F for the year ended December 31, 2022, which is required by April 30, 2023, we will receive a related notice of non-compliance from Nasdaq.

Appointment of Chief Medical Officer

In November 2022, we appointed John F. Neylan, III, MD, as Executive Vice President, Chief Medical Officer. Dr. Neylan has more than 20 years of experience in medical, clinical development, and R&D. Before joining Akari, he was Executive Vice President, Chief Medical Officer and Head of Research for Angion Biomedica Corporation, where he led the development of therapies for chronic fibrotic conditions of the lung and kidney, and acute organ injuries. Previously, he was Senior Vice President and Chief Medical Officer for Keryx Biopharmaceuticals and Senior Vice President, Clinical Development for Genzyme Corporation, where he headed up therapeutic development for specialty metabolic diseases including renal, cardiovascular, endocrine, and osteoarthritis indications. Dr. Neylan was the Vice President, Research & Development at Wyeth Research where he led development of transplant immunosuppressants, antivirals/antibacterials, antiarrhythmics, chemotherapeutics, and hemophilia factor replacements. He also served on multiple advisory committees for the FDA.

Ray Prudo Agreement

On March 1, 2023, we entered into an agreement with Ray Prudo, our former Executive Chairman. The agreement was affective as of January 1, 2023. Under the agreement, Dr. Prudo will hold office as Non-Executive Chairman and Class C Director for the remainder of his three-year term which began at our 2021 annual general meeting, and thereafter will seek reappointment in accordance with the Company's Articles of Association. Dr. Prudo's current annual director fee is $100,000.

Preliminary Financial Data for the Year ended December 31, 2022

Our consolidated financial statements for the year ended December 31, 2022 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, or compiled 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 is helpful to an investor's understanding of our operating performance.

Cash

As of December 31, 2022, we had cash of approximately $13 million.

NOTE REGARDING FORWARD-LOOKING STATEMENTS

This document contains forward-looking statements and readers are cautioned that our actual results may differ materially from those discussed in the forward-looking statements. All statements other than statements of historical facts contained in this document, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected market growth are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

Words such as "may," "anticipate," "estimate," "expects," "projects," "intends," "plans," "believes" and words and terms of similar substance used in connection with any discussion of future operating or financial performance, identify forward-looking statements. Forward-looking statements represent management's present judgment regarding future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially from those described in the forward-looking statements.

Such risks and uncertainties include, but are not limited to:

- our needs for additional capital to fund our operations;
- our ability to continue as a going concern;
- uncertainties of cash flows and inability to meet working capital needs;
- an inability or delay in obtaining required regulatory approvals for nomacopan and any other product candidates, which may result in unexpected cost expenditures;
- our ability to obtain orphan drug designation in additional indications;

- risks inherent in drug development in general;
- uncertainties in obtaining successful clinical results for nomacopan and any other product candidates and unexpected costs that may result therefrom;
- difficulties enrolling patients in our clinical trials;
- our ability to enter into collaborative, licensing, and other commercial relationships and on terms commercially reasonable to us;
- failure to realize any value of nomacopan and any other product candidates developed and being developed in light of inherent risks and difficulties involved in successfully bringing product candidates to market;
- inability to develop new product candidates and support existing product candidates;
- the approval by the FDA, MHRA and EMA and any other similar foreign regulatory authorities of other competing or superior products brought to market;
- risks resulting from unforeseen side effects;
- risk that the market for nomacopan may not be as large as expected;
- risks associated with the impact of the COVID-19 pandemic and the Russian invasion of Ukraine;
- inability to obtain, maintain and enforce patents and other intellectual property rights or the unexpected costs associated with such enforcement or litigation;
- inability to obtain and maintain commercial manufacturing arrangements with third party manufacturers or establish commercial scale manufacturing capabilities;
- the inability to timely source adequate supply of our active pharmaceutical ingredients from third party manufacturers on whom the Company depends; and
- unexpected cost increases and pricing pressures.

In light of these assumptions, risks and uncertainties, the results and events discussed in the forward-looking statements contained in this document might not occur. We are not under any obligation, and we expressly disclaim any obligation, to update or alter any forward-looking statements, whether as a result of new information, future events or otherwise. All subsequent forward-looking statements attributable to us or to any person acting on our behalf are expressly qualified in their entirety by the cautionary statements contained or referred to in this section.

You should read this document with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements whether as a result of new information, future events or otherwise, except as required by applicable law.

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 $17,424,237 and $17,081,617 for the years ended December 31, 2021 and 2020, respectively. In addition, our accumulated deficit as of December 31, 2021 and 2020 was $199,705,048 and $182,280,811, respectively. Losses have principally resulted from costs incurred for manufacturing, clinical trial and preclinical activities and general and administrative expenses. We have funded our operations primarily through the private placement and public offering of equity securities. As of June 30, 2022, we had cash of approximately $8.2 million and we believe we do not have sufficient funds to fund our operations for the next twelve months from the filing of these risk factors.

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 nomacopan or other future product candidates receive marketing authorization, sales and marketing activities.

Our failure to become and remain profitable could depress the market price of the American Depository Shares ("ADS") representing our ordinary shares, $0.0001 par value per share ("ordinary shares"), 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, 2022, we had cash of approximately $8.2 million. In September 2022, we raised gross proceeds of approximately $12.84 million in a registered direct offering. We believe we do not have sufficient funds to fund our operations for the next twelve months as of the filing of these risk factors. 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 is 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 nomacopan in hematopoietic stem cell transplant-associated thrombotic microangiopathy ("HSCT-TMA"), GA, 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 nomacopan for HSCT-TMA, geographic atrophy ("GA"), 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;
- the costs and timing of 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 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 delayed or unable to complete ongoing and planned clinical trials for nomacopan 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.

We will need to raise additional capital. In any financing transaction, we may sell ordinary shares or ADSs, convertible securities or other equity securities. To the extent that we raised additional funds by issuing equity securities, our shareholders may experience significant dilution. To the extent that we raise additional capital through the sale of equity or convertible debt securities by any other means, existing ownership interests will be diluted. The sale of a substantial number of ADSs, or anticipation of such sales, could cause the trading price of our ADSs to decline or make it more difficult for us to sell equity or equity-related securities in the future at a time and at a price that we might otherwise desire.

RISKS RELATED TO THE CLINICAL DEVELOPMENT AND MARKETING AUTHORIZATION OF OUR PRODUCT CANDIDATES

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

Nomacopan has been the primary focus of our product development. Successful continued development and ultimate marketing authorization of nomacopan for at least one indication 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 nomacopan. We will need to raise sufficient funds for, and successfully enroll and complete, our ongoing clinical development programs for nomacopan and for our planned clinical development programs for nomacopan in 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 nomacopan;
- we may not be able to obtain adequate evidence of efficacy and safety for nomacopan;
- we do not know the degree to which nomacopan will be adopted by the market, even if approved;
- in our clinical programs, we may experience difficulty in enrollment, adjustments to clinical trial protocols or the need for additional clinical trial sites, which could delay our clinical trial progress;
- our reliance on a sole manufacturer to supply drug substance and a sole manufacturer to provide drug product formulation of nomacopan that is being used in our clinical trials may negatively impact the availability of our drug product;

- we may encounter disruptions in the supply chain of nomacopan which could negatively impact our ability to supply our drug product to clinical trial sites, delaying clinical studies;

- the results of our clinical trials may not meet the level of statistical or clinical significance required by the FDA, MHRA, 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 nomacopan, which could delay or prevent further clinical development;

- the standards implemented by clinical or regulatory agencies may change at any time;

- the FDA, MHRA, EMA or foreign regulatory agencies may require efficacy endpoints for a clinical trial that differ from the endpoints of our current or future trials, which may require us to conduct additional clinical trials;

- the mechanism of action of nomacopan is complex and we do not know the degree to which it will translate into a medical benefit in certain indications; 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 biologics license application, or BLA, to the FDA, or a marketing authorization application, or MAA, to the EMA and even fewer are approved for commercialization. Furthermore, even if we do receive marketing authorization to market nomacopan, 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 that nomacopan will be successfully developed or commercialized. If we or any of our future development partners are unable to develop, or obtain marketing authorization for, or, if approved, successfully commercialize nomacopan, we may not be able to achieve forecasted revenues.

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, MHRA, EMA or other foreign regulatory agencies for nomacopan 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 HSCT-TMA and other diseases for each of our ongoing and planned clinical trials of nomacopan in these indications. To date, we have experienced delays in enrollment of patients in our clinical trials and supply chain issues due in particular to the COVID-19 pandemic for certain of our past clinical trials, including, without limitation, in our discontinued bullous pemphigoid ("BP") clinical program, and, in the case of enrollment delays, the fact that we are targeting a small patient population with a rare disease or indication.

Patient enrollment is affected by other factors, including:

- 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;
- actual or threatened public health emergencies and outbreaks of disease (including, for example, the COVID-19 outbreak);
- 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;
- number of specialist physicians that treat patients with these diseases;
- ability to identify and enroll such patients with a stage of disease appropriate for our ongoing or future clinical trials;
- the costs of finding and diagnosing patients;
- patient referral practices of physicians; and
- our ability to monitor patients adequately during and after treatment.

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 marketing authorization processes for nomacopan are prolonged, delayed or suspended, we may be unable to commercialize nomacopan 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 and may negatively impact our ability to obtain marketing authorization for, and to market and sell, a particular product candidate, including:

- conditions imposed on us by the FDA, MHRA, 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 or 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, MHRA, EMA or any other applicable foreign regulatory authority or the requirement of additional supportive studies by the FDA, MHRA, EMA or such foreign regulatory authority.

Public health epidemics or outbreaks could adversely impact our business. The situation surrounding the COVID-19 pandemic, including the mutation of variants, continues to remain fluid globally. The potential for a material impact on our business, financial condition and results of operation remains a risk. We cannot reasonably estimate with any degree of certainty any future impact of COVID-19. Pandemics such as this can adversely impact our business as a result of disruptions, such as travel bans, quarantines, staffing shortages, and interruptions to access the trial sites and supply chains, which could result in material delays and complications with respect to our research and development programs and clinical trials.

Moreover, as a result of COVID-19, there is an increased unease of conducting certain non-critical activities in medical centers. For example, while now open for enrollment, prior clinical trials have been halted or delayed due to COVID-19. 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 extent to which COVID-19 impacts operations will depend on future developments, including the scope of any new virus mutations and outbreaks, the nature of government public health guidelines and the public's adherence to those guidelines, the rate of individuals becoming fully vaccinated and the public's adherence to guidelines to receive booster vaccinations, and the extent to which new lockdowns may be needed or are required in particular countries, including China. In particular, the continued spread of COVID-19 globally could adversely impact our operations and workforce, including research and clinical trials and the ability to raise capital, could affect the operations of key governmental agencies, such as the FDA, which may delay the development of our product candidates, and could result in the inability of suppliers to deliver components or raw materials, including drug product and drug substance, on a timely basis or at all, each of which in turn could have an adverse impact on our business, financial condition and results of operation.

We may not receive a Priority Review Voucher (PRV) in connection with the development of nomacopan for the treatment of HSCT-TMA, which would permit priority review for a subsequent marketing application for a different product or may be sold to a third party.

In November 2022, the U.S. Food and Drug Administration (FDA) has granted the Rare Pediatric Disease Designation to nomacopan for the treatment of pediatric hematopoietic stem cell transplant-related thrombotic microangiopathy (HSCT-TMA). The FDA Rare Pediatric Disease Designation and Voucher Program is a recognition of the significant need that exists for approved treatments in rare pediatric diseases and is intended to encourage development of these treatments. Under this program, a sponsor who receives an approval of a new drug application (NDA) or biologics license application (BLA) for a rare pediatric disease may be eligible for a Priority Review Voucher (PRV), which is received concurrently with marketing approval. A PRV is valuable because it can be redeemed to obtain priority review for a subsequent marketing application for a different product or may be sold to a third party. However, there can be no assurance that we will receive marketing approval for nomacopan for the treatment of HSCT-TMA, and thereby receive a PRV that permits priority review of other product candidates, or if the PRV program will still exist at such time.

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

Nomacopan may fail to show the desired safety and efficacy at any phase in the clinical development programs. 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. If nomacopan does not demonstrate adequate 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. If further studies or trials are initiated, earlier preclinical studies or clinical trials may not predict the scope and phase of further trials, that these further studies or trials 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 marketing authorizations or to commercialize products. Results of clinical trials could be inconclusive, requiring additional or repeat trials. Data obtained from preclinical studies and clinical trials is subject to varying interpretations that could delay, limit or prevent marketing authorization. If the results achieved in our clinical trials are insufficient to proceed to further trials or to marketing authorization of our product candidates, we could be materially adversely affected. Failure of a clinical trial to achieve its pre-specified primary endpoint generally may require us to undertake additional studies or trials if we determine to continue development of the product candidate, may reduce the timely development of and marketing authorization to market the product candidate, and may decrease the chances for successfully achieving the primary endpoint in scientifically similar indications.

Long-term animal toxicity and long-term human safety studies of nomacopan could demonstrate that the administration of nomacopan results in serious adverse events.

While we have conducted toxicity studies in certain animals with no observed adverse effect at the highest dose tested, we intend to conduct further long-term animal toxicity studies, including reproductive and carcinogenicity studies, and will continue to collect safety data from ongoing and future clinical studies. Such studies may show that nomacopan results in serious adverse events or other adverse results. If animal toxicity and human safety studies do not yield favorable results, we may be required to abandon our development of nomacopan, which could have a material adverse effect on our financial condition, including our ability to generate forecasted revenues.

Chronic dosing of patients with nomacopan 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 nomacopan 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 side effect of nomacopan that has occurred in patients receiving currently marketed C5 inhibitors and C3 inhibitors is an increased incidence of meningitis. As a result, we expect that patients receiving nomacopan may also require meningitis immunization and prophylactic antibiotics as indicated.

Nomacopan has a secondary binding site that sequesters leukotriene B4, or LTB4. LTB4 synthesis from arachidonic acid can be induced by a variety of triggers including terminal complement activation. LTB4 is a pro-inflammatory mediator that attracts and activates white blood cells at the area of inflammation. LTB4 inhibition may lead to positive anti-inflammatory benefits, but like other drugs with immune modulating properties may increase the risk of infection. However, a particular risk of infection associated with inhibition of LTB4 has not been identified and the only marketed drug which inhibits leukotrienes including LTB4, does not carry a warning of elevated infection risk on its label.

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 nomacopan, which would have a material adverse effect on our financial condition and results of operation.

If nomacopan is not convenient for patients to use, then we might be prevented from successful commercialization.

Nomacopan may require cold storage prior to use and will likely require self-injection for certain indications. 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 not achieve forecasts. In addition, if nomacopan 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 nomacopan has not yet received marketing authorization, it is difficult to predict the time and cost of development and our ability to successfully complete clinical development and obtain the necessary marketing authorizations for commercialization.

Nomacopan has not yet received marketing authorization for the treatment of any indications, and unexpected problems may arise that could cause us to delay, suspend or terminate our development efforts. To date, only a limited number of patients have been enrolled in our clinical trials. Larger scale trials will be required to obtain marketing authorization and the efficacy or non-efficacy of nomacopan will ultimately be determined by the applicable regulatory agencies. The long-term safety consequences of inhibition of C5 and/or LTB4 with nomacopan is not known. Marketing authorization of product candidates such as nomacopan can be more expensive and take longer than approval with previously approved products.

We have obtained orphan drug designation for nomacopan in the United States for the use in BP and HSCT-TMA, and in the EU for GBS, PNH, and BP, but we may be unable to maintain the benefits associated with orphan drug designation, 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 nomacopan in Guillain-Barré syndrome ("GBS"), HSCT-TMA, paroxysmal nocturnal hemoglobinuria ("PNH") and BP and may in the future seek orphan product designation for nomacopan in further indications, we may never receive such additional designations and we are not currently pursuing a clinical development program targeting BP, GBS or PNH.

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 biologics license application, or 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 nomacopan 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 biological 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.

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; (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 orphan drug designation does not mean that marketing approval will be granted.

We have obtained fast track designation from the FDA for the treatment of HSCT-TMA, and may seek such designation in other indications. 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 may not result in nomacopan or any other product candidates receiving marketing approval.

In addition to the fast track designation we have received for HSCT-TMA, we may seek a breakthrough therapy or fast track designation for nomacopan in other indications. 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 nomacopan 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 nomacopan 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 nomacopan, we or our partners may never obtain approval or commercialize our product candidates outside of the United States and, conversely, even if we obtain marketing authorization of nomacopan 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 regarding clinical trial design, safety and efficacy. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and marketing authorization in one country does not mean that marketing authorization 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 marketing authorizations in other countries could result in significant delays, difficulties and costs for us, and may require additional preclinical studies or clinical trials, which could be costly and time consuming and could delay or prevent introduction of nomacopan in those countries. We rely on contract research organizations to run our clinical trials and on regulatory consultants for experience in obtaining marketing authorization in international markets. If we or our partners fail to comply with regulatory requirements or to obtain and maintain required approvals, our target market may be reduced and our ability to realize the forecasted revenues of nomacopan may 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 United Kingdom, or U.K., European Union, or EU, regulations, to provide accurate information to the UK, 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 organization 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 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 programs 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 General Data Protection Regulation (EU) 2016/679, or GDPR, lays down the legal framework for data protection and privacy. The GDPR applies directly in EU Member States and applies to companies with an establishment in the EEA and to certain other companies not in the EEA that offer or provide goods or services to individuals located in the EEA or monitor the behavior of individuals located in the EEA. Since January 1, 2021, the UK is not part of the EU. In the UK, the GDPR has been converted into UK domestic law, pursuant to the Data Protection, Privacy and Electronic Communications (Amendments etc) (EU Exit) Regulations 2019 (as amended), which makes some minor technical amendments to ensure the GDPR is operable in the UK (UK GDPR). The UK GDPR is also supplemented by the Data Protection Act 2018. UK and EU data protection law is therefore aligned. The GDPR and UK GDPR implement stringent operational requirements for controllers of personal data, including, for example, expanded disclosures about how personal information is to be used, limitations on retention of information, increased requirements pertaining to health data and pseudonymized (i.e., key-coded) data, increased cyber security requirements, mandatory data breach notification requirements and higher standards for controllers to demonstrate that they have obtained a valid legal basis for certain data processing activities. The activities of data processors are being regulated for the first time, and require companies undertaking processing activities to offer certain guarantees in relation to the security of such processing and the handling of personal data. Contracts with data processors will also need to be updated to include certain terms prescribed by the GDPR, and negotiating such updates may not be fully successful in all cases. The GDPR provides that EU Member States may make their own further laws and regulations in relation to the processing of genetic, biometric or health data, which could result in differences between Member States, limit our ability to use and share personal data or could cause our costs to increase, and harm our business and financial condition. We are also subject to evolving and strict rules on the transfer of personal data out of the EU and UK to the United States, under both the GDPR and the UK GDPR. Under the GDPR personal data cannot be transferred to a third country (i.e. outside of the EEA or UK, as applicable) unless certain safeguards are in place. These include, for example, where the transfer is to a country that the EU Commission has deemed "adequate" or where EU standard contractual clauses have been implemented. Further prospective revision of the Directive on privacy and electronic communications (Directive 2002/58/EC), or ePrivacy Directive, may affect our marketing communications. Failure to comply with EU laws, including failure under the GDPR and UK GDPR, Data Protection Act 2018, ePrivacy Directive and other laws relating to the security of personal data may result in fines up to €20,000,000 (or £17,500,000 under the UK GDPR) or up to 4% of the total worldwide annual turnover of the preceding financial year, if greater, and other administrative penalties including criminal liability, which may be onerous and adversely affect our business, financial condition, results of operations and prospects. Failure to comply with the GDPR and related laws may also give risk to increase risk of private actions from data subjects and consumer not-for-profit organizations, including a new form of class action that is available under the GDPR. Compliance with the GDPR and UK GDPR requires a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to the aforementioned fines and penalties, litigation, and reputational harm in connection with any European activities.

The UK is treated as a third country (for the purposes of data transfers). On June 28, 2021, the EU Commission published two adequacy decisions in respect of transfers under EU GDPR and the Law Enforcement Directive stating that the UK provides adequate protection for personal data transferred from the EU to the UK under EU GDPR. The adequacy decision is expected to last until June 27, 2025 but may end earlier, for example if an EU data subject or EU data protection authority challenges the adequacy decisions. In such a case, the Court of Justice of the European Union would need to determine whether the UK provides essentially equivalent protection.

The UK government has confirmed that the EEA is adequate, and so all transfers of personal data from the UK to the EEA will continue to be unrestricted after July 1, 2021.

The UK has issued a consultation with respect to future changes to data protection law. There is risk that in the event UK and EU data protection law diverges, that the adequacy decisions may come to an end. If this occurs, there will be cost implication due to dual compliance requirements and costs with respect to to international data transfers.

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 in part 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 competitive advantage. We have issued composition-of-matter patents in the United States and other countries for nomacopan, but we cannot be certain that the claims in our issued patents will not be found invalid or unenforceable if challenged. We cannot be certain that the claims in any patent applications covering our product candidates that are pending, or that we may file, 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 patents will not be found invalid or unenforceable if challenged. Even if any patent applications that we may file relating to specific formulations of our product candidates issue as patents, 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 patent may not be enforced against competitors making and marketing a product that has the same active pharmaceutical ingredient for use in a method not claimed by 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 may be difficult to prevent or prosecute. Also, as is the case for composition-of-matter patents, we cannot be certain that the claims in our issued method-of-use patents will not be found invalid or unenforceable if challenged. We cannot be certain that the claims in any patent applications covering methods of using our product candidates that are pending, or that we may file, 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 method-of-use patents will not be found invalid or unenforceable if challenged.

Our issued patents for nomacopan and its uses are expected to expire between 2024 and 2035 (excluding any patent term adjustment or potential patent term extension). Our pending patent applications for nomacopan and its uses, if issued, are expected to expire at various times that range from 2024 to 2040 (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;

- patents have a finite term and thus may expire before the technologies they protect are approved or marketed and thus may not provide any competitive advantage. For example, issued composition-of-matter patents for the nomacopan product will expire in 2024 (excluding any patent term adjustment or extension);

- 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;

- 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; and

- some countries in Europe and China have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we, or any of our licensors, are forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired and our business, financial condition and results of operations may be adversely affected.

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. Enforcing a claim that a third party obtained illegally and is using trade secrets and/or proprietary know-how is expensive, time consuming and unpredictable. The enforceability of confidentiality agreements may vary from jurisdiction to jurisdiction. 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.

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

As is the case with other biopharmaceutical companies, our success if heavily dependent on intellectual property, particularly patents. Obtaining and exploiting patents in the biopharmaceutical industry involve both technological and legal complexity. Therefore, obtaining and exploiting biopharmaceutical patents is costly, time-consuming and inherently uncertain. For example, the U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. These rulings have created uncertainty with respect to the validity and enforceability of patents, even once obtained. Depending on future actions and decisions by the U.S. Congress, the federal courts, and the U.S. Patent and Trademark Office, the laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain new patents or to enforce our existing patents and patents that we may obtain in the future.

RISKS RELATED TO OUR BUSINESS OPERATIONS

We currently have no marketing, sales or distribution infrastructure with respect to nomacopan. If we are unable to develop our sales, marketing and distribution capability on our own or through collaborations with partners, we may not be successful in commercializing any approved drugs.

We currently have no marketing, sales or distribution capabilities. If our product candidate nomacopan is approved, we intend either to establish a sales and marketing organization with technical expertise and supporting distribution capabilities to commercialize nomacopan, or to outsource this function to a third party. Either of these options could be expensive and time consuming. Some of these costs may be incurred in advance of any approval of nomacopan. In addition, we may not be able to hire a commercial team in the United States or other target market that is sufficient in size or has adequate expertise in the medical institutions that we intend to target. Any failure or delay in the development of our or third parties' internal sales, marketing and distribution capabilities could adversely impact the commercialization of nomacopan and/or other future product candidates, if and when approved by the FDA.

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 capabilities. Any future product revenue may be lower than if we directly marketed or sold our 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. If we are unable to enter into these arrangements on acceptable terms or at all, we may not be able to successfully commercialize our approved products. If we are not successful in commercializing our approved products, our future product revenue will suffer and we may incur significant losses.

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

As of December 31, 2022, we had 15 employees. Our limited financial resources have led us to focus on the development of nomacopan and to manage and operate our business in a highly efficient manner. We cannot make assurances that we will be able to hire and/or retain adequate staffing levels to develop nomacopan or run our operations and/or to accomplish all of the objectives that we otherwise would seek to accomplish.

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 marketing authorization and in manufacturing and marketing biologic products. Our competitors may succeed in obtaining marketing authorization 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. Our competitors may succeed in developing products that are more effective 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, which could materially adversely affect our business.

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

The Biologics Price Competition and Innovation Act, or BPCIA, was enacted in 2010, creating an abbreviated approval pathway for biosimilar products, referred to as the "351(k) pathway." A biosimilar application must contain information demonstrating: (1) biosimilarity to the reference product through data derived from analytical studies, animal studies (including an assessment of toxicity), and clinical studies (including an assessment of immunogenicity and pharmacokinetics or pharmacodynamics), unless the FDA determines that such data are unnecessary, (2) sameness of strength, dosage form, and route of administration to the reference product as well as sameness of mechanism of action (to the extent known), (3) approval of the reference product for the conditions of use prescribed, recommended, or suggested in the labeling indications proposed for the biosimilar product, and (4) appropriate manufacturing, processing, packing, and holding facilities that meet the standards designed to ensure a safe, pure and potent medicine. Unless the FDA waives the requirement, clinical studies must be sufficient to show the safety, purity and potency of the proposed product for one or more "appropriate" conditions of use for which licensure is sought and for which the reference product is licensed.

If physicians and patients do not adopt our future products or if the market size for indications for which any product candidate is approved is smaller than expected, we may be unable to achieve forecasted revenues, if any.

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

- timing of market introduction of competitive products;
- demonstration of clinical safety and efficacy;
- 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;
- availability of alternative treatments in clinical trials;
- understanding of the drug;
- other potential advantages of alternative treatment methods; and
- ineffective marketing and distribution capabilities.

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 achieve forecasted revenues, if any.

Our business either directly or indirectly through critical suppliers may be adversely affected by the impact of COVID-19.

Public health epidemics or outbreaks could adversely impact our business. The situation surrounding the COVID-19 pandemic, including the mutation of variants, continues to remain fluid globally. The potential for a material impact on our business, financial condition and results of operation remains a risk if there is a resurgence of COVID-19. While the COVID-19 pandemic has subsided with the normalization of living with COVID-19 following the increase in accessibility to COVID-19 vaccines and antiviral treatments, we cannot reasonably estimate with any degree of certainty any future impact of a resurgence of COVID-19. Pandemics such as this can adversely impact our business as a result of disruptions, such as travel bans, quarantines, staffing shortages, and interruptions to access the trial sites and supply chains, which could result in material delays and complications with respect to our research and development programs and clinical trials.

Moreover, as a result of COVID-19, there is a general unease of conducting certain non-critical activities in medical centers. For example, while now open for enrollment, prior clinical trials have been halted or delayed due to COVID-19. The extent to which COVID-19 impacts operations will depend on future developments, including the scope of any new virus mutations and outbreaks, the nature of government public health guidelines and the public's adherence to those guidelines, the rate of individuals becoming fully vaccinated and the public's adherence to guidelines to receive booster vaccinations, and the extent to which new lockdowns may be needed or are required in particular countries, including China. In particular, if there is a resurgence COVID-19 globally, this could adversely impact our operations and workforce, including research and clinical trials and the ability to raise capital, could affect the operations of key governmental agencies, such as the FDA, which may delay the development of our product candidates, and could result in the inability of suppliers to deliver components or raw materials, including drug product and drug substance, on a timely basis or at all, each of which in turn could have an adverse impact on our business, financial condition and results of operation.

The uncertainty associated with biologics 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 approved drugs, if any. 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 is particularly uncertain, and failure to obtain or maintain adequate coverage and reimbursement for nomacopan 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 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. We may 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 Former President Trump have expressed their intentions to repeal or repeal and replace the PPACA. Former 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. In November 2020, Joseph Biden was elected President and, in January 2021, the Democratic Party obtained control of the Senate. As a result of these electoral developments, it is unlikely that continued legislative efforts will be pursued to repeal PPACA. Instead, it is possible that legislation will be pursued to enhance or reform PPACA. We are not able to state with certainty what the impact of potential legislation will be on our business.

In December 2020, the Department of Health and Human Services has published a final regulation that may significantly restrict the availability of certain regulatory safe harbors under the federal Anti-Kickback Statute, effective January 1, 2022, that are used to facilitate certain types of transactions between manufacturers and pharmacy benefits managers that play a significant role in the pharmaceutical distribution chain. These changes to the Discount Safe Harbors available under the Anti-Kickback Statute would reduce some of the protections currently available to manufacturers that pay negotiated rebates to pharmacy benefits managers in exchange for these "PBMs" agreeing to include drugs and biologics on the formularies of the PBM's downstream customers, primarily the health plans that insure patients for both private commercial plans and government-sponsored plans. The Pharmaceutical Care Management Association has filed a lawsuit challenging this rule under the Administrative and Procedures Act. Should the regulation go into effect in 2022, it could have an impact on both our commercial supply arrangements with health plans and our supply arrangements to health plans that serve beneficiaries of federal health care programs such as Medicare Part D.

On January 5, 2017, the Health Resources and Services Administration (HRSA) at the U.S. Department of Health and Human Services (HHS) issued a final rule implementing Civil Monetary Penalties for manufacturers who knowingly and intentionally charge a covered entity more than the 340B ceiling price for a covered outpatient drug, as well as providing clarity as to the calculation of the 340B ceiling price. The final rule became effective on January 1, 2019. Since the final rule became effective, the HRSA has audited a number of manufacturers and concluded that they violated the 340B ceiling price requirement in some instances, suggesting that manufacturers are now at a higher risk of enforcement action for ceiling price noncompliance.

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

We face an inherent risk of product liability lawsuits related to the testing of our product candidates in seriously ill patients and may 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 any approved drugs.

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 any approved drugs. 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, investor relations 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 may be required to 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. With respect to investor relations agreements, we may indemnify the counterparty for losses resulting from our negligence or our supply of inaccurate information.

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 or security breaches.

Despite the implementation of security measures, our internal computer systems, and those of our contract research organizations, or CROs and other third parties on which we rely, are vulnerable to damage from computer viruses, unauthorized access, cyber-attacks, natural disasters, fire, terrorism, war, and telecommunication and electrical failures. If such an event were to occur and interrupt our operations, it could result in a material disruption of our drug development programs. For example, the loss of clinical trial data from ongoing or planned clinical trials could result in delays in our marketing authorization 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, loss of trade secrets or inappropriate disclosure of confidential or proprietary information, including protected health information or personal data of employees or former employees, access to our clinical data, or disruption of the manufacturing process, we could incur liability and the further development of our drug candidates could be delayed. We may also be vulnerable to cyber-attacks by hackers or other malfeasance. This type of breach of our cybersecurity may compromise our confidential information and/or our financial information and adversely affect our business or result in legal proceedings. If security breaches result in the loss of clinical trial data or other confidential information, we may be the subject of legal proceedings and suffer financial and reputational damage. Further, these cybersecurity breaches may inflict reputational harm upon us that may result in decreased market value and erode public trust.

During the preparation of our 2020 Form 20-F, we identified certain misstatements to our previously issued financial statements and previously restated certain of our consolidated financial statements. If we discover errors in our financial statements and are required to restate in the future, it could create additional risks and uncertainties that may have a material adverse effect on our business, financial position and results of operations.

In our Annual Report on Form 20-F for the year ended December 31, 2020, we discovered an error in our accounting treatment of certain options from 2015 that should have been accounted for as an equity instrument as opposed to a liability. Accordingly, we concluded that the financial statements contained in our Annual Reports on Form 20-F for the years ended December 31, 2015 through 2019, as well as the interim condensed consolidated financial statements contained in the quarterly reports on Form 6-K for each quarter within these years, as well as the quarterly periods ended March 31, 2020, June 2020 and September 2020, should be restated and therefore not relied upon. This was non-cash restatement and the options did not constitute a legal liability to us and will not affect our financial statements upon settlement.

As a result of these errors and the restatement, we became subject to a number of additional risks and uncertainties and unanticipated costs for accounting, legal and other fees and expenses. We may become subject to legal proceedings brought by regulatory or governmental authorities, or subject to other legal proceedings, as a result of the errors or the related restatement, which could result in a loss of investor confidence and other reputational harm, the loss of key employees, additional legal and other costs. Any of the foregoing impacts, individually or in aggregate, may have a material adverse effect on our business, financial position and results of operations.

We or the third parties upon whom we depend may be adversely affected by natural disasters and/or health epidemics and pandemics, and our business continuity and disaster recovery plans may not adequately protect us from natural disasters and/or health epidemics and pandemics.

Natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition and prospects. If a natural disaster, power outage, health epidemics or other event occurred that prevented us from using all or a significant portion of our office, that damaged critical infrastructure, such as the manufacturing facilities of our third-party contract manufacturers, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. As the global supply chain continues to see disruptions, there is higher risk for continued labor shortages, reduced labor capacity at supplier and third-party manufacturers, increased raw material costs and delays in production of our clinical product and clinical trials that will adversely impact our business. The extent to which the global supply chain disruptions may continue to impact our results of operations, including the long-term nature of the impact, depends on numerous evolving factors, which are highly uncertain and difficult to predict.

Public health pandemics, epidemics or outbreaks could adversely impact our business. The situation surrounding the COVID-19 pandemic, including the mutation of variants, continues to remain fluid. The potential for a material impact on our business, financial condition and results of operation remains a risk. We cannot reasonably estimate with any degree of certainty any future impact of COVID-19. Pandemics such as this can adversely impact our business as a result of disruptions, such as travel bans, quarantines, staffing shortages, and interruptions to access the trial sites and supply chains, which could result in material delays and complications with respect to our research and development programs and clinical trials.

Moreover, as a result of COVID-19, there is a general unease of conducting certain non-critical activities in medical centers. For example, while now open for enrollment, prior clinical trials have been halted or delayed due to COVID-19. The extent to which COVID-19 impacts operations will depend on future developments, including the scope of any new virus mutations and outbreaks, the nature of government public health guidelines and the public's adherence to those guidelines, the rate of individuals becoming fully vaccinated and the public's adherence to guidelines to receive booster vaccinations, and the extent to which new lockdowns may be needed or are required in particular countries, including China. In particular, the continued spread of COVID-19 globally could adversely impact our operations and workforce, including research and clinical trials and the ability to raise capital, could affect the operations of key governmental agencies, such as the FDA, which may delay the development of our product candidates, and could result in the inability of suppliers to deliver components or raw materials, including drug product and drug substance, on a timely basis or at all, each of which in turn could have an adverse impact on our business, financial condition and results of operation.

If we fail to develop and commercialize other product candidates, we may be unable to generate revenues.

Although the development and commercialization of nomacopan is our primary focus, as part of our longer-term growth strategy, we may 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, orphan or other disorders with high unmet medical needs and limited treatment options. These other product candidates may require additional, time-consuming development efforts prior to commercial sale, including preclinical studies, clinical trials and approval by the FDA, MHRA, 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 commercially available alternatives.

Our business could suffer if we are unable to attract and retain key employees.

Our success depends upon the continued service and performance of our senior management and other key personnel. The loss of the services of these personnel could delay or prevent the successful completion of our planned clinical trials or the commercialization of our therapeutic candidates or otherwise affect our ability to manage our company effectively and to carry out our business plan. We do not maintain key-man life insurance. Although we have entered into employment agreements with all of the members of our senior management team, members of our senior management team may resign at any time. High demand exists for senior management and other key personnel in the biopharmaceutical industry. There can be no assurance that we will be able to continue to retain and attract such personnel.

Our growth and success also depend on our ability to attract and retain additional highly qualified scientific, clinical, technical, sales, managerial and finance personnel. We experience intense competition for qualified personnel, and the existence of non-competition agreements between prospective employees and their former employers may prevent us from hiring those individuals or subject us to suit from their former employers. In addition, if we elect to independently commercialize any approved drug, we will need to expand our marketing and sales capabilities. While we attempt to provide competitive compensation packages to attract and retain key personnel, many of our competitors are likely to have greater resources and more experience than we have, making it difficult for us to compete successfully for key personnel. If we cannot attract and retain sufficiently qualified technical employees on acceptable terms, we may not be able to develop and commercialize competitive products. Further, any failure to effectively integrate new personnel could prevent us from successfully growing our company.

Class action lawsuits against us could lead to adverse outcomes.

We have in the past been, and may in the future become subject to class action litigation. 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 concerning the Phase II PNH trial of nomacopan and a report issued on April 26, 2017 titled "Akari's Coversin matches Soliris® in Phase II", or the Edison Report, by Edison Investment Research Ltd, or Edison, 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, a former Chief Executive Officer and our former Chief Financial Officer. These actions were consolidated, and plaintiffs amended their pleadings to include our Executive Chairman and Edison as defendants. On June 8, 2018, the parties entered into a memorandum of understanding to settle plaintiffs' claims for a total payment of $2.7 million in cash. On July 26, 2018, plaintiffs filed a notice with the Court voluntarily dismissing Edison from the action. On August 3, 2018, the remaining parties executed and filed a stipulation and agreement of settlement (the terms of which were consistent with the memorandum of understanding). On August 7, 2018, the Court granted plaintiffs' motion for preliminary approval of the settlement, and on November 28, 2018, following a hearing with the parties, the court ordered final approval of the settlement. Plaintiffs subsequently moved to distribute the settlement funds to the class, and the Court granted plaintiffs' motion on February 4, 2019. Separately, Edison Investment Research Ltd. sought indemnification from us including reimbursement of all legal expenses that Edison incurs in connection with the securities class action (to which, as discussed above, Edison was added as a defendant) and lost profits from customer relationships that Edison claims it lost as a result of the retraction of the Edison Report. The parties have finalized and consummated a settlement and the settlement payment has been made. If we become subject to any future class action litigation, we could incur substantial costs not covered by our liability insurance, suffer a significant adverse impact on our reputation and this could divert management's attention and resources from other priorities, any of which could have a material adverse effect on our business. In addition, any of these matters could require payments that are not covered by, or exceed the limits of, our available liability insurance, which could have a material adverse effect on our business, financial condition and results of operation.

Environmental, social and corporate governance (ESG) issues, including those related to climate change and sustainability, may have an adverse effect on our business, financial condition and results of operations and damage our reputation.

There is an increasing focus from certain investors, customers, consumers, employees and other stakeholders concerning ESG matters. Additionally, public interest and legislative pressure related to public companies' ESG practices continue to grow. If our ESG practices fail to meet regulatory requirements or investor, customer, consumer, employee or other stakeholders' evolving expectations and standards for responsible corporate citizenship in areas including environmental stewardship, support for local communities, board of director and employee diversity, human capital management, employee health and safety practices, product quality, supply chain management, corporate governance and transparency, our reputation, brand and employee retention may be negatively impacted, and our customers and suppliers may be unwilling to continue to do business with us.

Customers, consumers, investors and other stakeholders are increasingly focusing on environmental issues, including climate change, energy and water use, plastic waste and other sustainability concerns. Concern over climate change may result in new or increased legal and regulatory requirements to reduce or mitigate impacts to the environment. Changing customer and consumer preferences or increased regulatory requirements may result in increased demands or requirements regarding plastics and packaging materials, including single-use and non-recyclable plastic products and packaging, other components of our products and their environmental impact on sustainability, or increased customer and consumer concerns or perceptions (whether accurate or inaccurate) regarding the effects of substances present in certain of our products. Complying with these demands or requirements could cause us to incur additional manufacturing, operating or product development costs.

If we do not adapt to or comply with new regulations, including the SEC's published proposed rules that would require companies to provide significantly expanded climate-related disclosures in their periodic reporting, which may require us to incur significant additional costs to comply and impose increased oversight obligations on our management and board of directors, or fail to meet evolving investor, industry or stakeholder expectations and concerns regarding ESG issues, investors may reconsider their capital investment in our Company, we may become subject to penalties, and customers and consumers may choose to stop purchasing our products, if approved for commercialization, which could have a material adverse effect on our reputation, business or financial condition.

RISKS RELATED TO OUR RELIANCE ON THIRD PARTIES

We seek to partner with third-party collaborators with respect to aspects of the development and commercialization of our product candidates and we may not succeed in establishing and maintaining collaborative relationships, which may significantly limit our ability to develop and commercialize our product candidates successfully, if at all.

Our business strategy relies in part on partnering with pharmaceutical companies to supplement our internal development efforts. If we are not able to enter into collaboration arrangements, we may be required to undertake and fund further development, clinical trials, manufacturing and commercialization activities solely at our own expense and risk. If we are unable to finance and/or successfully execute those activities, or we delay such activities due to capital availability, our business could be materially and adversely affected, and potential future product launches could be materially delayed, be less successful, or we may be forced to discontinue clinical development of product candidates.

The process of establishing and maintaining collaborative relationships is difficult, time-consuming and involves significant uncertainty, including if a collaboration partner:

- may shift its priorities and resources away from our product candidates due to a change in business strategies, or a merger, acquisition, sale or downsizing;
- may seek to renegotiate or terminate their relationships with us due to unsatisfactory clinical results, manufacturing issues, a change in business strategy, a change of control or other reasons;
- may cease development in therapeutic areas which are the subject of our strategic collaboration;
- may not devote sufficient capital or resources towards our product candidates;
- may change the success criteria for a drug candidate thereby delaying or ceasing development of such candidate;
- experiences significant delays in initiating certain development activities, which will also delay payment of milestones tied to such activities, thereby impacting our ability to fund our own activities;
- develops a product that competes, either directly or indirectly, with our drug candidate;

- may not commit sufficient financial or human resources to the marketing, distribution or sale of our product;
- may encounter regulatory, resource or quality issues and be unable to meet demand requirements;
- may exercise a contractual right to terminate a strategic alliance;
- and us have a dispute arise concerning the research, development or commercialization of a drug candidate resulting in a delay in milestones, royalty payments or termination of an alliance and possibly resulting in costly litigation or arbitration which may divert management attention and resources; and
- may use our products or technology in such a way as to invite litigation from a third party.

If any collaborator fails to fulfill its responsibilities in a timely manner, or at all, our research, clinical development, manufacturing or commercialization efforts related to that collaboration could be delayed or terminated, or it may be necessary for us to assume responsibility for expenses or activities that would otherwise have been the responsibility of our collaborator. If we are unable to establish and maintain collaborative relationships on acceptable terms or to successfully transition terminated collaborative agreements, we may have to delay or discontinue further development of one or more of our product candidates, undertake development and commercialization activities at our own expense or find sources of additional capital.

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 marketing authorization for or commercialize our product candidates.

We use and heavily rely on third-party contract research organizations 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 FDA's, MHRA's and/or EMA's requirements and its general investigational plan and protocol.

The FDA, MHRA and EMA require us and our contract research organizations 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 nomacopan that is being used in our clinical trials. Although we believe that there are several potential alternative manufacturers who could manufacture nomacopan, 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 nomacopan 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, which may result in delays or inadequate supply of product;
- limitations on supply availability resulting from capacity and scheduling constraints of third-parties;
- limitation on supply availability due to difficulties in sourcing raw materials;
- the possible breach of manufacturing agreements by third-parties because of factors beyond our control;
- the possible termination or non-renewal of the manufacturing agreements by the third-party, at a time that is costly or inconvenient to us; and
- delays associated with the lack of availability of staff at third-party manufacturers.

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 marketing authorization 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, MHRA 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 FDA, MHRA, 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.

Moreover, the manufacturing of therapeutic biologics products is highly complex. Problems may arise during manufacturing for a variety of reasons, including but not limited to:

- equipment malfunction;
- failure to follow specific protocols and procedures;
- changes in product specification;
- low quality or insufficient supply of raw materials;
- delays in the construction of new facilities or the expansion of our existing manufacturing facilities as a result of changes in manufacturing production sites and limits to manufacturing capacity due to regulatory requirements;
- staffing shortages;

- advances in manufacturing techniques;
- physical limitations that could inhibit continuous supply; and
- man-made or natural disasters and other environmental factors.

Products with quality issues may have to be discarded, resulting in product shortages or additional expenses. This could lead to, among other things, increased costs, lost revenue, damage to customer relationships, time and expense spent investigating the cause and, depending on the cause, similar losses with respect to other batches or products. If problems are not discovered before the product is released to the market, recall and product liability costs may also be incurred.

Manufacturing methods and formulation are sometimes altered through the development of drug candidates from clinical trials to approval, and further to commercialization, in an effort to optimize manufacturing processes and results. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could cause the drug candidates to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the altered materials. This could delay the commercialization of any approved drugs and require bridging studies or the repetition of one or more clinical trials, which may result in increases in clinical trial costs, delays in drug approvals and may jeopardize our ability to commence product sales and generate revenue.

We may also experience shortages of qualified personnel, raw materials or key contractors, and experience unexpected damage to our facilities or the equipment in them. In these cases, we may be required to delay or suspend our manufacturing activities. We may be unable to secure temporary, alternative manufacturers for our drugs with the terms, quality and costs acceptable to us, or at all. Such an event could delay our clinical trials and/or the availability of our products for commercial sale. Moreover, we may spend significant time and costs to remedy these deficiencies before we can continue production at our manufacturing facilities.

In addition, the quality of our products, including drug candidates manufactured by us for research and development purposes and drugs manufactured by us for commercial use, depends significantly on the effectiveness of our quality control and quality assurance, which in turn depends on factors such as the production processes used in our manufacturing facilities, the quality and reliability of equipment used, the quality of our staff and related training programs and our ability to ensure that our employees adhere to our quality control and quality assurance protocol. However, there can be no assurances that our quality control and quality assurance procedures will be effective in consistently preventing and resolving deviations from our quality standards. Any significant failure or deterioration of our quality control and quality assurance protocol could render our products unsuitable for use, jeopardize any cGMP certifications we may have and/or harm our market reputation and relationship with business partners. Any such developments may have a material adverse effect on our business, financial condition and results of operations.

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

In order to produce sufficient quantities of nomacopan to meet the demand for future clinical trials and subsequent commercialization, our third party manufacturer of nomacopan will be required to increase its production 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 nomacopan, or if it is unable to produce increased amounts of nomacopan 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.

Our ADSs may be involuntarily delisted from trading on the Nasdaq Capital Market if we fail to comply with the continued listing requirements. A delisting of our ADSs could reduce the liquidity of our ADSs and may inhibit or preclude our ability to raise additional capital.

Nasdaq requires us to meet certain financial, public float, bid price and liquidity standards on an ongoing basis in order to continue the listing of our ADSs. Generally, we must maintain a minimum closing bid price of $1.00 and a minimum amount of shareholders equity (generally $2.5 million). On October 24, 2022, we were notified by Nasdaq that we were not in compliance with the minimum bid price requirements set forth in Nasdaq Listing Rule 5550(a)(2) for continued listing on the Nasdaq Capital Market, and in accordance with the applicable Nasdaq rules, we were provided with a grace period, through April 24, 2023, to regain compliance with this rule. In addition, as a result of the expected accounting classification of the warrants issued in connection with our September 2022 registered direct offering as liabilities, we believe our shareholders equity will fall below the $2,500,000 shareholders' equity requirement set forth in Nasdaq Listing Rule 5505(b)(1) for continued listing on the Nasdaq Capital Market as of December 31, 2022 and we expect that once we file our Annual Report on Form 20-F for the year ended December 31, 2022, which is required by April 30, 2023, we may receive a related notice of non-compliance from Nasdaq.

If we fail to regain compliance with the Nasdaq minimum closing bid price or shareholders equity requirement, or otherwise meet any of the continuing listing requirements, our ADSs may be subject to delisting and we may become subject to delisting proceedings. If our ADSs are delisted and we are not able to list our ADSs on another national securities exchange, we expect our securities would be quoted on an over-the-counter market. If this were to occur, our shareholders could face significant material adverse consequences, including limited availability of market quotations for our ADSs and reduced liquidity for the trading of our securities. In addition, we could experience a decreased ability to issue additional securities and obtain additional capital in the future. There can be no assurance that an active trading market for our ADSs will develop or be sustained. If we have not regained compliance with the minimum bid price rule described above before April 24, 2023, we intend to seek an 180-day extension to regain compliance with the minimum bid price requirement under the Nasdaq Listing Rules, but there can be no assurance that Nasdaq will grant such extension. We plan to raise additional capital in order to increase our shareholders' equity in order to meet the Nasdaq continued listing standards. Any additional equity financings may be financially dilutive to, and will be dilutive from an ownership perspective to our shareholders, and such dilution may be significant based upon the size of such financing. Additionally, we cannot assure that such funding will be available on a timely basis, in needed quantities, or on terms favorable to us, if at all.

Our business, operating results and growth rates may be adversely affected by current or future unfavorable economic and market conditions and adverse developments with respect to financial institutions and associated liquidity risk.

Our business depends on the economic health of the global economies. If the conditions in the global economies remain uncertain or continue to be volatile, or if they deteriorate, including as a result of the impact of military conflict, such as the war between Russia and Ukraine, terrorism or other geopolitical events, our business, operating results and financial condition may be materially adversely affected. Economic weakness, inflation and increases in interest rates, limited availability of credit, liquidity shortages and constrained capital spending have at times in the past resulted, and may in the future result, in challenging and delayed sales cycles, slower adoption of new technologies and increased price competition, and could negatively affect our ability to forecast future periods, which could result in an inability to satisfy demand for our products and a loss of market share.

In addition, increases in inflation raise our costs for commodities, labor, materials and services and other costs required to grow and operate our business, and failure to secure these on reasonable terms may adversely impact our financial condition. Additionally, increases in inflation, along with the uncertainties surrounding COVID-19, geopolitical developments and global supply chain disruptions, have caused, and may in the future cause, global economic uncertainty and uncertainty about the interest rate environment, which may make it more difficult, costly or dilutive for us to secure additional financing. A failure to adequately respond to these risks could have a material adverse impact on our financial condition, results of operations or cash flows.

More recently, the closures of SVB and Signature Bank and their placement into receivership with the FDIC created bank-specific and broader financial institution liquidity risk and concerns. Although the Department of the Treasury, the Federal Reserve and the FDIC jointly released a statement that depositors at SVB and Signature Bank would have access to their funds, even those in excess of the standard FDIC insurance limits, under a systemic risk exception, future adverse developments with respect to specific financial institutions or the broader financial services industry may lead to market-wide liquidity shortages, impair the ability of companies to access near-term working capital needs, and create additional market and economic uncertainty. There can be no assurance that future credit and financial market instability and a deterioration in confidence in economic conditions will not occur. Our general business strategy may be adversely affected by any such economic downturn, liquidity shortages, volatile business environment or continued unpredictable and unstable market conditions. If the current equity and credit markets deteriorate, or if adverse developments are experienced by financial institutions, it may cause short-term liquidity risk and also make any necessary debt or equity financing more difficult, more costly, more onerous with respect to financial and operating covenants and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and stock price and could require us to alter our operating plans. In addition, there is a risk that one or more of our service providers, financial institutions, manufacturers, suppliers and other partners may be adversely affected by the foregoing risks, which could directly affect our ability to attain our operating goals on schedule and on budget.

We identified a material weakness in our internal control over financial reporting in 2021, and in the future, we may identify additional material weaknesses or fail to maintain an effective system of controls. If we identify additional material weaknesses in the future or otherwise fail to maintain an effective system of internal controls, we may not be able to accurately or timely report our financial condition or results of operations, which may adversely affect our business and stock price.

The Sarbanes-Oxley Act of 2002 requires, among other things, that we maintain effective internal control over financial reporting and disclosure controls and procedures. In particular, we are required, under Section 404 of the Sarbanes-Oxley Act of 2002, to perform system and process evaluations and testing of our internal control over financial reporting to allow management to report on the effectiveness of our internal control over financial reporting. This assessment must include disclosure of any material weaknesses in our internal control over financial reporting identified by our management. A material weakness is a control deficiency, or combination of control deficiencies, in internal control over financial reporting that results in more than a reasonable possibility that a material misstatement of annual or interim consolidated financial statements will not be prevented or detected on a timely basis.

We identified a material weakness in our internal control over financial reporting in 2021, and concluded that our internal control over financial reporting was not effective as of December 31, 2020, which resulted in an error in the accounting treatment of the RPC options, or the RPC Options. We remediated the material weakness regarding the RPC Options in 2021, which were originally recorded as a $26 million liability (as related to options and warrants), by re-classifying and re-valuing the RPC Options in the year ended December 31, 2015 (and for each subsequent year) as $22.6 million of equity (additional paid-in capital) as discussed in “Item 15. Controls and Procedures” of the Annual Report on Form 20-F for the year ended December 31, 2021. In addition, we updated our policies and procedures regarding the accounting for significant non-routine transactions, specifically to periodically re-evaluate the accounting analysis and conclusions of these transactions to ensure that the accounting conclusions reached at the inception of the transaction remain appropriate.

We cannot assure you that the measures we have taken to date and may take in the future will be sufficient to prevent or avoid potential future material weaknesses. The effectiveness of our internal control over financial reporting is subject to various inherent limitations, including cost limitations, judgments used in decision making, assumptions about the likelihood of future events, the possibility of human error, and the risk of fraud. If we are unable to prevent or avoid future material weaknesses, our ability to record, process, and report financial information accurately, and to prepare financial statements within the time periods specified by the forms of the SEC, could be adversely affected which, in turn, may adversely affect our reputation and business and the market price of our common stock. In addition, any such failures could result in litigation or regulatory actions by the SEC or other regulatory authorities, loss of investor confidence, delisting of our securities, and harm to our reputation and financial condition, or diversion of financial and management resources from the operation of our business.

In addition, it is possible that control deficiencies could be identified by our management or by our independent registered public accounting firm in the future or may occur without being identified. Such a failure could result in regulatory scrutiny and cause investors to lose confidence in our reported financial results, lead to a default under our current or future indebtedness and otherwise have a material adverse effect on our business, financial condition, cash flows, or results of operations.

If we are deemed or become a passive foreign investment company, or PFIC, for U.S. federal income tax purposes in 2023 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 were not a PFIC for 2022. Because the PFIC determination is highly fact sensitive, there can be no assurance that we will not be a PFIC for 2023 or for any other taxable year. If we were to be characterized as a PFIC for U.S. federal income tax purposes in any taxable year during which a U.S. shareholder owns our ADSs, and such U.S. shareholder 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 such 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. shareholder'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, or IRS, 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. shareholders who hold our ADSs during a period when we are a PFIC will be generally subject to the foregoing rules, even if we cease to be a PFIC in subsequent years, subject to certain exceptions, including 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 intend to 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. investors are urged to consult their own tax advisors regarding the possible application of the PFIC rules.

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 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, marketing authorizations or new product introductions;
- a serious adverse event in a clinical trial and/or a long-term safety issue;
- developments concerning our licensors or product manufacturers;
- litigation and other developments relating to our patents or other proprietary rights or those of our competitors;
- conditions in the pharmaceutical or biotechnology industries;
- variations in our anticipated or actual operating results;
- governmental regulation and legislation, actual or anticipated;
- 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, MHRA 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 marketing authorization;
- announcement of FDA, MHRA or EMA approval or non-approval of our product candidates or delays in or adverse events during the FDA, MHRA or EMA review process;
- actions taken by regulatory agencies with respect to our product candidates or products, our clinical trials or our future 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, MHRA, 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 our ordinary shares or ADSs by our executive officers, directors and significant shareholders;
- managerial costs and expenses;
- changes in accounting principles or practices;
- the loss of any of our key scientific or management personnel; and
- natural disasters and political and economic instability, including wars, terrorism, political unrest, results of certain elections and votes, emergence of a pandemic, or other widespread health emergencies (or concerns over the possibility of such an emergency, including for example, the COVID-19 outbreak), boycotts, adoption or expansion of government trade restrictions, and other business restrictions.

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, 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 own a significant amount of our outstanding shares 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 March 1, 2023, our directors and executive officers, together with their affiliates and related persons, beneficially own, in the aggregate, approximately 20% of our outstanding ordinary shares. Our chairman Dr. Ray Prudo, beneficially owns approximately 18% 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. Additionally, any ordinary shares or ADSs issued pursuant to our equity incentive plan may result in material dilution to our existing shareholders.

The withdrawal of the United Kingdom from the European Union (Brexit) could adversely affect our business, financial condition, results of operations and prospects.

Prior to January 1, 2021, the UK was part of the EU so that there was some commonality with respect to EU laws and the UK was a member of the Customs Union and the Single Market.

Since January 1, 2021 the UK is no longer part of the EU and is considered by the EU as a “third country”. The trade relationship between the EU and the UK is principally governed by a trade and co-operation agreement, or the EU-UK Trade Agreement. Alongside agreements for co-operation on economic, social, environmental and other matters, the EU-UK Trade Agreement incorporates an extensive free trade agreement that provides for zero tariffs and quotas on goods, provided that certain conditions are met. Nevertheless, additional administrative and regulatory burdens may increase costs. Following Brexit, EU laws were mostly transitioned into UK law but UK laws may diverge in future from those in the EU. Parallel regulatory regimes could result in the regulatory compliance and patent costs associated with our business increasing significantly so as to adversely affect our financial condition, results of operations and prospects. Further, our regulatory compliance costs may increase, as the UK has adopted standalone UK medicines regulations. The UK medicines regulatory regime is currently similar to EU regulations but the UK has enacted the Medicines and Medical Devices Act 2021, under which the UK may adopt changed regulations which may diverge from the EU legislative regime for medicines, their research, development and commercialization. Separate regulatory regimes will require us to comply with separate regimes in the UK and the EU, or to develop new policies and procedures or reorganize our operations, any of which could increase our compliance costs. 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. Any of the aforementioned possible effects of Brexit, and others that 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 might 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 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 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 a "foreign private issuer" and as a result of this and other reduced disclosure requirements applicable to foreign private issuers, our ADSs may be less attractive to investors.

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 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 of 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.

Provisions in the UK City Code on Takeovers and Mergers may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our shareholders.

The UK City Code on Takeovers and Mergers, or the Takeover Code, applies, among other things, to an offer for a public company whose registered office is in the United Kingdom and whose securities are not admitted to trading on a regulated market in the United Kingdom if the company is considered by the Panel on Takeovers and Mergers, or the Takeover Panel, to have its place of central management and control in the United Kingdom. This is known as the "residency test." The test for central management and control under the Takeover Code is different from that used by the UK tax authorities. Under the Takeover Code, the Takeover Panel will determine whether we have our place of central management and control in the United Kingdom by looking at various factors, including the structure of our board of directors, the functions of the directors and where they are resident. Whilst the Takeover Panel has not informed us of any such determination, on account of the current constitution of our board, we believe that we are currently subject to the Takeover Code.

If at the time of a takeover offer the Takeover Panel determines that we have our place of central management and control in the United Kingdom, we will be subject to a number of rules and restrictions, including but not limited to the following: (1) our ability to enter into deal protection arrangements with a bidder will be extremely limited; (2) we may not, without the approval of our shareholders, be able to perform certain actions that could have the effect of frustrating an offer, such as issuing shares or carrying out acquisitions or disposals; and (3) we will be obliged to provide equality of information to all bona fide competing bidders.

Further, the Takeover Code contains certain rules in respect of mandatory offers. Under Rule 9 of the Takeover Code, if a person: (a) acquires an interest in our shares which, when taken together with shares in which he or persons acting in concert with him are interested, carry 30% or more of our voting rights; or (b) who, together with persons acting in concert with him, is interested in shares that in the aggregate carry not less than 30% of our voting rights and does not hold shares carrying more than 50% of our voting rights, 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, will be required (except with the consent of the Takeover Panel) to make a cash offer for our outstanding shares at a price not less than the highest price paid for any interest in our shares by the acquirer or its concert parties during the previous 12 months.

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 a general meeting is 14 clear days' notice (or, for an annual general meeting, 21 clear days' notice (unless, in the case of an annual general meeting, all members entitled to attend and vote at the meeting, or, in the case of any other general meeting, a majority in number 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.

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.