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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549
FORM 20-F

(Mark One)

☐ **REGISTRATION STATEMENT PURSUANT TO SECTION 12(b) OR (g) OF THE SECURITIES EXCHANGE ACT OF 1934**

OR

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended **December 31, 2022**

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

OR

☐ **SHELL COMPANY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

Date of event requiring this shell company report_____

For the transition period from_____ to _____

Commission file number 001-36288

Akari Therapeutics, Plc

(Exact name of Registrant as specified in its charter)

The Laws of England and Wales
(Jurisdiction of incorporation or organization)

75/76 Wimpole Street
London W1G 9RT
United Kingdom
(Address of principal executive offices)

Rachelle Jacques
President and Chief Executive Officer
75/76 Wimpole Street
London W1G 9RT
United Kingdom
Telephone +44 20 8004 0270

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

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
American Depositary Shares, each representing 100 Ordinary Shares, par value $0.0001 per share	**AKTX**	**The Nasdaq Capital Market**
Ordinary Shares, $0.0001 par value per share*		

* Not for trading, but only in connection with the registration of American Depositary Shares (ADS) representing such Ordinary Shares pursuant to the requirements of the Securities and Exchange Commission.

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

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

The number of outstanding shares of each of the issuer's classes of capital or common stock as of the close of the period covered by the annual report: 7,444,917,123 Ordinary Shares, $0.0001 par value per share.

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act.

☐ Yes ☒ No

If this report is an annual or transition report, indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934.

☐ Yes ☒ No

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days.

☒ Yes ☐ No

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files).

☒ Yes ☐ No

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

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

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

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

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statement. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

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

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

If "Other" has been checked in response to the previous question, indicate by check mark which financial statement item the registrant has elected to follow.

☐ Item 17 ☐ Item 18

If this is an annual report, indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act).

☐ Yes ☒ No

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INTRODUCTION

Unless the context otherwise requires, all references to “Akari,” “we,” “us,” “our,” the “Company” and similar designations refer to Akari Therapeutics, Plc and its subsidiaries.

Market data and certain industry data and forecasts used throughout this Annual Report on Form 20-F were obtained from sources we believe to be reliable, including market research databases, publicly available information, reports of governmental agencies, and industry publications and surveys. We have relied on certain data from third-party sources, including internal surveys, industry forecasts, and market research, which we believe to be reliable based on our management’s knowledge of the industry. While we are not aware of any misstatements regarding the industry data presented in this Annual Report, our estimates involve risks and uncertainties and are subject to change based on various factors, including those discussed under the heading “Risk Factors” and elsewhere in this prospectus.

All trademarks, service marks, trade names and registered marks used in this report are trademarks, trade names or registered marks of their respective owners.

Statements made in this Annual Report on Form 20-F concerning the contents of any agreement, contract or other document are summaries of such agreements, contracts or documents and are not complete description of all of their terms. If we filed any of these agreements, contracts or documents as exhibits to this Report or to any previous filing with the Securities and Exchange Commission, or SEC, you may read the document itself for a complete understanding of its terms.

FORWARD-LOOKING STATEMENTS

This Annual Report on Form 20-F contains forward-looking statements. All statements other than statements of historical facts contained in this Annual Report on Form 20-F, 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 marketing authorizations 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;
- our ability to attract and retain key employees;
- 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 our disclosure controls and procedures not been ineffective due to a material weakness;
- 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 we depend;
- unexpected cost increases and pricing pressures;
- risks related to unfavorable economic and market conditions and adverse developments with respect to financial institutions and associated liquidity risk;
- risks related to any resurgence of the COVID-19 pandemic and the Russian invasion of Ukraine; and
- those factors referred to in "Item 3.D. Risk Factors," "Item 4. Information on the Company," and "Item 5. Operating and Financial Review and Prospects", as well as in this Annual Report on Form 20-F generally.

In light of these assumptions, risks and uncertainties, the results and events discussed in the forward-looking statements contained in this Annual Report on Form 20-F 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.

We have obtained the statistical data, market data and other industry data and forecasts used throughout this Annual Report on Form 20-F from publicly available information. We have not sought the consent of the sources to refer to the publicly available reports in this Annual Report on Form 20-F.

You should read this Annual Report on Form 20-F and the documents that we have filed as exhibits to the Annual Report on Form 20-F 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.

PART I

ITEM 1. IDENTITY OF DIRECTORS, SENIOR MANAGEMENT AND ADVISERS

Not applicable.

ITEM 2. OFFER STATISTICS AND EXPECTED TIMETABLE

Not applicable.

ITEM 3. KEY INFORMATION

A. [Reserved]

B. Capitalization and Indebtedness

Not applicable.

C. Reasons for the Offer and Use of Proceeds

Not applicable.

D. Risk Factors

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

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

Risk Factor Summary

The following summarizes some, but not all, of these risks. Please carefully consider all of the information discussed in "Item 3. Key Information—D. Risk Factors" in this Annual Report on Form 20-F for a more thorough description of these and other risks.

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.
- Our auditor's report on our consolidated financial statements states that our recurring operating losses, negative cash flows and dependence on additional financial support raises substantial doubt about our ability to continue as a going concern, which may have a detrimental effect on our ability to obtain additional funding.
- 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.

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 could be materially harmed.
- If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.
- 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 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.
- 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.
- Results of earlier preclinical studies or clinical trials may not be predictive of advancement to the next phase of development.
- Long-term animal toxicity and long-term human safety studies of nomacopan could demonstrate that the administration of nomacopan results in serious adverse events.
- Chronic dosing of patients with nomacopan could lead to an immune response that causes adverse reactions or impairs the activity of the drug.
- If nomacopan is not convenient for patients to use, then we might be prevented from successful commercialization.
- 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.

- We have obtained orphan drug designation for nomacopan in the United States for the use in bullous pemphigoid, or BP, and hematopoietic stem cell transplant-associated thrombotic microangiopathy, or HSCT-TMA, paroxysmal nocturnal hemoglobinuria, or PNH, Guillain-Barré syndrome, or GBS, 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.

- 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.

- 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.

- 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.

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

Risks Related to our Intellectual Property

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

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.

- 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.

- 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.

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

- 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.

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

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

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.

- 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 commercialization may be slowed.

Risks Related to our Ordinary Shares and ADSs

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

- 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.

- 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.

- The rights of our shareholders may differ from the rights typically offered to shareholders of a U.S. corporation.

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 $17.7 million and $17.4 million for the years ended December 31, 2022 and 2021, respectively. In addition, our accumulated deficit as of December 31, 2022 and 2021 was $217.5 million and $199.7 million, 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.

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 ADS representing our 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.

Our auditor's report on our consolidated financial statements states that our recurring operating losses, negative cash flows and dependence on additional financial support raises substantial doubt about our ability to continue as a going concern, which may have a detrimental effect on our ability to obtain additional funding.

The report of our U.S. independent registered public accounting firm on our consolidated financial statements for the period ended December 31, 2022, includes an explanatory paragraph raising substantial doubt about our ability to continue as a going concern as a result of our recurring losses from operations and net capital deficiency. Our future is dependent upon our ability to obtain financing in the future. This opinion could materially limit our ability to raise funds. If we fail to raise sufficient capital when needed, we will not be able to complete our business plan. As a result, we may have to liquidate our business and investors may lose their investment in our ADSs.

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 December 31, 2022, we had cash of approximately $13.2 million. In September 2022, we raised gross proceeds of approximately $12.8 million in a registered direct offering and on March 30, 2023 we raised gross proceeds of approximately $4.0 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 this Annual Report on Form 20-F. 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, which raises substantial doubt about our ability to continue as a going concern. The report from our U.S. independent registered public accounting firm for our consolidated financial statements for the year ended December 31, 2022 included an emphasis of matter paragraph expressing substantial doubt about our ability to continue as a going concern. The inclusion of this going concern emphasis of matter paragraph could materially limit our ability to raise additional funds through the issuance of equity or debt securities or otherwise.

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 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, 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 could 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.

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 of previously approved products.

We have obtained orphan drug designation for nomacopan in the United States for the use in HSCT-TMA, BP, PNH and GBS, 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 HSCT-TMA, GBS, 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.

Future changes associated with pharmaceutical product or drug reimbursement may adversely affect our business.

Market acceptance and sales of any one or more of our products will depend in part 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. Obtaining coverage and reimbursement approval for a product from a government or other third-party payor is a time consuming and costly process that could require us to provide supporting scientific, clinical, and cost-effectiveness data for the use of our products to the payor. We may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. 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.

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.

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, 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. Congress through the passage of the Inflation Reduction Act, the Infrastructure Investment and Jobs Act, and the Bipartisan Safer Communities Act delayed implementation of this safe harbor until 2032. Should the regulation go into effect in 2023, 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.

Most recently, in August 2022, the Inflation Reduction Act of 2022 (the “IRA”) became law. Among other things, the IRA has multiple provisions that may impact the prices of drug products that are both sold into the Medicare program and throughout the United States. Starting in 2023, a manufacturer of a drug or biological product covered by Medicare Parts B or D must pay a rebate to the federal government if the product’s price increases faster than the rate of inflation. This calculation is made on a drug product by drug product basis and the amount of the rebate owed to the federal government is directly dependent on the volume of a drug product that is paid for by Medicare Parts B or D. Additionally, starting in payment year 2026, the Centers for Medicare and Medicaid Services (CMS) will negotiate drug prices annually for a select number of single source Part D drugs without generic or biosimilar competition. CMS will also negotiate drug prices for a select number of Part B drugs starting for payment year 2028. If a drug product is selected by CMS for negotiation, it is expected that the revenue generated from such drug will decrease. The effect of the IRA on our business and the healthcare industry in general is not yet known. There remains a large amount of uncertainty regarding the federal government’s approach to paying for pharmaceutical products.

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 could 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. Pandemics such as COVID-19 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.

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 for the treatment of autoimmune, inflammatory or 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 marketing 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, if any.

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 attract and retain 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 products. Further, any failure to effectively integrate new personnel could prevent us from successfully growing our company.

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.

Our business either directly or indirectly through critical suppliers may be adversely affected by the impact of any resurgence 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.

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 in accordance with the applicable Nasdaq rules, we were provided with a grace period, through April 24, 2023, to regain compliance with this rule. On April 25, 2023, Nasdaq granted us an additional 180 calendar day period, or until October 23, 2023, in which to regain compliance with the minimum $1.00 bid price requirement. 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, our shareholders equity fell 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 this Annual Report on Form 20-F for the year ended December 31, 2022, 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. 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 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, inflation raises 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, inflation, along with the uncertainties surrounding a resurgence of 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.

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 may have been a PFIC for 2022, but we have not performed a detailed analysis to determine PFIC status for 2022. Because the PFIC determination is highly fact sensitive, there can be no assurance that we were not a PFIC for 2022 and 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, a resurgence of COVID-19), 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 31, 2023, our directors and executive officers, together with their affiliates and related persons, beneficially own, in the aggregate, approximately 24.7% of our outstanding ordinary shares. Our chairman Dr. Ray Prudo, beneficially owns approximately 21.8% 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.

We may lose our foreign private issuer status in the future, which could result in additional costs.

We are a foreign private issuer, and therefore, we are not required to comply with all of the periodic disclosure and current reporting requirements of the Exchange Act. The determination of foreign private issuer status is made annually on the last business day of an issuer's most recently completed second fiscal quarter. We would lose our foreign private issuer status if, for example, more than 50% of our ordinary shares are directly or indirectly held by residents of the U.S. and we fail to meet additional requirements necessary to maintain our foreign private issuer status. If we lose our foreign private issuer status on this date, we would be required to file with the SEC periodic reports and registration statements on U.S. domestic issuer forms beginning with the following fiscal year, which are more detailed and extensive than the forms available to a foreign private issuer, and require the filing with the SEC of quarterly reports on Form 10-Q containing unaudited financial and other specified information, as well as current reports on Form 8-K upon the occurrence of specified significant events. In addition, foreign private issuers are not required to file their annual report on Form 20-F until four months after the end of each financial year, while U.S. domestic issuers that are accelerated filers are required to file their annual report on Form 10-K within 75 days after the end of each fiscal year. Foreign private issuers are also exempt from the Regulation Fair Disclosure, aimed at preventing issuers from making selective disclosures of material information. We would also have to mandatorily comply with U.S. federal proxy requirements, and our officers, directors and principal shareholders would become subject to the short-swing profit disclosure and recovery provisions of Section 16 of the Exchange Act. In addition, we would lose our ability to rely upon exemptions from certain corporate governance requirements under the Nasdaq listing rules. As a U.S. listed public company that is not a foreign private issuer, we would incur additional legal, accounting and other expenses that we would not incur as a foreign private issuer, and accounting, reporting and other expenses in order to maintain a listing on a U.S. securities exchange.

ITEM 4. INFORMATION ON THE COMPANY

A. History and Development of the Company

Our Corporate History

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

On September 18, 2015, we completed an acquisition of all of the capital stock of Volution Immuno Pharmaceuticals SA, or Volution, a private Swiss company, from RPC Pharma Limited, or RPC, Volution's sole shareholder, in exchange for our ordinary shares, in accordance with the terms of a Share Exchange Agreement, dated as of July 10, 2015. In connection with the acquisition, our name was changed to Akari Therapeutics, Plc and the combined company focused on the development and commercialization of life-transforming treatments for a range of rare and orphan autoimmune and inflammatory diseases caused by dysregulation of complement C5.

Our ADSs have been listed on the Nasdaq Capital Market under the symbol "AKTX" since September 21, 2015 and under the symbol "CLTX" from January 31, 2014 until September 18, 2015. Prior to that, our ADSs were quoted on the OTCQB under the symbol "CLSXD" from January 3, 2014 to January 30, 2014 and were quoted on the OTCQB under the symbol "CLSXY" from September 16, 2013 until January 2, 2014 and under the symbol "MRRBY" from February 19, 2013 to September 15, 2013. Effective January 3, 2014, our ratio of ADSs to ordinary shares changed from one ADS per each two ordinary shares to one ADS per each ten ordinary shares and, effective as of September 17, 2015, our ratio of ADSs to ordinary shares changed from one ADS per each ten ordinary shares to one ADS per each one hundred ordinary shares. Currently, each ADS represents one hundred ordinary shares. Effective December 8, 2020, the currency of our ordinary shares was changed from pounds sterling to US dollars and the nominal (par) value of an ordinary share was reduced to $0.0001.

Our principal office is located at 75/76 Wimpole Street, London W1G 9RT, United Kingdom, and our telephone number is +44 20 8004 0270. Our website address is www.akaritx.com. The information contained on, or that can be accessed through, our website is neither a part of nor incorporated into this Annual Report. We have included our website address in this annual report solely as an inactive textual reference. Puglisi & Associates, or Puglisi, serves as our agent for service of process in the United States. Puglisi's address is 850 Library Avenue, Suite 204, Newark, Delaware 19711.

We use our website (www.akaritx.com), Linkedin (https://www.linkedin.com/company/akaritx/) and Twitter (https://twitter.com/AkariTX) as a channel of distribution of Company information. The information we post through this channel may be deemed material. Accordingly, investors should monitor our website, LinkedIn and Twitter, in addition to following our press releases, SEC filings and public conference calls and webcasts. The contents of our website are not, however, a part of this Annual Report.

Capital Expenditures

We had no capital expenditures for the years ended December 31, 2022, 2021 and 2020.

B. Business 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 to eye, inhaled and intravitreous 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 the ticks 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, GBS, PNH 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, 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. We have also received Rare Pediatric Disease Designation from the FDA for the treatment of pediatric HSCT-TMA. The Rare Pediatric Disease Designation 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 or biologics license application for a rare pediatric disease may be eligible for a Priority Review Voucher, which is received concurrently with marketing approval as discussed further below.

Our clinical targets for nomacopan are autoimmune and inflammatory diseases where the inhibition of both C5 and LTB4 are implicated, including pediatric HSCT-TMA. We additionally have a pre-clinical program developing long-acting PASylated-nomacopan (PAS-nomacopan) for treatment of geographic atrophy (GA) secondary to dry age-related macular degeneration (dry AMD).

Clinical Development Programs — Past and Current

Phase 1a Single Ascending Dose Trial

Nomacopan entered clinical development in 2013 when a Phase 1a clinical trial was initiated under a Clinical Trials Authorization (CTA) issued by the Medicines and Healthcare products Regulatory Agency (MHRA), an executive agency of the Department of Health and Social Care in the United Kingdom. The primary objective of this single ascending dose, first-in-man study was to explore the safety profile of nomacopan in 24 subjects. The drug was well tolerated, and no serious or dose-related serious adverse events were reported. The secondary objective of this Phase 1a clinical trial was to examine the effect of nomacopan on complement activity at the highest, therapeutic dose. This showed that the peak onset of action was about nine hours after injection, and that the effect of a single dose was detectable for more than 96 hours. The effects were consistent between all subjects and showed 100% inhibition of the complement system within 12 hours.

Phase 1b Dose Range Finding Trial

A Phase 1b repeat dose study was initiated in the first quarter of 2016. In this double-blind, randomized Phase 1b trial, each cohort of six normal healthy volunteers was given either a loading dose of subcutaneous placebo twice a day for two days followed by five days of a single daily placebo dose (n=2) or a loading dose of 30 mg of subcutaneous nomacopan twice a day for two days followed by five days of a single daily subcutaneous maintenance dose (n=4) of either 15 mg, 22.5 mg or 30 mg.

Data from the 22.5 mg once daily maintenance cohort and 30 mg once daily maintenance cohort demonstrated that subcutaneous nomacopan achieved complete complement inhibition (ELISA CH50 < 8 Eq/ml, lower limit of quantification) within the first day, and demonstrated complete complement inhibition at the end of dosing on day 7 whether measured using the ELISA or lytic CH50 assays.

The data from the 15 mg once daily maintenance cohort demonstrated that subcutaneous nomacopan achieved complete complement inhibition (ELISA CH50 < 8 Eq/ml, lower limit of quantification) within the first day following an ablating dose but by day three was unable to maintain complete complement inhibition at the 24-hour trough measurement. A final cohort of 4 healthy volunteers was given 22.5 mg of nomacopan as a maintenance dose for 21 days. Complete complement inhibition was demonstrated at the end of the 21 day period of once daily dosing and there were no neutralizing antibodies detected. One volunteer receiving the nomacopan in the 30 mg 7 day cohort stopped dosing on day three due to a non-serious adverse event possibly related to antibiotics administered for meningitis prophylaxis. The trial was conducted at Hammersmith Medicines Research Ltd, in London.

HSCT-TMA Clinical Program

HSCT-TMA is an orphan condition with severe cases having an estimated fatality rate of more than 80% patients with the disease. Complement activity is known to be implicated in HSCT-TMA with sC5b-9 and CH50 identified as key markers of disease progression; LTB4, which is also inhibited by nomacopan, may also be implicated by causing uncontrolled functioning of certain immune cells, such as neutrophils, that may lead to inflammation, tissue damage, and development of thrombosis. Currently, there are no approved treatment options for adult or pediatric patients in the U.S. or Europe.

In December 2019, we opened a two-part, multi-center Phase 3 study for the treatment of pediatric HSCT-TMA with nomacopan, based upon guidance from our end-of-phase 2 meeting with FDA. The primary endpoints are focused on disease response defined primarily by renal improvement and reduced transfusion dependence. This two-part pivotal Phase 3 study of nomacopan in pediatric patients with HSCT-TMA is based on guidance from our end-of-Phase 2 meeting with the FDA. Part A of the trial is a dose confirmation study. The pivotal Part B of the trial is a responder-based safety and efficacy study. As a result of the COVID-19 outbreak, we experienced delays in openings and enrollment. However, Part A of the trial in pediatric HSCT-TMA has now fully enrolled two of three pediatric age cohorts.

In November 2022, the FDA granted the Rare Pediatric Disease Designation to nomacopan for the treatment of pediatric HSCT-TMA, which 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, or NDA, or BLA for a rare pediatric disease may be eligible for a Priority Review Voucher, or PRV. 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.

In February 2023, based on Type C guidance from the FDA, we announced our plans to move forward into design and planning for pivotal Part B of the Phase 3 clinical trial of nomacopan for treatment of pediatric HSCT-TMA in patients between 2 years and <18 years of age. Part A of the Phase 3 clinical trial of nomacopan in pediatric HSCT-TMA was designed to include three cohorts: ages 0.5 to <2 years, ≥2 to <9 years and ≥9 to <18 years. We enrolled patients in the two older age groups and, based on feedback from the FDA, the PK/PD data from these patients from the Part A study are consistent with the predictions derived from our latest PK/PD model. Since enrollment for the youngest age cohort (ages 0.5 to <2 years) in the Part A pediatric study is not completed, we are keeping the study open for this youngest group of pediatric patients while advancing the pivotal Part B study of nomacopan in the older pediatric patients. We participated in the FDA Model-Informed Drug Development (MIDD) program to refine the our PK/PD model suitability and doses for the Phase 3 clinical trial of nomacopan in pediatric HSCT-TMA. Clinical data from 38 subjects (in previous clinical studies and healthy volunteers) were included in the PK/PD model, which was used to predict dosing for pediatric HSCT-TMA patients through 10,000 virtual patient simulations. These informed FDA MIDD interactions that confirmed PK/PD model suitability and doses selected for the nomacopan Phase 3 Part A clinical trial in pediatric HSCT-TMA. An expanded PK/PD model using data from 55 patients treated with nomacopan was reviewed in a Type C interaction with the FDA along with PK/PD data from the Part A study. According to FDA feedback, the model is predictive and supports a simple, fixed dosing regimen of nomacopan in the upcoming Phase 3 pivotal Part B clinical trial in pediatric HSCT-TMA patients who are ages 2 years and older. Study enrollment in the pivotal Part B portion of the trial is expected to begin by the end of 2023.

In addition, in February 2023, 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.

In March 2023, we presented a case study of the first patient to complete treatment in the Part A portion of the Phase 3 clinical study of nomacopan in pediatric HSCT-TMA at the late-breaker at the Transplantation & Cellular Therapy Tandem Meetings as a poster presentation at the European Society for Blood and Marrow Transplantation (EBMT) 49th Annual Meeting. A 6-year-old male patient at Royal Manchester Children's Hospital, Manchester University NHS Foundation Trust in Manchester, UK received a 6/8 HLA-mismatched unrelated cord blood HSCT conditioned with fludarabine, treosulfan and thiotepa, for relapsed refractory acute myelogenous leukemia (AML). The patient received 7 granulocyte infusions peri-transplant as part of an experimental protocol to augment the graft-versus-leukemia effect. His immediate post-transplant course was complicated by engraftment syndrome, acute gut graft-versus-host disease (GVHD) grade 3 and cytomegalovirus (CMV) viraemia. At day +66 after transplant, the patient developed features consistent with TMA, was enrolled in the clinical trial, and began treatment with nomacopan on day +74. A single-age and weight-based ablating dose was followed by maintenance dosing for 21 days. After initial pharmacodynamic analysis at day 14 of treatment, the patient was found to have pre-dose terminal complement activity (TCA) slightly higher (value 14.4) than the LLOQ (CH50 >10 U Eq/ml). Although his TCA had been reduced by 95% from a high baseline CH50 of 299.6U Eq/ml and sC5b9 had normalized, dose was increased in line with the study protocol. A few days later the patient developed neurological symptoms following a period of hypertension and was diagnosed with posterior reversible encephalopathy syndrome (PRES). Nomacopan was stopped for 3 days and restarted after the diagnosis was deemed to be unrelated to nomacopan treatment. Treatment continued for 46 days until the patient's urine protein creatinine ratio was corrected for ≥28 days. Gut pathology and thrombocytopenia were resolved. The patient was discharged from the hospital and remains well and in remission. No adverse events related to nomacopan were experienced during the 72-day treatment period.

Front And Back Of The Eye Programs

Results in a rodent model of Experimental Immune Conjunctivitis (EIC), undertaken at Moorfields Hospital Institute of Ophthalmology, showed that nomacopan demonstrated significant anti-inflammatory activity. In this preclinical model of severe eye surface inflammation, nomacopan, applied topically, resulted in a statistically significant reduction (64%, $p<0.001$) in late phase inflammation versus placebo.

During the third quarter of 2018, we commenced a Phase 1/2 randomized, double blinded, placebo-controlled trial with an initial three patients (Part A) prior to the blinding (Part B) to evaluate the safety and efficacy of nomacopan in patients with the inflammatory mediated eye disorder aopic keratoconjunctivitis, or AKC. In Part A of the Phase 1/2 study, three patients were treated with twice daily nomacopan eye drops in addition to standard of care for up to 56 days in order to establish the safety and tolerability of the drops in preparation for Part B, a randomized, double-masked placebo-controlled comparison in 16 patients. The drops were found to be comfortable and well-tolerated throughout the trial for all three patients. There were no serious adverse events reported. On that basis, the independent safety committee gave permission for the trial to proceed to Part B. Enrollment in the Part B placebo-controlled efficacy arm of the study was halted in H1 2020 due to the COVID-19 outbreak. Of the 12 patients recruited, a complete data set was available on 10 patients – two from Part A and eight from Part B. In Part B, of the eight patients recruited, six were placebo (four AKC patients and two other surface of the eye diagnosis) and two were treated with nomacopan (two AKC patients). As a first-in-eye Phase 1/2 study, the primary endpoint measure was safety. Aggregating data from the eight AKC patients from Part A and Part B shows no ocular treatment emergent serious adverse events during the eight-week treatment period. Nomacopan is delivered topically as eye drops without preservatives and is pH neutral. A comfort score measured after each eye drop installation showed the drug was comfortable and well tolerated. Although the four nomacopan treated AKC patients achieved a higher improved mean efficacy score than the four placebo AKC patients, the patient numbers are too small to show statistical significance on efficacy measures between the two treatment groups.

During 2020 and 2021, we announced preclinical data comparing the therapeutic efficacy of nomacopan, long acting PAS-nomacopan, and a monoclonal anti-VEGF antibody all administered intravitreally. PAS-nomacopan was found to reduce intraocular VEGF levels by as much as the anti-VEGF antibody with 74% (p=0.04) and 68% (p=0.05) reductions respectively, compared to saline control. Furthermore, based on a clinical score measurement, inflammation increased in both the control and anti-VEGF groups by 49% and 33%, respectively, PAS-nomacopan treatment showed a 9% reduction in inflammation assessed by retinal fundoscopy (p=0.02). This therapeutic activity across multiple pathogenic pathways (VEGF, inflammation and complement) supports the potential for nomacopan as a new mode of action for the treatment of back of the eye diseases.

During the fourth quarter of 2020, we announced the publication of the results of a two-year research collaboration with the UCL Institute of Ophthalmology. The results showed that the therapeutic intravitreal (IVT) administration of long-acting PAS-nomacopan mitigated both the severity and progress of retinal damage in two models of autoimmune uveitis, a severe inflammatory eye disease where steroids are the primary treatment option. In addition, results showed the presence of inflammatory cells expressing both complement C5 and LTB4 receptors in retinal tissue from donor patients with uveitis as compared to healthy donor eyes.

During the second quarter of 2022, we announced positive results from two preclinical studies of investigational PAS-nomacopan in diseases of the eye. These preclinical results confirm bioavailability of PAS-nomacopan in the retina and suggested that a clinical dose interval of three months or more may be possible. Studies have shown that due to adverse effects, such as infection, increase in intraocular pressure and discomfort and anxiety, intravitreal or IVT, injection of PAS-nomacopan presents a heavy burden on patients therefore a longer dosing interval may be beneficial.

During the third quarter of 2022, we announced further positive results from these recent pre-clinical studies on the tolerability and extended dose interval of long-acting PAS-nomacopan, which, together with data previously presented, suggest PAS-nomacopan may be a potential novel and effective treatment option for GA, a chronic progressive degeneration of the macula in the aging eye leading to lesions on the outer retina that can cause irreversible vision loss.There is currently one FDA-approved therapy for treatment of GA and one filed with the FDA, both are complement inhibitors; treatments are administered to patients through monthly or every-other-month needle injections into the eye (intravitreal injections/IVTs). Frequent needle injections into the eye are a source of fear, discomfort, disruption for patients and has been shown to decrease patient compliance with optimal dosing regimens.

Our preclinical results show that PAS-nomacopan has the potential to make IVT injection long-lasting in the back of the eye and may provide a more than three-month dosing interval that is less burdensome and thus more attractive for patients. Sight-threatening choroidal neovascularization (CNV) is a safety risk associated with approved and late-stage complement-only inhibitors used for the treatment of GA. CNV is typically treated with anti-VEGF injections. Currently approved and late-stage GA treatments have shown increased risks of developing CNV in clinical trials 4X and 2X compared to sham, respectively. Dual-action PAS-nomacopan may offer the well-understood benefits of complement C5 inhibition in slowing the progression of GA lesions, while LTB4 inhibition also has the potential to help prevent VEGF-A over-expression, a key driver of CNV. These positive results support the potential of long-acting PAS-nomacopan to advance toward IND/IMPD for clinical trials in GA / advanced dry AMD. The program is on -track to submit an IND to the FDA in the first half of 2024.

BP Clinical Program De-Prioritization

In patients with BP there is evidence that both C5 and LTB4 have a central role in driving the disease. Ex vivo data, from a study at Lubeck University, Germany in BP patients showed a pronounced accumulation of LTB4 and C5 and its activation products in the inflamed skin of bullous pemphigoid disease patients.

Following positive topline results from our fully recruited Phase 2 study of nomacopan in nine BP patients, in 2021 we submitted an IND with the FDA and initiated a Phase 3 program for the treatment of BP. Supply chain issues resulted in delays in the study, and in May 2022, some sites started recruiting. Following positive FDA and EMA meetings in 2020, we created a trial design in two parts, with Part A and Part B having the same structure, duration, endpoints and target population of moderate and severe BP patients. In the third quarter of 2022, we announced the prioritization of the Phase 3 clinical trial of nomacopan in severe pediatric HSCT-TMA and the promising pre-clinical program of PAS-nomacopan in GA and discontinuation of the clinical program evaluating nomacopan in BP.

The decision to narrow the pipeline focus is based on Akari's thorough reassessment of development timelines and associated costs to maximize value in its pipeline. It is not related to BP clinical trial data.

Other Program De-Prioritization

We have been in the early stages of exploring opportunities in inflammatory lung diseases with severe exacerbations where complement and leukotriene pathways are implicated, and had in process a PNH program consisting of four separate studies. We provide below a summary of the promising results of nomacopan from our discontinued PNH clinical program.

The PNH program consisted of four separate studies, each of which is closed.

Phase 2 PNH Eculizumab-Resistant Trials which opened in Q1 2016 and has treated two patients.

Phase 2 COBALT PNH Trial which opened in Q4 2016 and has treated eight patients.

Phase 3 CAPSTONE PNH Trial which opened in Q1 2018 and has treated nine patients.

Long-Term Safety and Efficacy CONSERVE Study which treated 15 patients.

In December 2020, we announced new data on the efficacy and safety profile of long-term self-administration of nomacopan for treatment of patients with PNH.

The data from 19 PNH patients treated for a median of 18.5 months are derived from the Phase 2 COBALT trial (n=8 patients), the Phase 2 trial which specifically recruited eculizumab-resistant patients (n=2 patients), the Phase 3 CAPSTONE trial (n = 9 patients), and from the long-term safety study CONSERVE (n = 15), which accepted patients from the Phase 2 and Phase 3 studies. Sixteen of the 19 PNH patients were transfusion dependent prior to treatment with nomacopan, of whom 14 were treated with nomacopan for six months or more.

The data show that long term self-administration of nomacopan by PNH patients:

1) Reduced transfusion dependence (the most clinically relevant efficacy endpoint) by 79% in the 14 formerly transfusion dependent patients treated with nomacopan for at least six months, with a median time since last transfusion of 13.8 months.

2) In the Phase 3 CAPSTONE trial, all patients dosed with nomacopan (n=4) were transfusion independent for the six-month treatment period while all patients on placebo (n=5) remained transfusion dependent, which was the primary end point of the study. The difference is statistically significant at the p=0.034 level. The active and placebo groups were very similar in terms of transfusion requirements prior to treatment.

3) The number of units of packed red blood cells (U PRBC) received per month declined in all 16 of the transfusion dependent PNH patients by 77% from a mean value of 0.91 U PRBC per month prior to treatment with nomacopan to 0.21 U PRBC per month on nomacopan3.

4) The three PNH patients who were transfusion independent prior to treatment with nomacopan remained transfusion independent on nomacopan.

5) None of the 19 PNH patients treated with nomacopan for over 30 cumulative patient-years had a reported major adverse vascular event (MAVE).

6) There has only been a single reported serious adverse event (urinary tract infection) in one patient that was considered possibly related to nomacopan. None of the patients has had a meningococcal infection reported.

7) Terminal complement activity was below the lower limit of assay quantification (10 CH50 U Equivalent/ml) in all patients at all time points measured during long-term treatment on nomacopan.

Immunogenicity

A chronic (28 day) dosing experiment in mice investigated whether daily subcutaneous administration of the expected therapeutic dose of nomacopan induces an antibody response, and whether the antibodies neutralize complement inhibition by nomacopan. The data from this chronic dosing experiment showed nomacopan was well-tolerated with no injection site allergic reactions or behavioral changes. Nomacopan can induce formation of low titre anti-drug IgG antibodies in mice after four weeks of daily inoculation, which is not uncommon, but these antibodies were not neutralizing and had no effect on nomacopan's ability to inhibit complement.

No neutralizing antibodies have been detected, including in the healthy volunteers in the Phase 1a and 1b trials, and the PNH studies. Pharmacokinetic analysis in PNH patients show that nomacopan serum drug levels do not fall in the presence of anti-drug antibodies and pharmacodynamic analyses show that terminal complement activity was fully inhibited (ELISA CH50 <10 U Eq/mL) throughout nomacopan dosing.

PAS-Nomacopan

Using PASylation®, a proprietary technology licensed from of XL-protein GmbH, XL-protein has modified nomacopan by adding a 600 amino acid proline/alanine/ serine (PAS) N-terminal fusion tag to generate PAS-nomacopan (68kDa). The unstructured and uncharged PAS polypeptide increases the apparent molecular size to approximately 600kDa, slowing kidney clearance and extending the systemic half-life of nomacopan.

Data from mouse, rat and dog studies of PAS-nomacopan demonstrated that the expected terminal half-life in humans may be approximately 4 days. Based on these data, PK modeling supports that a once weekly subcutaneous dosing regimen in human may be feasible. In addition, work in a rabbit eye model has demonstrated the potential for intravitreal dosing interval of once every three months or more using PAS-nomacopan.

In addition, data in a porcine model has shown a similar PK profile for the higher concentrated formulation which may be used in future chronic dosing subcutaneous programs. This new highly concentrated formulation with small (0.3mL) volume and water-like viscosity is intended to allow ease of administration and increased patient comfort and as described above is in pre-clinical development for GA.

Target Indications

Hemopoietic Stem Cell Transplant - Thrombotic Microangiopathy (HSCT-TMA)

TMAs are a group of diseases in which thrombosis occurs in small blood vessels as a result of damage to the endothelium (lining) of the vessels. This leads to hemolytic anaemia, low platelet count (thrombocytopenia), end organ damage which may result in complications including renal failure, stroke and pulmonary hypertension. The major varieties of TMA are hemolytic uremic syndrome (HUS), atypical hemolytic uremic syndrome (aHUS), thrombotic thrombocytopenic purpura (TTP), antiphospholipid syndrome (APS), disseminated intravascular coagulation (DIC), malignant hypertension, scleroderma renal failure and TMA associated with hemopoietic stem cell transplant (HSCT). The latter is often linked to toxicity of calcineurin inhibitors which are used to protect against graft versus host disease (GvHD). There are no currently approved drugs for the treatment of HSCT-TMA and, untreated, the condition in its more severe forms has a high risk of death.

Geographic Atrophy (GA) Secondary to dry Age-Related Macular Degeneration (dry AMD)

GA secondary to dry age-related macular degeneration (dAMD) is a degenerative disease of the retina that leads to progressive loss of retinal pigment epithelium (RPE) and ultimately to photoreceptors. These areas of loss manifest as atrophic lesions on the macula, which reduce photosensitivity and if they overlap the fovea impair vision and ultimately lead to blindness. The pathogenesis of GA is multifactorial and is generally thought to be triggered by intrinsic and extrinsic stress acting on the poorly regenerative retinal pigment epithelium as people age. The stress results in the appearance of drusen and lipofuscin deposits. Components of drusen and lipofuscin, include complement, as well as products of oxidative stress such as advanced glycation end products, and may trigger inflammation via multiple pathways. The resulting inflammation can ultimately lead to the retinal cell death characteristic of GA. Development of AMD, including dAMD, is associated with polymorphisms in various complement proteins and recently a complement inhibitor against C3 has become the first FDA-approved drug for treatment of GA.

Market Opportunity in Complement Mediated Diseases

The NIH estimates that approximately 23.5 million Americans may suffer from an autoimmune disorder, although this number is almost certainly an underestimate of the actual prevalence as it includes only 24 diseases for which good epidemiology studies were available. It is estimated that an additional 1.18 million people in the US will acquire/develop an autoimmune disease every five years. Women are 2.7 times more likely than men to develop an autoimmune disease. Researchers have identified 80 – 100 different autoimmune diseases and suspect at least 40 additional diseases of having an autoimmune basis. Patients with one autoimmune disease are at increased risk of other diseases with an autoimmune basis. These diseases are chronic and can be life-threatening. Autoimmune disease is one of the top 10 leading causes of death in female children and women in all age groups up to 64 years of age. The NIH estimates annual direct health care costs for autoimmune diseases to be in the range of $100 billion.

Both the complement and leukotriene pathways work as part of the immune system to disable and clear out foreign invaders and unwanted cells, and as such, plays an important role in the pathology of many autoimmune diseases. The term “Complement Mediated Diseases” applies to diseases and conditions where a patient’s immune system attacks and destroys healthy body tissue by mistake, causing direct damage mediated by complement and via a plethora of mediators induced by complement activation. In addition to those conditions where complement activity is believed to be the primary driver of disease, there are many other poorly treated diseases where in addition to complement activation other inflammatory pathways are implicated. These diseases, such as HSCT-TMA, GA, PNH, aHUS, GBS, Myasthenia Gravis, NMOSD, BP and AKC, are potential targets for bi-specific nomacopan.

Mortality in patients who develop severe transplant-related TMAs is estimated to be 80%. There are no approved therapeutics for HSCT-TMA. We believe the size of the potential patient population for moderate to severe complement mediated HSCT-TMA is approximately 200-300 in the pediatric population and 3,100-3,200 in the adult population in the US alone. With respect to GA, approximately 5 million people worldwide are estimated to be affected with nearly 1 million in the U.S.

Competition in Complement and Leukotriene Mediated Diseases

The development and commercialization of new drugs is highly competitive. We will face competition with respect to all product candidates that we may develop or commercialize in the future from pharmaceutical and biotechnology companies worldwide. The key factors affecting the success of any approved product will be its efficacy, safety profile, drug interactions, method of administration, pricing, reimbursement and level of promotional activity relative to those of competing drugs.

Our potential competitors may have substantially greater financial, technical, and personnel resources than we do. In addition, many of these competitors have significantly greater commercial infrastructures. Our ability to compete successfully will depend largely on our ability to leverage our collective experience in drug discovery, development and commercialization to:

- discover and develop drugs that are differentiated from other products in the market;
- obtain patent and/or proprietary protection for our product candidates and technologies;
- obtain required marketing authorizations;
- commercialize our product candidates ourselves and/or through partners, if approved; and
- attract and retain high-quality personnel, including those with research, development and commercial skills.

There has been a broad research effort in complement-based therapy to date, with eculizumab being the first therapy approved that directly inhibits C5. Although there is currently less research and development effort in the leukotriene field there are approved leukotriene inhibitors used as a treatment for severe asthma. However, we are aware of certain other companies and academic institutions that are continuing their efforts to discover and develop alternate complement and/or C5 inhibitors, including, but not limited to, Alexion Pharmaceuticals, a subsidiary of AstraZeneca, Apellis, Omeros, Amgen, Iveric, Novartis, Roche and UCB.

Sales and Marketing

Because we have been focused on discovery and development of drugs, we currently have limited sales, marketing and distribution capabilities in order to commercialize nomacopan or any approved product candidates. If our lead 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 some or all of this function to third parties. We may take different approaches to commercialization in different geographies. We will adopt a similar strategy for the other compounds in our pipeline.

Manufacturing

We currently employ third-party contract manufacturers, or CDMOs, which manufacture in accordance with current good manufacturing practice (GMP) requirements, for investigational medical products, including active pharmaceutical ingredients, drug substance and drug products for our preclinical research and clinical studies for nomacopan. Analytical methods have been established and qualified for release testing of drug substance and drug products. We have successfully manufactured nomacopan drug substance and drug product batches in 2016 and manufactured multiple lots of nomacopan in recent years through to 2022.

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We currently rely, and expect to continue to rely, on CDMOs for the manufacture of nomacopan and PAS-nomacopan and any other product candidates that we may develop for larger scale preclinical and clinical testing, as well as for commercial quantities of any product candidates that are approved.

In January 2021, we announced that the FDA has agreed, via a Type C meeting, to the clinical use of nomacopan derived from a next generation manufacturing process. This process increases the final yield of nomacopan at least 5-fold, compared to the previous manufacturing process, which may significantly decrease future commercial cost of goods and reduce the cost of ongoing Phase 3 and future clinical development programs for nomacopan.

In the future 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.

Intellectual Property

We will be able to protect our technology and products from unauthorized use by third parties only to the extent it is covered by valid and enforceable patents or is effectively maintained as trade secrets. Patents and other proprietary rights are thus an essential element of our business.

Our success will depend in part on our ability to obtain and maintain proprietary protection for our product candidates, technology, and know-how, to operate without infringing on the proprietary rights of others, and to prevent others from infringing our proprietary rights. Our policy is to seek to protect our proprietary position by, among other methods, filing U.S. and foreign patent applications related to our proprietary technology, inventions, and improvements that are important to the development of our business and defending our patent applications and patents if they are subjected to challenge by a third party. We also rely on trade secrets, know-how, continuing technological innovation, and in-licensing opportunities to develop and maintain our proprietary position.

We own or have exclusive rights to patents and patent applications based on 15 international patent applications. This includes eight issued United States patents, nine patents granted by the European Patent Office and foreign issued patents in other jurisdictions. This further includes pending patent applications in the United States and other jurisdictions. Our patents and patent applications relate to the complement C5 inhibitor protein nomacopan and to its use in the treatment of key disease indications, as well as to nomacopan variants, and histamine binding proteins. Our current patent portfolio includes granted patents in the jurisdictions of United States, Canada, major European countries, Japan, China, Brazil, Israel, Hong Kong, Mexico, Russia, Australia, New Zealand and pending applications in the jurisdictions of United States, Canada, Europe, Japan, China, Brazil, Israel, Republic of Korea, Australia and New Zealand.

Issued patents in the US and other countries which cover our product candidate nomacopan and its uses will expire between 2024 and 2038, excluding any patent term extensions that might be available following the grant of marketing authorizations. We have pending patent applications for our product candidate nomacopan and its uses that, if issued, would expire in the United States and in countries outside of the United States between 2024 and 2040, excluding any patent term adjustment that might be available following the grant of the patent and any patent term extensions that might be available following the grant of marketing authorizations. These patent and patent applications relate to subject matters including: complement inhibitor molecule; methods for treating myasthenia gravis; methods for treating peripheral nerve disorders; methods for treating respiratory disorders; methods for treating viral infections of the respiratory tract; methods of treating complement-mediated diseases in patients with C5 polymorphisms, methods of treating acute graft versus host disease; methods of treating cicatrizing eye inflammatory disorders; methods of treating autoimmune blistering diseases; methods of treating rheumatic diseases; methods of treating proliferative retinal diseases; methods of treating HSCT-TMA, and nomacopan variants lacking C5 or LTB4 binding.

We have licensed rights to patents and patent applications relating to PAS polypeptides and nucleic acids encoding PAS polypeptides, which include patents/applications which cover PAS-nomacopan fusion proteins. We also own a GB patent application directed to certain PAS-nomacopan fusion proteins and their use in the treatment of key disease indications, including GA. If granted, this GB patent would expire in 2042. This application was filed on 1st December 2022, meaning it is possible to file further applications including in the United States claiming priority to this application until 1st December 2023. If filed and granted, those priority-claiming patents would expire in 2043.

If we are unable to obtain, maintain, defend and enforce patent and other intellectual property rights for our technologies and product candidate nomacopan, or if the scope of the patent and other intellectual property rights obtained is not sufficiently broad, our competitors and other third parties could develop and commercialize technology, biologics and/or biosimilars similar or identical to ours, and erode or negate any competitive advantage that we may have, which could harm our business and ability to achieve profitability.

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. Composition-of-matter patents on the biological or chemical active pharmaceutical ingredients are generally considered to offer the strongest protection of intellectual property and provide the broadest scope of patent protection for pharmaceutical products, as such patents provide protection without regard to any method of use or any method of manufacturing. While we have issued composition-of-matter patents in the United States and other countries for nomacopan, we cannot be certain that the claims in our issued composition-of-matter patents will not be found invalid or unenforceable if challenged. We cannot be certain that the claims in any patent applications covering composition-of-matter or formulations of 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 composition-of-matter 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.

Government Regulation

Government Regulation and Product Approval

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

U.S. Drug Development Process

In the U.S., the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and in the case of biologics, also under the Public Health Service Act, or PHSA, and implementing regulations. The process of obtaining marketing authorizations and the subsequent compliance with applicable federal, state, local, and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to administrative or judicial sanctions. These sanctions could include the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, warning letters, requesting product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement, or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us. The process required by the FDA before a drug or biologic may be marketed in the U.S. generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies according to Good Laboratory Practices or other applicable regulations;

- submission to the FDA of an IND which must become effective before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials according to Good Clinical Practices to establish the safety and efficacy of the proposed drug for its intended use;
- submission to the FDA of an NDA or BLA;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with current good manufacturing practice, or cGMP, to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity; and
- FDA review and approval of the NDA or BLA.

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

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

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

- ***Phase 1:*** The product candidate is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion. In the case of some products for severe or life-threatening diseases, such as cancer, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing may be conducted in patients.
- ***Phase 2***: This phase involves studies in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- ***Phase 3***: Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical study sites. These studies are intended to establish the overall risk-benefit ratio of the product candidate and provide, if appropriate, an adequate basis for product labeling.

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

During the development of a new drug, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to submission of an IND, at the end of Phase 2, and before an NDA or BLA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice, and for the sponsor and FDA to reach agreement on the next phase of development. Sponsors typically use the end of Phase 2 meeting to discuss their Phase 2 clinical results and present their plans for the pivotal Phase 3 clinical trial that they believe will support approval of the new drug.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA. Safety reports must be submitted to the FDA and the investigators 15 calendar days after the trial sponsor determines that the information qualifies for reporting. The sponsor also must notify FDA of any unexpected fatal or life-threatening suspected adverse reaction as soon as possible but in no case later than 7 calendar days after the sponsor's initial receipt of the information. Sponsors of clinical trials of FDA-regulated products, including drugs, are required to register and disclose certain clinical trial information, which is publicly available at www.clinicaltrials.gov.

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

U.S. Review and Approval Processes

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

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

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

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

Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of FDA approval of our drugs, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as partial compensation for effective patent term lost due to time spent during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND, and the submission date of an NDA or BLA, plus the time between the submission date of an NDA or BLA and the approval of that application, except that the period is reduced by any time during which the applicant failed to exercise due diligence. Only one patent applicable to an approved drug may be extended, and the extension must be applied for prior to expiration of the patent. The United States Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration.

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

Biologics Price Competition and Innovation Act of 2009

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

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

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

Orphan Drug Designation

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

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

Fast Track Designation and Accelerated Approval

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

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

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

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

Post-Approval Requirements

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

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

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

Regulation and Marketing Authorization in the European Union

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

- preclinical laboratory tests, animal studies and formulation studies all performed in accordance with the applicable EU Good Laboratory Practice regulations;
- submission to the relevant national authorities of a clinical trial application, or CTA, which must be approved before human clinical trials may begin;
- performance of adequate and well-controlled clinical trials to establish the safety and efficacy of the product for each proposed indication

- submission to the relevant competent authorities of a MAA, which includes the data supporting safety and efficacy as well as detailed information on the manufacture and composition of the product in clinical development and proposed labelling;

- satisfactory completion of an inspection by the relevant national authorities of the manufacturing facility or facilities, including those of third parties, at which the product is produced to assess compliance with strictly enforced current cGMP;

- potential audits of the non-clinical and clinical trial sites that generated the data in support of the MAA; and

- review and approval by the relevant competent authority of the MAA before any commercial marketing, sale or shipment of the product.

Preclinical Studies

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

Clinical Trial Approval

Clinical trials in the European Union are governed by the Clinical Trials Regulation, (EU) No 536/2014, or the CT Regulation. The CT Regulation was adopted in 2014 and replaces the Clinical Trials Directive 2001/20/EC. To ensure that the rules for clinical trials are identical throughout the European Union, the new EU clinical trials legislation was passed as a "regulation" that is directly applicable in all EU member states. All clinical trials performed in the European Union are required to be conducted in accordance with the CT Regulation. Although the CT Regulation entered into force on June 16, 2014 the timing of its application depended on the development of a fully functional Clinical Trial Information System (CTIS), which had to be confirmed by an independent audit. After the process was delayed several times for various reasons, the audit eventually took place in 2021, and the European Commission published the respective notice on July 31, 2021. As a result, the CT Regulation has become applicable on January 31, 2022, with the CTIS going live on the same day.

The New CT Regulation aims to harmonize, simplify and streamline the approval of clinical trials in the European Union. The main characteristics of the CT Regulation include:

- A streamlined application procedure via a single-entry point, the EU portal.

- A single set of documents to be prepared and submitted for the application as well as simplified reporting procedures that will spare sponsors from submitting broadly identical information separately to various bodies and different member states.

- A harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts. Part I is assessed jointly by all member states concerned. Part II is assessed separately by each member state concerned.

- Strictly defined deadlines for the assessment of clinical trial application.

- The involvement of the ethics committees in the assessment procedure in accordance with the national law of the member state concerned but within the overall timelines defined by the New CT Regulation.

Before the CT Regulation became applicable, requirements for the conduct of clinical trials in the EU were regulated by the Clinical Trials Directive 2001/20/EC and the GCP Directive 2005/28/EC. To some extent, these legal frameworks may continue to be applicable under the transitional provisions of the CT Regulation. These transitional provisions allow that where the request for authorization of a clinical trial had been submitted before January 31, 2022 pursuant to the Clinical Trials Directive, that clinical trial shall continue to be governed by the Clinical Trials Directive for three more years, and where the request for authorization of a clinical trial is submitted within 12 months from January 31, 2022, it may be started in accordance with Articles 6, 7 and 9 of the Clinical Trials Directive 2001/20/EC and in that case shall continue to be governed by the Clinical Trials Directive for three more years (i.e. until January 31, 2025).

Marketing Authorization

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

Centralized Authorization Procedure

The centralized procedure enables applicants to obtain a marketing authorization that is valid in all EU member states based on a single application. Certain medicinal products, including products developed by means of biotechnological processes, must undergo the centralized authorization procedure for marketing authorization, which, if granted by the European Commission, is automatically valid in all 27 EU member states. The EMA and the European Commission administer this centralized authorization procedure pursuant to Regulation (EC) No 726/2004.

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

- medicinal products developed by means of one of the following biotechnological processes:
- recombinant DNA technology;
- controlled expression of genes coding for biologically active proteins in prokaryotes and eukaryotes including transformed mammalian cells; and
- hybridoma and monoclonal antibody methods;
- advanced therapy medicinal products as defined in Article 2 of Regulation (EC) No. 1394/2007 on advanced therapy medicinal products;
- medicinal products for human use containing a new active substance that, on the date of effectiveness of this regulation, was not authorized in the European Union, and for which the therapeutic indication is the treatment of any of the following diseases:
- acquired immune deficiency syndrome;
- cancer;
- neurodegenerative disorder;
- diabetes;
- auto-immune diseases and other immune dysfunctions;
- viral diseases; and
- medicinal products that are designated as orphan medicinal products pursuant to Regulation (EC) No 141/2000.

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

Administrative Procedure

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

Conditional Approval

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

Marketing Authorization under Exceptional Circumstances

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

Enhanced Pathways

Enhanced pathways including a potential rolling review of clinical data by EMA have become more common as a result of the COVID-19 pandemic, but significant requirements have to be met to benefit from such enhanced or facilitated pathways to approval.

Market Authorizations Granted by Authorities of EU Member States

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

- The decentralized procedure allows applicants to file identical applications to several EU member states and receive simultaneous national approvals based on the recognition by E.U. member states of an assessment by a reference member state.
- The national procedure is only available for products intended to be authorized in a single EU member state.
- A mutual recognition procedure similar to the decentralized procedure is available when a marketing authorization has already been obtained in at least one EU member state.

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

Pediatric Studies

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

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

Periods of Authorization and Renewals

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

Orphan Drug Designation and Exclusivity

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

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

Regulatory Data Protection

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

Regulatory Requirements after a Marketing Authorization Has Been Obtained

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

Pharmacovigilance and Other Requirements

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

Manufacturing

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

Marketing and Promotion

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

Patent Term Extension

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

A six-month pediatric extension of an SPC may be obtained where the patentee has carried out an agreed pediatric investigation plan, the authorized product information includes information on the results of the studies and the product is authorized in all member states of the EU. The six-month pediatric extension of SPCs is not available for medicinal products that are designated as orphan medicinal products, as such products benefit from a separate two-year pediatric extension of orphan status and exclusivity. The six-month pediatric extension of SPCs is, however, available for medicinal products which were originally designated as orphan medicinal products but were subsequently (voluntarily) removed from the EU's Community Register of Orphan Medicinal Products; according to a first instance court judgment, an SPC pediatric extension is also available where a designation as orphan drug had been sought but never granted.

On July 1, 2019, EU Regulation 2019/933 entered into force. The Regulation introduced manufacturing waivers for exporting and stockpiling active pharmaceutical ingredients and medicinal products. If certain requirements are met, those actions are now exempted from SPC protection. The patent reform of 2012 that laid the ground for the creation of unitary patent protection in the EU did not explicitly provide for a "unitary SPC". To ensure that companies which choose unitary patent protection can benefit from the SPC extension, the European Commission is working on the articulation of unitary patent protection and SPC legislation.

UK Regulation

From January 1, 2021, EU law no longer directly applies in the UK. The UK has adopted existing EU medicines regulation as standalone UK legislation with some amendments to reflect procedural and other requirements with respect to marketing authorizations and other regulatory provisions.

In order to market medicines in the UK, manufacturers must hold a UK marketing authorization. Applications may be made through several national routes including the 150-day assessment for national applications and rolling review for marketing authorizations. For a period of two years from January 1, 2021, as part of the application for a UK marketing authorization, Great Britain may rely on a decision taken by the European Commission on the approval of new marketing authorizations in the centralized community marketing authorization procedure (EC Decision reliance Procedure). Such applications must include all information provided to the EMA during the relevant licensing procedure including the final CHMP opinion and must also state whether the applicant intends to apply for orphan designation in the UK. The UK has the power to take into account marketing authorizations made under the EU decentralized and mutual recognition procedures.

UK medicines legislation is subject to future regulatory change under the Medicines and Medical Devices Act 2021. This act sets out a new framework for the adoption of medicines regulation.

Different rules will apply in Northern Ireland following implementation of the Northern Ireland Protocol. In Northern Ireland, EU central marketing applications will continue to apply.

The EU-UK Trade Agreement contains an Annex in relation to medicinal products with the objective of facilitating availability of medicines, promotion of public health and consumer protection in respect of medicinal products between the UK and the EU. The Annex provides for mutual recognition of Good Manufacturing Practice (GMP) inspections and certificates, meaning that manufacturing facilities do not need to undergo duplicate inspections for the two markets. The Annex establishes a Working Group on Medicinal Products to deal with matters under the EU-UK Trade Agreement, facilitate co-operation and for the carrying out of technical discussions. It is expected that further bilateral discussions will continue with respect to regulatory areas not the subject of the EU-UK Trade Agreement, including pharmacovigilance. The EU-UK Trade Agreement also does not include reciprocal arrangements for the recognition of batch testing certification. The UK has listed approved countries, including the EEA which will enable UK importers and wholesales to recognize certain certification and regulatory standards. The UK has unilaterally agreed to accept EU batch testing and batch release for a period of at least two years until January 1, 2023. However, the EU continues to apply EU laws that require batch testing and batch release to take place in the EU territory. This means that medicinal products that are tested and released in the UK must be retested and re-released when entering the EU market for commercial use. As regards marketing authorizations, Great Britain has a separate regulatory submission process, approval process and a national markting authorization. Northern Ireland will, however, continue to be covered by the marketing authorizations granted by the European Commission.

The separate UK authorization system, albeit with transitional recognition procedures in the UK, will lead to additional regulatory costs. In addition, additional regulatory costs will be incurred with respect to the lack of mutual recognition of batch testing and related regulatory measures.

Foreign Regulation

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

Pharmaceutical Pricing and Reimbursement

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

Medicare is a U.S. federal government insurance program that covers individuals aged 65 years or older, as well as individuals of any age with certain disabilities, and individuals with End-Stage Renal Disease. The primary Medicare programs that may affect reimbursement for Akari are Medicare Part B, which covers physician services and outpatient care, and Medicare Part D, which provides a voluntary outpatient prescription drug benefit. Medicare Part B provides limited coverage of certain outpatient drugs and biologicals that are reasonable and necessary for diagnosis or treatment of an illness or injury. Under Medicare Part B, reimbursement for most drugs is based on a fixed percentage above the applicable product's average sales price, or ASP. Manufacturers calculate ASP based on a statutory formula and must report ASP information on a quarterly basis to the Centers for Medicare and Medicaid Services (CMS), the federal agency that administers Medicare and the Medicaid Drug Rebate Program. The current reimbursement rate for drugs and biologicals in both the hospital outpatient department setting and the physician office setting is ASP + 6%. The rate for the physician clinic setting is set by statute, but CMS has the authority to adjust the rate for the hospital outpatient setting on an annual basis. This reimbursement rate may decrease in the future. In both settings, the amount of reimbursement for a product's usage is updated quarterly based on the manufacturer's submission of new ASP information about its product or based on the submission of ASP information of each manufacturer that sells a product for which there are multiple competitors in that product market. On November 27, 2020, CMS issued an interim final rule (November 2020 IFR) setting prices for certain drugs based on prices paid in other nations. Under the November 2020 IFR, beginning on January 1, 2021 and extending until December 30, 2027, CMS would use a model called Most Favored Nation to allow Medicare to more closely align its Medicare payment amount for selected Part B drugs with prices paid in other nations. On December 28, 2020, the U.S. District Court for the Northern District of California issued a nationwide preliminary injunction enjoining the implementation of the November 2020 IFR. CMS, on February 28, 2022, formally rescinded the November 2020 IFR.

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

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

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

On November 27, 2020, the Centers for Medicaid and Medicare Services issued an interim final rule implementing a "Most Favored Nation" model for Medicare Part B drugs and biologicals (single source drugs, biologicals, and biosimilars). On December 28, 2020, the U.S. District Court for the Northern District of California granted temporary nationwide injunctions for the drug pricing model proposed to be effective January 1, 2021, precluding its implementation. CMS, on February 28, 2022, formally rescinded the November 2020 IFR. We are not able to state with certainty what the impact of these changes will have on our business with regard to these drug pricing initiatives.

As part of its reform of the 340B discount drug program, on October 31, 2018, the HRSA at HHS issued a notice of proposed rulemaking to move up the effective date of a final rule that would give HHS authority to impose Civil Monetary Penalties on pharmaceutical manufacturers who knowingly and intentionally charged a covered entity more than the statutorily allowed ceiling price for a covered outpatient drug. The final rule is intended to encourage compliance by manufacturers in offering the mandatory 340B ceiling purchase price to eligible purchasers, such as certain qualified health systems or individual hospitals.

Various states, such as California, have also taken steps to consider and enact laws or regulations that are intended to increase the visibility of the pricing of pharmaceutical products with the goal of reducing the prices at which we are able to sell our products. Because these various actual and proposed legislative changes are intended to operate on a state-by-state level rather than a national one, we cannot predict what the full effect of these legislative activities may be on our business in the future. Medicaid is a government health insurance program for low-income children, families, pregnant women, and people with disabilities. It is jointly funded by the federal and state governments, and it is administered by individual states within parameters established by the federal government. Coverage and reimbursement for drugs and biologics thus varies by state. Drugs and biologics may be covered under the medical or pharmacy benefit. State Medicaid programs may impose utilization management controls, such as prior authorization, step therapy, or quantity limits on drugs and biologics. Medicaid also includes the Medicaid Drug Rebate Program, under which, as a condition of coverage for our future products by the individual state Medicaid programs, we will be required to pay a retrospective rebate to each state Medicaid program for the quarterly utilization of our products by those respective state Medicaid programs we would be required to pay a rebate to each state Medicaid program for quantities of any future products that are dispensed to Medicaid beneficiaries and paid for by a state Medicaid program as a condition of having federal funds being made available to the states for any future products under Medicaid and Medicare Part B. Those rebates are based on pricing data that would be reported by us on a monthly and quarterly basis to CMS. These data include the average manufacturer price and the best price for each product we sell. As further described below under "U.S. Healthcare Reform and Other U.S. Healthcare Laws," the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, the PPACA, made significant changes to the Medicaid Drug Rebate Program that could negatively impact our results of operations.

Federal law requires that any company that participates in the Medicaid Drug Rebate Program also participate in the Public Health Service's 340B drug discounted pricing program in order for federal funds to be available for the manufacturer's drugs under Medicaid and Medicare Part B. The 340B pricing program requires participating manufacturers to agree to charge statutorily-defined covered entities no more than the 340B "ceiling price" for the manufacturer's covered outpatient drugs. These 340B covered entities include a variety of community health clinics and other entities that receive health services grants from the Public Health Service as well as hospitals that serve a disproportionate share of low-income patients. The 340B ceiling price is calculated using a statutory formula, which is based on the average manufacturer price and rebate amount for the covered outpatient drug as calculated under the Medicaid Drug Rebate Program. Changes to the definition of average manufacturer price and the Medicaid rebate amount under PPACA and CMS's issuance of final regulations implementing those changes also could affect the 340B ceiling price calculation for any future products and could negatively impact our results of operations. As described below under "U.S. Healthcare Reform and Other U.S. Healthcare Laws," PPACA expanded the 340B program to include additional types of covered entities but exempts "orphan drugs" designated under section 526 of the FDCA from the ceiling price requirements for these newly-eligible entities. CMS has also implemented new regulations that further define and further expand which health care provider entities are eligible to purchase approved drugs at the discounted 340B prices. As part of its reform of the 340B program, on October 31, 2018, the HRSA at HHS issued a notice of proposed rulemaking to move up the effective date of a final rule that would give HHS authority to impose Civil Monetary Penalties on pharmaceutical manufacturers who knowingly and intentionally charged a covered entity more than the statutorily allowed ceiling price for a covered outpatient drug.

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

Pursuant to the VHCA, knowing provision of false information in connection with a Non-FAMP filing can subject a manufacturer to significant civil monetary penalties for each item of false information.

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

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

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

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

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

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

In 2011, Directive 2011/24/EU was adopted at the EU level. This Directive concerns the application of patients' rights in cross-border healthcare. The Directive is intended to establish rules for facilitating access to safe and high-quality cross-border healthcare in the EU. Pursuant to Directive 2011/24/EU, a voluntary network of national authorities or bodies responsible for HTA in the individual EU Member States was established. The purpose of the network is to facilitate and support the exchange of scientific information concerning HTAs.

On December 13, 2021, a new Regulation on HTA on EU level was adopted, Regulation (EU) 2021/2282 of the European Parliament and of the Council of December 15, 2021 on health technology assessment and amending Directive 2011/24/EU (HTA Regulation).

With the "European Network for Health Technology Assessment, "EUnetHTA21" a consortium of thirteen EUnetHTA member organizations has now been commissioned to prepare the implementation of the EU HTA Regulation and thus the future binding joint HTA work.

The regulation covers new medicines and certain new medical devices, "providing the basis for permanent and sustainable cooperation at the EU level for joint clinical assessments in these areas." Member states will be able to use common HTA tools, methodologies and procedures across the EU, working together in four main areas: 1) joint clinical assessments focusing on the most innovative health technologies with the most potential impact for patients; 2) joint scientific consultations whereby developers can seek advice from HTA authorities; 3) identification of emerging health technologies to identify promising technologies early; and 4) continuing voluntary cooperation in other areas.

Individual member states will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technology, and making decisions on pricing and reimbursement.

The HTA Regulation was adopted and entered into force on January 11, 2022, and will become applicable three years later, i.e. on January 12, 2025.

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

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

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

- The federal civil False Claims Act, or FCA, prohibits, among other things, knowingly presenting, or causing to be presented claims for payment of government funds that are false or fraudulent, or knowingly making, using or causing to be made or used a false record or statement material to such a false or fraudulent claim, or knowingly concealing or knowingly and improperly avoiding, decreasing, or concealing an obligation to pay money to the federal government. This statute also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery. The FCA prohibits anyone from knowingly presenting, conspiring to present, making a false statement in order to present, or causing to be presented, for payment to federal programs (including Medicare and Medicaid) claims for items or services, including drugs, that are false or fraudulent, claims for items or services not provided as claimed, or claims for medically unnecessary items or services. This law also prohibits anyone from knowingly underpaying an obligation owed to a federal program. Increasingly, U.S. federal agencies are requiring nonmonetary remedial measures, such as corporate integrity agreements in FCA settlements. The U.S. Department of Justice announced in 2016 its intent to follow the "Yates Memo," taking a far more aggressive approach in pursuing individuals as FCA defendants in addition to the corporations. FCA liability is potentially significant in the healthcare industry because the statute provides for treble damages and mandatory penalties of $ 12,537to $25,076 per false claim or statement for penalties assessed after May 9, 2022. Government enforcement agencies and private whistleblowers have investigated pharmaceutical companies for or asserted liability under the FCA for a variety of alleged promotional and marketing activities, such as providing free product to customers with the expectation that the customers would bill federal programs for the product; providing consulting fees and other benefits to physicians to induce them to prescribe products; engaging in promotion for "off-label" uses; and submitting inflated best price information to the Medicaid Rebate Program.

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

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

- The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of, or payment for, healthcare benefits, items or services; similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

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

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

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

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

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

PPACA contains several provisions that have or could potentially impact our business. PPACA made significant changes to the Medicaid Drug Rebate Program. Effective March 23, 2010, rebate liability expanded from fee-for-service Medicaid utilization to include the utilization of Medicaid managed care organizations as well. With regard to the amount of the rebates owed, PPACA increased the minimum Medicaid rebate from 15.1% to 23.1% of the average manufacturer price for most innovator products; changed the calculation of the rebate for certain innovator products that qualify as line extensions of existing drugs; and capped the total rebate amount for innovator drugs at 100% of the average manufacturer price. In addition, PPACA and subsequent legislation changed the definition of average manufacturer price. In early 2016, CMS issued final regulations to implement the changes to the Medicaid Drug Rebate Program under PPACA, which became effective on April 1, 2016. Finally, PPACA requires pharmaceutical manufacturers of branded prescription drugs to pay a branded prescription drug fee to the federal government. Generally, a fee is imposed by the IRS on each manufacturer or importer of branded prescription drug sales of over $5 million to specific government programs, such as Medicare and Medicaid. Sales of "orphan drugs" are excluded from this fee. "Orphan drugs" are specifically defined for purposes of the fee. For each indication approved by the FDA for the drug, such indication must have been designated as orphan by the FDA under section 526 of the FDCA, an orphan drug tax credit under section 45C of the Internal Revenue Code must have been claimed with respect to such indication, and such tax credit must not have been disallowed by the IRS. Finally, the FDA must not have approved the drug for any indication other than an orphan indication for which a section 45C orphan drug tax credit was claimed (and not disallowed).

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

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

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

There is significant interest in the United States in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access, including increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices, particularly with respect to drugs that have been subject to relatively large price increases over relatively short time periods. There have been several recent U.S. Congressional inquiries and proposed bills designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. Although multiple bills to repeal or repeal and replace portions of the PPACA were introduced in 2017, none of these measures have successfully passed both houses of Congress. Congress may consider other legislation to repeal and replace elements of the PPACA or other health reform measures in the future. However, with the election of Joseph Biden and a change in control of the Senate, it is less likely that Congress will pass legislation to repeal and replace PPACA, but legislation to modify or expand PPACA may be considered.

Other Regulations

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

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

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

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

Legal Proceedings

We are not involved in any material legal proceedings.

Employees

As of December 31, 2022, we had 15 full-time employees.

C. Organizational Structure

Our corporate structure consists of Akari Therapeutics Plc and four subsidiaries, one of which is an indirect subsidiary. The following is a list of our subsidiaries:

Name of Subsidiary	Jurisdiction	Activity	% Holding
Volution Immuno Pharmaceuticals SA	Switzerland	Research & Development	100 %
Celsus Therapeutics Inc.	Delaware, USA	Research & Development	100 %
Morria Biopharma Ltd	Israel	Inactive	100 %
Akari Malta Limited	Malta	Research & Development	100 %

D. Property, Plant and Equipment

We do not currently own any property.

We currently lease office space in New York, New York on a short term basis for approximately $3,000 per month.

We also lease office space in London, England on a short-term basis for approximately $12,200 per month.

Item 4A. UNRESOLVED STAFF COMMENTS

None.

Item 5. OPERATING AND FINANCIAL REVIEW AND PROSPECTS

A. Operating Results

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our consolidated financial statements and related notes appearing elsewhere in this Annual Report on Form 20-F. In addition to historical information, this discussion and analysis contains forward-looking statements that involve risks, uncertainties and assumptions. Our actual results may differ materially from those anticipated in the forward-looking statements as a result of certain factors. We discuss factors that we believe could cause or contribute to these differences below and elsewhere in this report, including those set forth under Item 3D "Risk Factors" in this Annual Report on Form 20-F.

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 to eye, inhaled and intravitreous 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 the ticks 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, PNH, GBS 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, for the treatment of PNH in patients who have polymorphisms conferring Soliris(R) (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. We have also received Rare Pediatric Disease Designation from the FDA for the treatment of pediatric HSCT-TMA. The Rare Pediatric Disease Designation 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 or biologics license application for a rare pediatric disease may be eligible for a Priority Review Voucher, which is received concurrently with marketing approval as discussed further below.

Our clinical targets for nomacopan are autoimmune and inflammatory diseases where the inhibition of both C5 and LTB4 are implicated, including pediatric HSCT-TMA. We additionally have a pre-clinical program developing long-acting PASylated-nomacopan (PAS-nomacopan) for treatment of geographic atrophy (GA) secondary to dry age-related macular degeneration (dry AMD).

Impact of COVID-19 Outbreak

Public health epidemics or outbreaks could adversely impact our business. While the direct effects of the pandemic on our business have significantly lessened since the first quarter of fiscal year 2022 as a result of declining infection rates and the normalization of living with COVID-19 following the increase in accessibility to COVID-19 vaccines and antiviral treatments, the situation surrounding the COVID-19 pandemic, including the mutation of variants, continues to remain fluid globally. We cannot reasonably estimate with any degree of certainty any future impact of a resurgence of the COVID-19. Future pandemics may 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. Delays in our clinical trials would 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.

Results of Operations

For the Years Ended December 31, 2022 and December 31, 2021

Research and development expenses

Research and development expenses for the year ended December 31, 2022 were approximately $9,561,000 compared to approximately $9,133,000 for the year ended December 31, 2021, representing an increase of 5% or $428,000. The change was the net impact of multiple factors. Our research and development expenses increased due to the receipt of a lower tax credit in 2022 as compared to 2021 and increased maintenance and renewal costs for our patents. These increases were partially offset by decreases in staffing costs and decreases in clinical trial costs resulting from our decision to close the BP trial in August 2022.

We expect our clinical expenses including other research and development expenses to increase in the future as we plan to conduct additional trials to support the development of nomacopan, and advance PAS-nomacopan toward clinical development.

General and administrative expenses

General and administrative expenses for the year ended December 31, 2022 were approximately $13,527,000 compared to approximately $8,081,000 for the year ended December 31, 2021. This 67% or $5,446,000 increase was primarily due to increases in the following areas (i) $2,429,000 in payroll, sign-on incentives and stock-based compensation relating to new executives, including our CEO and COO, severance relating to our former CEO, and recruiting costs; (ii) $1,704,000 of issuance costs related to the September 2022 Registered Offering that were expensed due to liability classification for the September 2022 Warrants; (iii) $655,000 in consulting fees including outsourced services, strategic and expert advisors, communications / investor relations, and compliance; and (iv) $150,700 in insurance expenses.

Other Income (expenses)

Other income for the year ended December 31, 2022 was approximately $5,340,000 compared to other expense of $210,000 for the year ended December 31, 2021. This change was primarily attributed to (i) the September 2022 Warrants, which are accounted for as liabilities and whose fair value decreased by $6,946,000 between their issuance date and December 31, 2022; (ii) a positive foreign currency exchange impact of $646,000 as compared to the prior year; and (iii) an increase of $35,400 in interest income earned on higher cash balances as compared to the prior year, offset by $1,963,000 of expense recognized for the excess fair value of warrants issued over cash proceeds in connection with our September 2022 Registered Offering and an increase in New York City taxes of $112,800.

For the Years Ended December 31, 2021 and December 31, 2020

For a discussion of our results of operations for the year ended December 31, 2021, including a year-to-year comparison between 2021 and 2020, and a discussion of our liquidity and capital resources for the year ended December 31, 2021, refer to Item 5. “Operating and Financial Review and Prospects” in our Annual Report on Form 20-F for the year ended December 31, 2021.

B. Liquidity and Capital Resources

At December 31, 2022, we had $13.2 million in cash and an accumulated deficit in the amount of $217.5 million. Since inception, we have funded our operations primarily through the sale of equity securities.

In March 2023, we sold to certain accredited and institutional investors, led by our existing investors, including Dr. Ray Prudo, our Chairman, an aggregate of 26,666,667 ADSs in a registered direct offering, or the March 2023 Registered Offering, at $0.15 per ADS for aggregate gross proceeds of approximately $4.0 million. We also entered into a letter agreement with Paulson Investment Company, LLC, or the March 2023 Placement Agent, to serve as our placement agent in connection with this offering.

In September 2022, we sold to certain accredited and institutional investors, including our former Executive Chairman and current Chairman of the Board of Directors, Dr. Ray Prudo, an aggregate of 15,100,000 ADSs in a registered direct offering, or the September 2022 Registered Offering, at $0.85 per ADS for aggregate gross proceeds of approximately $12.8 million. In addition, we issued to the investors in a private placement that closed simultaneously with the September 2022 Registered Offering, the September 2022 Private Placement, and together with the September 2022 Registered Offering, (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, and we refer to the Series A and B warrants together as the September 2021 Warrants. The Series A warrants and Series B warrants became exercisable immediately following the date of issuance and 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 paid 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, for an aggregate of $1,000,700 in placement agent fees and expenses.

In March 2022, we sold to certain accredited and institutional investors, led by our existing investors, including Dr. Ray Prudo, our Chairman, an aggregate of 7,440,833 ADSs in a registered direct offering, or the March 2022 Registered Offering, at $1.20 per ADS for aggregate gross proceeds of approximately $8.9 million. We also entered into a letter agreement with Paulson Investment Company, LLC, or the March 2022 Placement Agent, to serve as our placement agent in connection with this offering. In connection with this offering, we issued to the investors and the March 2022 Placement Agent registered warrants to purchase 3,720,409 ADSs at $1.40 per ADS and 297,633 ADSs at $1.75 per ADS, respectively.

In December 2021, we sold to certain accredited and institutional investors, led by our existing investors, including Dr. Ray Prudo, our Chairman, an aggregate of 4,311,019 ADSs in a registered direct offering, or the 2021 Registered Offering, at $1.40 per ADS for aggregate gross proceeds of approximately $6.0 million, which closed on January 5, 2022. In connection with the offering, we issued to the investors and Paulson Investment Company, LLC, as placement agent, or the December 2021 Placement Agent, registered warrants to purchase 2,155,507 ADSs at $1.65 per ADS and 172,441 ADSs at $1.75 per ADS, respectively.

In July 2021, we sold to certain accredited and institutional investors, led by some of our existing investors, including Praxis Trustees Limited as trustee of Sonic Healthcare Holding Company EFRBS which is beneficially owned by Dr. Ray Prudo, our Chairman, an aggregate of 7,947,529 ADSs in a private placement, or the 2021 Private Placements, at $1.55 per ADS for aggregate gross proceeds of approximately $12.3 million. In connection with the offering, we issued to Paulson Investment Company, LLC, as placement agent, or the July 2021 Placement Agent, unregistered warrants to purchase 398,384 ADSs at $2.32 per ADS.

In June 2020, we entered into a Purchase Agreement with Aspire Capital, or the 2020 Purchase Agreement, which provided that, upon the terms and subject to the conditions and limitations set forth therein, Aspire Capital was committed to purchase up to an aggregate of $30.0 million of our ADSs during a 30 month period beginning on July 27, 2020. Prior to the 2020 Purchase Agreement's termination on January 27, 2023, we sold to Aspire Capital a total of approximately $8.0 million of ordinary shares. See "Aspire Capital Financing Arrangement below".

In February and March 2020, we sold to certain accredited and institutional investors, led by some of our existing investors, including Dr. Ray Prudo, our Chairman, an aggregate of 5,620,296 ADSs in a private placement, or the 2020 Private Placements, at $1.70 per ADS for aggregate gross proceeds of approximately $9.5 million. In connection with the offering, we issued to the investors and Paulson Investment Company, LLC, as placement agent, or the 2020 Placement Agent, unregistered warrants to purchase 2,810,136 ADSs at $2.20 per ADS and 449,623 ADSs at $2.55 per ADS, respectively.

As of April 28, 2023, we expect our existing cash, which includes net proceeds of $3.7 million received from the issuance of share capital in our March 2023 registered direct offering, will be sufficient to fund our operations through October 2023. We have experienced significant negative cash flows from operations since inception including net losses of $17.7 million, $17.4 million and $17.1 million for the years ended December 31, 2022, 2021 and 2020, respectively. We expect to incur substantial operating losses and negative cash flows from operations for the foreseeable future. To fund our future capital needs, we plan to raise additional funds through equity or debt financings or other sources, such as strategic partnerships, alliance and/or licensing arrangements, government grants and in the long term, proceeds from sales of commercial product.

Based on our recurring losses from operations incurred since inception, our expectation of continuing operating losses for the foreseeable future, negative operating cash flows for the foreseeable future, and the need to raise additional capital to finance its future operations, we have concluded that there is substantial doubt regarding our ability to continue as a going concern within one year after the date that these consolidated financial statements are issued. Because of these uncertainties, the accompanying consolidated financial statements have been prepared assuming that we will continue as a going concern, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business. As such, the accompanying consolidated financial statements do not reflect any adjustments relating to the recoverability and classification of recorded assets and liabilities that might be necessary if we are unable to continue as a going concern.

Aspire Capital Financing Arrangement

2020 Purchase Agreement

On June 30, 2020, we entered into the 2020 Purchase Agreement, which provided that, upon the terms and subject to the conditions and limitations set forth therein, Aspire Capital was committed to purchase up to an aggregate of $30.0 million of our ADSs, during a 30-month period beginning July 27, 2020, the effective date of a registration statement related to the transaction.

Under the 2020 Purchase Agreement, we had the right, in our sole discretion, to present Aspire Capital with a purchase notice, each, a Purchase Notice, directing Aspire Capital (as principal) to purchase up to 150,000 ADSs per business day and up to $30.0 million of our ADSs in the aggregate at a per share price, or the Purchase Price, equal to the lesser of:

1) the lowest sale price of our ADSs on the purchase date; or

2) the arithmetic average of the three (3) lowest closing sale prices for the ADSs during the ten (10) consecutive business days ending on the business day immediately preceding such Purchase Date (to be appropriately adjusted for any reorganization, recapitalization, non-cash dividend, stock split, reverse stock split or other similar transaction).

In addition, on any date on which we submitted a Purchase Notice to Aspire Capital in an amount of 150,000 ADSs, we also had the right, in its sole discretion, to present Aspire Capital with a volume-weighted average price purchase notice, each, a VWAP Purchase Notice, to direct Aspire Capital to purchase an amount of ADSs equal to up to 30% of the aggregate shares of our ADSs traded on our principal market on the next trading day, or the VWAP Purchase Date, subject to a maximum number of 250,000 ADSs. The purchase price per share pursuant to such VWAP Purchase Notice was generally 97% of the volume-weighted average price for our ADSs traded on our principal market on the VWAP Purchase Date.

The 2020 Purchase Agreement provided that we and Aspire Capital not effect any sales under the 2020 Purchase Agreement on any purchase date where the closing sale price of our ADSs was less than $0.25. Additionally, governing law in the United Kingdom, where we are incorporated, requires a minimum payment per ADS to be issued pursuant to a Purchase Notice equal to the nominal value of an ADS (i.e., £1). In accordance with ASC 815-40-15, *Determining Whether an Instrument (or Embedded Feature) Is Indexed to an Entity's Own Stock*, since the ultimate floor price which was effectively the nominal value of the ADS which was denominated in GBP at the time of entering into the 2018 Purchase agreement as well as the 2020 Purchase Agreement (together "the Purchase Agreements") prior to the 2020 Redenomination, the number of shares issuable under the contract was impacted by foreign currency, therefore ASC 815-40-15-7I precluded the Purchase Agreements from being indexed to our own stock. We determined that the right to sell shares to Aspire Capital under the Purchase Agreements represented a freestanding put option that met the criteria of a derivative pursuant to ASC 815 *Derivatives and Hedging*. Since the purchase price per share pursuant to the Purchase Agreements was at the market, we concluded that the put option had a fair value of zero, and therefore no additional accounting related to the put option was required.

In consideration for entering into the 2020 Purchase Agreement, we issued to Aspire Capital 40,760,900 ordinary shares, the 2020 Commitment Shares, which had a fair value of approximately $900,000. Because we determined that the 2020 Purchase Agreement was a freestanding put option derivative, we recorded the value of the 2020 Commitment Shares during the year ended December 31, 2020 in general and administrative expenses in the consolidated statements of operations and comprehensive loss.

Prior to the 2020 Purchase Agreement's termination on January 27, 2023, we sold to Aspire Capital a total of approximately $8.0 million of ordinary shares.

Cash Flows

Net cash used in operating activities was $21,505,000 during the year ended December 31, 2022 compared to $18,847,000 during the year ended December 31, 2021. Net cash flow used in operating activities was primarily attributed to our ongoing research activities to develop nomacopan, including manufacturing, clinical trial and preclinical activities, as well as our general and administrative expenses and the change in fair value of the September 2022 Warrants, which have been classified as liabilities. During the twelve months ended December 31, 2022, we received research and development tax credits in the amount of approximately $2,318,000 compared to research and development tax credits of approximately $3,067,000 during the twelve months ended December 31, 2021.

There was no net cash provided by or used in investing activities during the years ended December 31, 2022 and 2021.

Net cash provided by financing activities, after related expenses, was approximately $25,288,000 during the year ended December 31, 2022. This was primarily from net proceeds from our December 2021 Registered Direct Offering received in January 2022 in the approximate amount of $4,289,000, net proceeds from our March 2022 Registered Direct Offering in the approximate amount of $8,070,000 and gross proceeds from our September 2022 Registered Direct Offering in the amount of $12,835,000 (issuance costs associated with our September 2022 Registered Direct Offering were expensed as incurred).

Net cash provided by financing activities, after related expenses, was approximately $14,293,000 during the year ended December 31, 2021. This was from net proceeds from our 2021 Private Placements in the approximate amount of $11,179,000, issuance of shares to Aspire Capital under the Purchase Agreement in the approximate amount of $1,994,000 and proceeds received prior to closing in connection with the 2021 Registered Direct Offering of approximately $1,120,000 during the twelve months ended December 31, 2021.

Contractual Obligations

We do not have any significant contractual obligations as of December 31, 2022. We lease office space in London, UK and New York, NY on a short-term basis.

C. Research and Development, Patents and Licenses

Our research and development expenditures were approximately $9,561,000, $9,133,000 and $8,820,000 for the years ended December 31, 2022, 2021 and 2020 respectively. Most of such research and development expenditures were in the form of payments to third parties to carry out our manufacturing, pre-clinical and clinical research and development activities.

We incurred the following research and development expenses for the years ended December 31, 2022, 2021 and 2020:

	Years ended December 31, (in $000's)		
	2022	2021	2020
Direct Expenses:			
Nomacopan	$ 3,912	$ 3,970	$ 4,363
Clinical trials	4,414	4,517	4,281
Other	476	586	626
Total direct expenses	$ 8,802	$ 9,073	$ 9,270
Indirect Expenses:			
Staffing	2,086	2,267	2,348
Other indirect	991	860	574
Total indirect expenses	$ 3,077	$ 3,127	$ 2,922
Tax credits	(2,318)	(3,067)	(3,372)
Total Research and Development	$ 9,561	$ 9,133	$ 8,820

D. Trend Information

We are a clinical-stage drug development company and it is not possible for us to predict with any degree of accuracy the outcome of our research, development or commercialization efforts. As such, it is not possible for us to predict with any degree of accuracy any significant trends, uncertainties, demands, commitments or events that are reasonably likely to have a material effect on our net sales or revenues, income from continuing operations, profitability, liquidity or capital resources, or that would cause financial information to not necessarily be indicative of future operating results or financial condition. However, to the extent possible, certain trends, uncertainties, demands, commitments and events are identified in the preceding subsections of this Item 5.

E. Critical Accounting Estimates

We prepare our consolidated financial statements in accordance with U.S. GAAP. In doing so, we must make estimates and assumptions that affect our reported amounts of assets, liabilities and expenses, as well as related disclosure of contingent assets and liabilities. In some cases, we could reasonably have used different accounting policies and estimates. Changes in the accounting estimates are reasonably likely to occur from period to period. Accordingly, actual results could differ materially from our estimates. To the extent that there are material differences between these estimates and actual results, our financial condition or results of operations will be affected. Significant estimates include, but are not limited to, those related to stock-based compensation and fair value of warrants classified as liabilities. For further significant accounting policies please see Note 2 to our audited consolidated financial statements of this annual report. We believe that our accounting policies contained therein are critical in fully understanding and evaluating our financial condition and operating results.

Share-Based Compensation

We measure all stock-based awards granted to employees, directors and non-employees based on the estimated fair value on the date of grant and recognizes compensation expense of those awards over the requisite service period, which is generally the vesting period of the respective awards. Forfeitures are accounted for as they occur. We classify stock-based compensation expense in our consolidated statements of operations and comprehensive loss in the same manner in which the award recipient's payroll costs are classified or in which the award recipient's service payments are classified.

The fair value of each restricted ordinary share award is estimated on the date of grant based on the fair value of our ordinary shares on that same date. The fair value of each option grant is estimated on the date of grant using the Black-Scholes option pricing model, which requires inputs based on certain subjective assumptions, including the expected stock price volatility, the expected term of the award, the risk-free interest rate, and expected dividends. We estimate our expected stock price volatility based on the historical volatility of publicly traded peer companies. The expected term of our options has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is based on the fact that we have never paid cash dividends on ordinary shares and do not expect to pay any cash dividends in the foreseeable future.

Warrants issued in connection with the September 2022 Registered Direct Offering

On September 14, 2022, our sale of ADSs to accredited and institutional investors also included the issuance of Series A and Series B warrants. The Series A warrants allow the investors to purchase an aggregate of 15,100,000 ADSs at $0.85 per ADS. The Series A warrants are immediately exercisable and expire two years from issuance (September 14, 2024). The Series B warrants allow the investors to purchase an aggregate of 15,100,000 ADSs at $0.85 per ADS. The Series B warrants are immediately exercisable and expire seven years from issuance (September 14, 2029). The Series A warrants and the Series B warrants may be exercised on a cashless basis if six months after issuance there is no effective registration statement registering the ADSs underlying the warrants. Pursuant to the cashless exercise provision, the warrant holder must make an additional payment to us equal to the nominal value of an ADS (i.e., $0.0001) per warrant ADS to be issued pursuant to the cashless exercise.

We determined that the Series A and Series B warrants represent freestanding financial instruments because, based on the warrant term, their volatility input would preclude an option contract from being considered indexed to an entity's own stock. For this reason, the September 2022 Private Placement warrants are recorded as liability-classified instruments and recorded at fair value. Such warrants are remeasured to fair value at each reporting date until the warrant is exercised or expires. Changes in the fair value of the warrant liability are recognized in the consolidated statements of operations and comprehensive loss.

The fair value of the Series A and Series B warrants was determined using the Black-Scholes Option Pricing Model, which uses various assumptions, including (i) fair value of our ADS, (ii) exercise price of the warrant, (iii) expected term of the warrant, (iv) expected volatility and (v) expected risk-free interest rate.

Warrants issued in connection with the March 2022 Registered Direct Offering

In connection with the sale of the ADSs in the March 2022 Registered Direct Offering, we issued to the investors registered warrants to purchase an aggregate of 3,720,409 ADSs at $1.40 per ADS and we issued an aggregate of 297,633 ADS at $1.50 per ADS to the March 2022 Placement Agent, on the same terms. We determined that, at the time of their issuance, these warrants met the requirements for classification as equity under ASC 815-40-25. In connection with the March 2022 Registered Direct Offering, the costs directly attributable to realizing proceeds of issuing ADSs such as placement agent fees, commissions, legal and accounting fees pertaining to the financing and other external, incremental fees and expenses paid to advisors were recognized in additional paid-in capital of the Shareholders' Equity in the Consolidated Balance Sheets. At grant date on March 10, 2022, the fair value of these warrants was $3,693,622 and was recorded within additional paid-in capital of shareholders' equity.

Warrants issued in connection with the December 2021 Registered Direct Offering

In connection with the sale of the ADSs in the December 2021 Registered Direct Offering, we issued to investors registered warrants to purchase an aggregate of 2,155,507 ADSs, or the December 2021 Investor Warrants. The December 2021 Investor Warrants are immediately exercisable at an exercise price of $1.65 per ADS, subject to adjustment as set forth therein and will expire five years from issuance. We also issued registered warrants to the Placement Agent to purchase an aggregate of 172,441 ADSs, or theDecember 2021 Placement Agent Warrants, on the same terms as the December 2021 Investor Warrants, except that the December 2021 Placement Agent Warrants are exercisable at $1.75 per ADS. We have determined that, at the time of their issuance, the December 2021 Investor Warrants and the December 2021 Placement Agent Warrants, or, together, the December 2021 Warrants, met the requirements for classification as equity under ASC 815-40-25. In accordance with ASC 820, we measured the December 2021 Warrants at grant date fair value. The total grant date fair value of the December 2021 Warrants was $2,613,016 and was recorded within additional paid-in capital of shareholders' equity.

Warrants issued in connection with the 2021 Private Placements

In connection with the sale of the ADSs in the 2021 Private Placements, we issued unregistered warrants to the July 2021 Placement Agent to purchase an aggregate of 398,384 ADSs, or the 2021 Warrants. The 2021 Warrants are immediately exercisable at an exercise price of $2.32 per ADS, subject to adjustment as set forth therein and will expire five years from issuance. We determined that, at the time of their issuance, the 2021 Warrants met the requirements for classification as equity under ASC 815-40-25. In connection with the 2021 Private Placements, the costs directly attributable to realizing proceeds of issuing ADSs such as placement agent fees, commissions, legal and accounting fees pertaining to the financing and other external, incremental fees and expenses paid to advisors are recognized in additional paid-in capital of the Shareholders' Equity in the Consolidated Balance Sheets in accordance with ASC 814-40. At grant date on July 16, 2021, the fair value of the 2021 Warrants was $231,063 and was recorded within additional paid-in capital of shareholders' equity.

Warrants issued in connection with the 2020 Private Placements

In connection with the sale of the ADSs in the 2020 Private Placements, we issued to investors unregistered warrants to purchase an aggregate of 2,810,136 ADSs in a private placement, or the 2020 Investor Warrants. The warrants are immediately exercisable at an exercise price of $2.20 per ADS, subject to adjustment as set forth therein and will expire five years from issuance. We also issued unregistered warrants to the 2020 Placement Agent to purchase an aggregate of 449,623 ADSs, or 2020 Placement Agent Warrants, on the same terms as the 2020 Investor Warrants, except that the 2020 Placement Agent Warrants are exercisable at $2.55 per ADS. The total amount of warrants issued in connection with this private placement amounted to warrants to purchase an aggregate of 3,259,759 ADSs. 3,247,259 of these warrants were outstanding as of December 31, 2021. At grant date, the 2020 Investor Warrants and the 2020 Placement Agent Warrants, or, together, the 2020 Warrants were recorded as liability-classified awards and accounted for in accordance with ASC 815-40-25, *Accounting for Derivative Financial Instruments Indexed to, and Potentially Settled in, a Company's Own Stock* and ASC 815-40-15, *Determining Whether an Instrument (or Embedded Feature) Is Indexed to an Entity's Own Stock*. In accordance with ASC 820, we measured the 2020 Warrants at grant date fair value. The total grant date fair value of the 2020 Warrants was $2,749,369. We concluded that due to the 2020 Redenomination, the 2020 Warrants now meet the requirements for classification as equity under ASC 815-40-25 as of December 8, 2020, the date of the 2020 General Meeting. We updated the carrying amount of the warrant liability to its fair value on December 8, 2020, with any changes recorded in the consolidated statements of operations and comprehensive loss and then reclassed the warrant liability balance to additional paid in capital within shareholders' equity.

Commitment Shares issued in connection with the 2020 Purchase Agreement

In consideration for entering into the 2020 Purchase Agreement, we agreed to issue to Aspire Capital 40,760,900 ordinary shares (the "2020 Commitment Shares") which had a fair value of approximately $900,000. Since we have determined that the 2020 Purchase Agreement includes a freestanding put option that meets the criteria of a derivative in accordance with ASC 815-40-15, *Determining Whether an Instrument (or Embedded Feature) Is Indexed to an Entity's Own Stock*, we recorded the fair value of the 2020 Commitment Shares in general and administrative expenses in the consolidated statements of operations and comprehensive loss.

Functional Currency

Our functional currency is U.S. dollars as that is the primary economic environment in which we operate as well as the currency in which we have been financed.

Our reporting currency is U.S. dollars. We translate our non-U.S. operations' assets and liabilities denominated in foreign currencies into U.S. dollars at current rates of exchange as of the balance sheet date and income and expense items at the average exchange rate for the reporting period. Translation adjustments resulting from exchange rate fluctuations are recorded as foreign currency translation adjustments, a component of accumulated other comprehensive loss. Gains or losses from foreign currency transactions are included in foreign currency exchange gains/(losses).

Item 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES

A. Directors and Senior Management

The following table presents the names of the current members of our board of directors and executive officers as of the date of this Annual Report on Form 20-F.

Name	Age	Position
James Hill, M.D.	77	Class A Director
Stuart Ungar, M.D.	79	Class A Director
David Byrne	63	Class A Director
Donald Williams	64	Class A Director
Michael Grissinger	69	Class A Director
Rachelle Jacques	51	Class B Director — President and Chief Executive Officer
Ray Prudo	78	Class C Director — Chairman of the Board(1)
Dr. Torsten Hombeck	53	Chief Financial Officer
Melissa Bradford-Klug	53	Chief Operating Officer
Miles Nunn	54	Chief Scientific Officer
John Neylan, M.D.	70	Chief Medical Officer

(1) Dr. Prudo served as Executive Chairman of our board of directors from September 2015 until December 2022. Dr. Prudo assumed the role of Chairman of our board of directors effective January 1, 2023.

Biographical information of the members of our board of directors and executive officers is set forth below.

James Hill, M.D., age 77, has served as a member of our board of directors since September 2015. Prior to joining our board of directors, Dr. Hill was a non-executive director and Chairman of Genetix Group Plc from 2001 to 2009, an AIM listed company providing scientists with intelligent solutions for cell imaging and analysis. Previously Dr. Hill was a director and Senior Vice President of Corporate Affairs with SmithKline Beecham, from 1994 to 2001, with global responsibility for Investor Relations, Government Affairs, Communication and was a member of the corporate management team which oversaw corporate strategy. Dr. Hill's prior experience was in the field of strategic product development working closely with research and development and the global markets. Dr. Hill qualified in medicine at Guy's Hospital and became a fellow of the Royal Colleges of Physicians in both London and Edinburgh and was earlier awarded a Hunterian Professorship by the Royal College of Surgeons in England.

Stuart Ungar, M.D., age 79, has served as a member of our board of directors since September 2015. After pursuing post-graduate studies in Internal Medicine and research in neuro-pharmacology at the Royal Post-Graduate Medical School, UK, Dr. Ungar was in practice as an Internist at The Princess Grace Hospital, London. Following fifteen years of practice he, jointly with Dr. Raymond Prudo, founded The Doctors Laboratory PLC, a general pathology laboratory, which provided analytical services to clinicians and pharmaceutical organizations throughout the United Kingdom and abroad. During his tenure as Chairman and Board Director, The Doctors Laboratory PLC grew from a start-up to become one of the largest pathology laboratories in the United Kingdom. It was sold to Sonic Healthcare, a quoted Australian PLC in 2002. Dr. Ungar studied medicine and biochemistry in the University of London at the Royal Free Hospital School of Medicine. As a post-graduate he was admitted to the Royal College of Physicians of the United Kingdom. Dr. Ungar is a Life Fellow of the Royal Society of Medicine and a founder and former Vice-President of the Independent Doctors Federation. Dr. Ungar is a non-executive director of Pharmacierge Ltd., a private company providing prescription dispensing services to the public.

David Byrne, age 63, has served as a member of our board of directors since April 2016. Mr. Byrne is currently Group Chief Executive Officer of Sonic Healthcare UK Group, the United Kingdom's largest NGO clinical diagnostics organization, a position that he has held since 1997. Mr. Byrne is also the CEO of The Doctors Laboratory which is a subsidiary of Sonic. Mr. Byrne also currently serves as a Main Board Director for CIS Healthcare Limited and served as a Main Board Finance Director for Clinisys Solutions Ltd from 2000 to 2007. He is a UK Chartered Certified Accountant with over 25 years' experience in corporate finance and developing early stage biotechnology and medical services companies.

Donald Williams, age 63, has served as a member of our board of directors since June 2016 and is an "audit committee financial expert". Mr. Williams is a 35-year veteran of the public accounting industry who retired in 2014. Mr. Williams spent 18 years as a partner at Ernst & Young and the last seven years as a partner at Grant Thornton. During the last seven years at Grant Thornton, he served as the National Leader of Grant Thornton's Life Sciences Practice and the Managing Partner of the San Diego Office. He was the lead partner for both Ernst & Young and Grant Thornton on multiple initial public offerings, secondary offerings, and private and public debt financings, as well as numerous mergers and acquisitions. Mr. Williams serves as a director of Forte Biosciences, Inc. (NASDAQ: FBRX), Impedimed Limited (XASX: IPD), Palisade Bio, Inc. (NASDAQ: PALI), and Monia Cap. Mr. Williams is a graduate of Southern Illinois University with a B.S. degree.

Michael Grissinger, age 69, has served as a member of our board of directors since January 2018. Mr. Grissinger spent 22 years at Johnson & Johnson, retiring in 2018. During his Johnson and Johnson tenure, Mr. Grissinger served in a variety of senior-level management roles including Vice President- Corporate Development, Vice President- Worldwide Business Development & Licensing and Vice President and Head- Mergers & Acquisitions for the pharmaceuticals group. Prior to Johnson & Johnson, Mr. Grissinger spent 12 years at Ciba-Geigy in finance, marketing, and business development roles. In addition to Akari, Mr. Grissinger also serves as a member of the board of directors of Aprea Therapeutics, Inc. (NASDAQ: APRE), Atriva Therapeutics and Kira Biotech. Mr. Grissinger holds a B. Sc. in Chemistry from Juniata College and an MBA from Temple University- Fox School of Business.

Rachelle Jacques, President and Chief Executive Officer, age 51, has served as our President and Chief Executive Officer and a member of our board of directors since March 2022. Before joining the Company, Ms. Jacques served as Chief Executive Officer of Enzyvant Therapeutics Inc., a commercial-stage biotechnology company developing transformative regenerative therapies for rare diseases. Prior to Enzyvant, she served as the Senior Vice President and Global Complement Franchise Head at Alexion Pharmaceuticals, Inc., where she was responsible for global franchise strategy development and execution of the C5 complement inhibitors, eculizumab and ravulizumab, across the therapeutic areas of hematology, nephrology and neurology. She was Vice President of U.S. Hematology Marketing at Baxalta Inc. and then Shire plc, following Shire's acquisition of Baxalta in 2016. At Baxalta, she served as Vice President of Business Operations after its spinoff from Baxter International Inc. Ms. Jacques held multiple leadership positions at Baxter, including Vice President of Finance, U.S. BioScience Business. Earlier in her career, Ms. Jacques served in various roles at Dow Corning Corporation, including operational management positions in the U.S., Europe, and China. She serves on the boards of directors of uniQure N.V. (NASDAQ: QURE) and Corbus Pharmaceuticals (NASDAQ: CRBP) and is a founding member of the Alliance for Regenerative Medicine (ARM) Action for Equality Task Force. Ms. Jacques received her B.A. in business administration from Alma College and is currently a member of the school's Board of Trustees.

Raymond Prudo-Chlebosz, M.D., Chairman of the Board, age 78, served as our Executive Chairman from September 2015 through December 2022. Effective January 1, 2023 Dr. Prudo began serving as the Chairman of our board of directors. Dr. Prudo has been an active investor and developer of healthcare companies for 25 years. Dr. Prudo was the Founder, Chairman, and Chief Executive Officer of Volution and its predecessor company, Varleigh Immuno Pharmaceuticals, since its inception in 2008. He is currently a board member of several UK healthcare companies. Dr. Prudo holds an MBBS from the University of London, and an FRCP(C) from the Royal College of Physicians and Surgeons of Canada.

Dr. Torsten Hombeck, age 53, has served as our Chief Financial Officer since June 2020. Dr. Hombeck has extensive experience in the biotechnology industry, finance, capital markets and M&A transactions as well as clinical and commercial drug development and regulatory filings. His previous positions include Chief Commercial and Strategy Officer and Managing Director at Promethera Biosciences, a private biopharmaceutical company, and Co-Chief Executive Officer and Chief Business Officer at Cytonet, where he played an integral role in its acquisition by Promethera in 2016. Dr. Hombeck also served as Chief Financial Officer at both Agennix and GPC Biotech. He holds a Masters in Business Administration and a Ph.D. in Finance.

Melissa Bradford-Klug, age 53, has served as our Chief Operating Officer since July 2022. She brings significant biotechnology experience, strategy, business development, and in public and private financing. Since January 2020, she has served President and Chief Business Officer of RareStone Inc., a private venture backed rare disease company focused on creating a portfolio of products for the Chinese market through in-licensing, co-development and joint ventures with European and US biotechnology companies. Melissa has extensive experience in strategy and corporate development, spending the last twenty years in strategy, financial planning, and business development roles at private and public companies. She has experience in mergers and acquisitions, cross-border licensing and divestments. From April 2019 to December 2019, she served as co-founder and CEO of Mayfield Pharmaceuticals, a private women's healthcare company leading the Series A financing for the company created by Harrow Health (NASDAQ: HROW). From December 2016 to December 2018, she divided her time between corporate strategy, financial planning, and business development as Chief Business Officer at Keryx Biopharmaceuticals (NASDAQ: KERX), where led the successful merger with Akebia Pharmaceuticals (NASDAQ: AKBA) that closed in December 2018. From June 2014 to December 2016, she served as Senior Vice President, Strategy and Business Development at AMAG Pharmaceuticals (NASDAQ: AMAG) focusing on the diversification of the company's portfolio through business development and mergers and acquisitions to become a leading women's health company. She executed over $1.4 billion in M&A to reshape AMAG's portfolio and was key member of the financing team to secure $800 million in equity and debt funding and ratings agency accreditation. From 2004-2014, Melissa was the Vice President of Corporate Development & Strategy at Mallinckrodt Pharmaceuticals (NYSE: MNK), formerly Covidien (NYSE:COV). She played a key role in the spin-out of Mallinckrodt to public listing on the New York Stock Exchange. She executed over $700 million of licensing, acquisition and carve out business unit and product divestments that revitalized Mallinckrodt's portfolio. Melissa has experience across a variety of functions including research and development, marketing, business development and finance in various roles at Baxter, Eli Lilly, Monsanto, and G.D. Searle. Ms. Bradford Klug received an M.B.A. in Finance from DePaul University and a B.S. in chemistry from Maryville University. She has completed executive education courses at Kellogg and Harvard Business School and Harvard Public Health. She serves on the board of directors of Massachusetts Biotechnology Council and is a founding member of Boston's Chief Business Officer networking association.

Dr. Miles Nunn, age 54, has served as our Chief Scientific Officer since September 2015. Dr. Nunn served as Chief Scientific Officer for Volution from November 2014 to September 2015. From June 2009 to July 2010 and November 2013 to November 2014, Dr. Nunn served as a consultant to Varleigh Immuno Pharmaceuticals, or Varleigh. Dr. Nunn has worked in the biotechnology industry for over 20 years and is the inventor of our lead drug, nomacopan. Prior to working for Volution and Varleigh, Dr. Nunn was Head of Research at Evolutec Group Limited, a biotech spin out from the Natural Environment Research Council (NERC), where he was employed as a Senior Scientific Officer and Principal Investigator. Dr Nunn holds a D.Phil. in Biochemistry from Oxford University and M.Sc. in Biotechnology and Molecular Biology from University College London.

Dr. John Neylan, age 70, has served as our Chief Medical Officer since November 2022. Prior to joining the Company, he was Executive Vice President, Chief Medical Officer and Head of Research for Angion Biomedica Corporation (Nasdaq: ANGN), where he led the development of therapies for chronic fibrotic conditions of the lung and kidney, and acute organ injuries. Dr. Neylan previously held a number of leadership roles in the biotechnology and pharmaceutical industry, working in clinical research for over twenty years. Prior to joining the private sector, Dr. Neylan spent 12 years in academic medicine, including as the Professor of Medicine at Emory University and Medical Director of the Emory Renal Transplant Program. He also previously served as President of the American Society of Transplantation and was a member of multiple FDA advisory committees. After completing his Internal Medicine residency at Vanderbilt University, Dr. Neylan completed a clinical fellowship in Nephrology and a research fellowship in Transplantation and Immunogenetics at Brigham & Women's Hospital. Dr. Neylan holds a B.S. from Duke University and an M.D. from Rush Medical School.

Director or Officer Involvement in Certain Legal Proceedings

Our directors and executive officers were not involved in any legal proceedings as described in Item 401(f) of Regulation S-K in the past ten years, other than the fact that Mr. Williams had served as a member of the Board of Directors of Proove Biosciences, Inc., a private company, from January 2015 until May 2017, which entity went into receivership in approximately September 2017.

B. Compensation

Summary Compensation Table

The following table shows the compensation paid or accrued during the last two fiscal years ended December 31, 2022 and 2021 for our senior executive officers.

Name and Principal Position	Year	Salary ($)	Bonus ($)	Stock Awards ($) [1]	Option Awards ($) [2]	Non-Equity Incentive Plan Compensation ($)	Nonqualified Deferred Compensation Earnings ($)	All Other Compensation ($) [3]	Total ($)
Ray Prudo, Former Executive Chairman(4)	2022	412,000	206,000	—	—	—	—	—	618,000
	2021	412,000	206,000	—	—	—	—	—	618,000
Rachelle Jacques President and Chief Executive Officer(5)	2022	458,333	875,000	253,410	1,965,991	—	—	49,865	3,602,600
	2021	—	—	—	—	—	—	—	—
Clive Richardson, Former Chief Executive Officer and Chief Operating Officer(6)	2022	118,195	657,764	—	—	—	—	317,175	1,093,134
	2021	525,981	206,826	—	—	—	—	86,066	818,873
Torsten Hombeck Chief Financial Officer(7)	2022	300,150	72,036	—	32,448	—	—	44,111	448,744
	2021	290,000	137,000	—	38,118	—	—	27,885	493,003

(1) This amount represents the fair value of restricted stock units on the date of grant.

(2) These amounts represent the aggregate grant date fair value for option awards for fiscal years 2022 and 2021, respectively, computed in accordance with FASB ASC Topic 718. A discussion of the assumptions used in determining grant date fair value may be found in our Financial Statements, included in our Annual Report on Form 20-F for the years ended December 31, 2022 and 2021.

(3) Consists of company contributions to a 401K plan or pension scheme, amounts accrued for paid leave and Mr. Richardson's consulting compensation.

(4) Dr. Prudo served as Executive Chairman of our board of directors from September 2015 until December 2022, and assumed the role of Chairman of the Board effective January 1, 2023.

(5) Ms. Jacques was appointed our President and Chief Executive Officer in March 2022. Ms. Jacques received a sign-on bonus in the amount of $650,000.

(6) Mr. Richardson resigned as Chief Executive Officer and Chief Operating Officer in March 2022. Mr. Richardson received cash severance of approximately $658,000. In addition, we entered into a consulting agreement with Mr. Richardson, in which Mr. Richardson earned approximately $305,000, which is presented as other compensation.

(7) Dr. Hombeck was appointed as our Chief Financial Officer in June 2020.

Narrative Disclosure to Summary Compensation Table

Ray Prudo. On September 21, 2015, in connection with the Acquisition, we entered into an agreement with our Chairman (and former Executive Chairman from September 2015 through December 2022) and director, Ray Prudo. The agreement was effective as of September 18, 2015 until December 2022. Under the agreement, Dr. Prudo held office as Executive Chairman and Class C Director for a three-year term and thereafter provided he will seek reappointment in accordance with our Articles of Association. Dr. Prudo's appointment was subject to early termination in accordance with the Articles of Association or if he ceases to be a director.

Dr. Prudo's annual salary was $412,000 beginning January 1, 2020 through his resignation as Executive Chairman. Under the agreement, Dr. Prudo was required to maintain the confidentiality of our confidential information.

In a separately entered into agreement with Dr. Prudo on September 2015, Dr. Prudo was entitled to an additional cash payment each calendar year in the discretion of our board of directors based on Dr. Prudo's performance. Dr. Prudo's annual cash bonus was set at 50% of base salary for the year ended December 31, 2022.

On March 1, 2023, we entered into an agreement with Dr. Prudo, which was affective as of January 1, 2023. Under this 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.

Rachelle Jacques. On March 2, 2022, we entered into an executive employment agreement with our President and Chief Executive Officer, Rachelle Jacques. The employment agreement is effective as of March 28, 2022 and shall continue in effect until terminated by either party upon at least thirty days' prior written notice.

Ms. Jacques current annual base salary is $600,000, beginning on March 28, 2022. Ms. Jacques is also entitled to (i) an annual cash bonus with a target of 50% of base salary, provided that the actual amount of such bonus shall be based on the achievement of performance goals established by the executive chairman of the Board and the Board and (ii) commencing with annual long-term incentive awards to senior executives in 2023, an award under the Company's equity incentive plan not less frequently than annually with a target grant value of 100% of Ms. Jacques's annual base salary in 2023 and thereafter otherwise commensurate with awards to executives in similarly situated companies as recommended by a reputable compensation consultant engaged by the Board. Any cash bonus for a year in which Ms. Jacques is employed for less than the full year will be prorated. The Employment Agreement also provides that Ms. Jacques is entitled following the Start Date to (i) if such start date is on or before March 28, 2022, (x) a one-time cash bonus of $650,000, which is subject to partial repayment in the event that Ms. Jacques's employment is terminated by her without good reason or by the Company for cause in the first two years and (y) restricted stock units having a value, on the basis of the last closing price of an ADS on Nasdaq before her start date, of $262,000 and (ii) a stock option to purchase an amount of ordinary shares in the Company (which may be held through ADSs) equal to 4% of the Company's issued share capital on her start date under the Company's Amended and Restated 2014 Equity Incentive Plan. The option will have a term of ten years with an exercise price equal to the closing price of the grant date and will vest ratably on an semiannual basis over four years, beginning on the grant date, subject to customary provisions pertaining to Ms. Jacques's continued employment with the Company (including in the event of a change of control) and disability or

death. Additionally, Ms. Jacques shall be entitled to receive restricted stock units having a value, on the basis of the last closing price of an ADS on Nasdaq before the respective anniversary date, of $446,000 on each of the first and second anniversaries of the Start Date. All of the above restricted stock unit awards will vest over two-year periods; in the event of a change of control, involuntary termination without cause, resignation for good reason or termination due to death or disability, vesting of these awards will be fully accelerated or, if they have not yet been granted, Ms. Jacques will receive a cash lump payment equal to their value.

Upon termination of Ms. Jacques's employment by the Company for cause or by Ms. Jacques without good reason or in the case of Ms. Jacques's disability or death, she shall be entitled to any accrued but unpaid base salary, expense reimbursement and vested and accrued benefits. Additionally, in the case of Ms. Jacques's death or disability, Ms. Jacques or her estate or beneficiaries shall be entitled to receive (i) any unpaid annual bonus relating to the previous year and (ii) the target annual performance bonus to which Ms. Jacques might have been entitled for the year in which the employment terminates on a pro rata basis based on number of days employed.

Upon termination of Ms. Jacques's employment without cause, or by Ms. Jacques for good reason, in addition to any accrued but unpaid base salary, expense reimbursement and vested and accrued benefits, she shall be entitled to receive (i) the sum of the annual base salary and target annual performance bonus in effect for the year in which the date of Ms. Jacques's termination occurs, (ii) any unpaid annual bonus relating to the previous year and (iii) the target annual performance bonus to which Ms. Jacques might have been entitled for the year in which the employment terminates on a pro rata basis based on number of days employed. In any such instance of termination, Ms. Jacques shall also be entitled to reimbursement for any monthly COBRA premium paid by Ms. Jacques on her behalf and on behalf of her dependents until the earliest of (i) 12 months following the date of termination, (ii) the date on which Ms. Jacques is no longer eligible to receive such coverage, and (iii) the date on which Ms. Jacques becomes eligible to receive similar coverage from another employer or other source.

Upon termination of Ms. Jacques's employment by us without cause or by Ms. Jacques for good reason within eighteen months of a change of control, in addition to any accrued but unpaid base salary, expense reimbursement and vested and accrued benefits, she shall be entitled to receive an amount equal to (i) the sum of the annual base salary and target annual performance bonus in effect for the year in which the date of Ms. Jacques's termination occurs (or, if greater, the previous year), (ii) any unpaid annual bonus relating to the previous year and (iii) the target annual performance bonus to which Ms. Jacques might have been entitled for the year in which the employment terminates (or, if greater, the previous year). In such instance of termination, Ms. Jacques shall also be entitled to reimbursement for any monthly COBRA premium paid by Ms. Jacques on her behalf and on behalf of her dependents until the earliest of (i) 12 months following the date of termination, (ii) the date on which Ms. Jacques is no longer eligible to receive such coverage, and (iii) the date on which Ms. Jacques becomes eligible to receive similar coverage from another employer or other source.

The employment agreement also contains restrictive covenants for the Company's benefit and Ms. Jacques is required to maintain the confidentiality of our confidential information.

Clive Richardson. On September 21, 2015, in connection with the Acquisition, we entered into an executive employment agreement with our Chief Operating Officer and director, Clive Richardson. Mr. Richardson departed as Chief Executive Officer and Chief Operations Officer in March 2022.

Mr. Richardson's most recent base salary was $525,981. Mr. Richardson was also entitled to an annual cash bonus with a target of 40% of base salary, provided that the actual amount of such bonus may be greater or less that the target amount. The employment agreement also provided that Mr. Richardson was entitled to a stock option grant to purchase 16,271,850 ordinary shares (equivalent to 162,718 ADSs). This option was granted under our 2014 Plan on September 21, 2015, had a ten-year term, exercisable at a price equal to $0.3221 per share (or $32.21 per ADS) and vested ratably on a semi-annual basis over four years, with a minimum 25% vesting, subject to acceleration in the case of change of control or non-renewal of the employment agreement.

Mr. Richardson entered into a settlement agreement in connection with his separation from the Company in April 2022, which provided that Mr. Richardson receive £535,228 (representing approximately $699,542 as of the date of the settlement agreement) in installments through March 2023 in lieu of the severance payment contemplated by his executive employment agreement. In such settlement agreement Mr. Richardson agreed to work for the Company as a consultant for one year following his departure. Mr. Richardson's options continued to vest according to their applicable vesting schedules and the exercise period of such options was extended to end no earlier than one unrestricted year after termination of his consultancy in April 2023. At the end of Mr. Richardson's consultancy in April 2023 he was given the opportunity to exercise all unexercised options.

Torsten Hombeck. On June 30, 2020, we entered into an executive employment agreement with our Chief Financial Officer, Torsten Hombeck. The employment agreement was effective as of June 30, 2020 and has a term of one year from June 30, 2020 with automatic renewals for successive one-year periods. Either party may give written notice of non-renewal of the current term at least three months prior to the expiration of the current term.

Dr. Hombeck's current annual base salary is $300,150, beginning January 1, 2022. Dr. Hombeck is also entitled to an annual cash bonus with a target of 30% of base salary, provided that the actual amount of such bonus may be greater or less that the target amount. The employment agreement also provides that Dr. Hombeck is entitled to a stock option grant to purchase 7,000,000 ordinary shares (equivalent to 70,000 ADSs). This option was granted under our 2014 Plan on June 30, 2020, has a ten-year term, is exercisable at a price equal to $0.0218 per share (or $2.18 per ADS) and vests ratably on a semi-annual basis over four years, provided that Dr. Hombeck remains employed with the Company, subject to acceleration in the case of change of control or non-renewal of the employment agreement. Dr. Hombeck additionally received a stock option grant to purchase 3,000,000 Ordinary Shares (equivalent to 30,000 ADSs) consistent with the aforementioned terms on January 1, 2021.

Upon termination of Dr. Hombeck's employment by the Company for cause or by Dr. Hombeck without good reason or in the case of Dr. Hombeck's disability or death or by non-renewal by Dr. Hombeck, then he shall be entitled to any accrued but unpaid base salary, expense reimbursement and vested and accrued benefits.

Upon termination of Dr. Hombeck's employment without cause, or by Dr. Hombeck for good reason or upon non-renewal by the Company of the term, in addition to any accrued but unpaid base salary, expense reimbursement and vested and accrued benefits, he shall be entitled to receive (a) prior to July 1, 2021, an amount equal to 50% of the sum of (i) 12 months of base salary in effect before the employment terminates, plus (ii) the target annual performance bonus to which Dr. Hombeck may have been entitled for the year in which the employment terminates and (b) after July 1, 2021, an amount equal to the sum of (i) 12 months of base salary in effect before the employment terminates, plus (ii) the target annual performance bonus to which Dr. Hombeck may have been entitled for the year in which the employment terminates; provided further that, (x) in the event of non-renewal of the term, such performance bonus is not owed unless termination occurs within one year of a change in control and (y) in the event that such termination occurs within one year of a change of control, the aforementioned sums in either clause (a) or (b) shall be multiplied by 1.5 times. In each such instance of termination, Dr. Hombeck shall also be entitled to an amount equal to the Company's share of the medical insurance premium that the Company pays for Dr. Hombeck under its health care plan for 12 months (18 months in the event of a change of control) following the date of termination and Dr. Hombeck's employment.

The employment agreement also contains restrictive covenants for our benefit and Dr. Hombeck is required to maintain the confidentiality of our confidential information.

Outstanding Equity Awards at Fiscal Year-End

The following table provides information regarding all outstanding equity awards for (1) our President and Chief Executive Officer, (2) our Chief Financial Officer as of December 31, 2022 and (3) our former Chief Executive Officer and Chief Operating Officer:

	Option Awards[1]					Stock Awards			
Name	Number of Securities Underlying Unexercised Options (#) Exercisable[(1)]	Number of Securities Underlying Unexercised Options (#) Unexercisable[(1)]	Equity Incentive Plan Awards: Number of Securities Underlying Unexercised Unearned Options (#)	Option Exercise Price ($)	Option Expiration Date	Number of Shares or Units of Stock That Have Not Vested (#) [(4)]	Market Value of Shares or Units of Stock that Have Not Vested ($) [(5)]	Equity Incentive Plan Awards; Number of Unearned Shares, Units or Other Rights that Have Not Vested (#)	Equity Incentive Plan Awards; Market or Payout Value of Unearned Shares, Units or Other Rights that Have Not Vested ($)
Rachelle Jacques	3,720,287 [(2)]	26,042,013 [(2)]	—	$ 0.0124	3/28/2032				
	25,954,300 [(3)]	181,680,100 [(3)]	—	$ 0.0124	3/28/2032				
						21,475,400	10,093,438	—	—
Dr. Torsten Hombeck	1,500,000 [(6)]	1,500,000 [(6)]	—	$ 0.0181	12/31/2030				
	4,375,000 [(7)]	2,625,000 [(7)]	—	$ 0.0218	6/30/2030				
	— [(8)]	10,000,000 [(8)]	—	$ 0.0132	2/3/2032				
	— [(9)]	10,000,000 [(9)]	—	$ 0.0047	10/31/2032				
Clive Richardson	4,500,000 [(10)]	— [(10)]	—	$ 0.035992	9/1/2027				
	20,000,000 [(11)]	— [(11)]	—	$ 0.0187	8/15/2028				

(1) Amounts represent options to purchase ordinary shares.

(2) These options were granted on July 29, 2022, have a ten-year term and vest semi-annually over a four-year period.

(3) These options were granted on June 1, 2022, have a ten-year term and vest semi-annually over a four-year period.

(4) The grant is a restricted stock award that vests 1/2 on June 1, 2023, and then in equal monthly installments thereafter.

(5) Based on AKTX's closing share price of $0.47 on December 31, 2022.

(6) These options were granted on January 4, 2021, have a ten-year term and vest semi-annually over a four-year period.

(7) These options were granted on June 30, 2020, have a ten-year term and vest semi-annually over a four-year period.

(8) These options were granted on February 3, 2022, have a ten-year term and vest annually over a four-year period.

(9) These options were granted on October 31, 2022, have a ten-year term and vest annually over a four-year period.

(10) These options were granted on September 1, 2017, have a ten-year term and vest annually over a four-year period.

(11) These options were granted on August 15, 2018, have a ten-year term and vest annually over a four-year period.

Director Compensation

Our director compensation program is administered by our board of directors with the assistance of the compensation committee. The compensation committee conducts an annual review of director compensation and makes recommendations to the board with respect thereto.

The shareholders approved our Directors Remuneration Policy on June 30, 2020 to provide a framework for the Director's compensation package. In addition, the Company has a non-employee director compensation policy, which was amended and restated on November 19, 2015 and was subsequently amended on June 29, 2016, January 26, 2017, January 23, 2018, January 8, 2019 and on January 9, 2020. On December 10, 2021, our board resolved that the cash compensation and committee membership fees would remain the same in 2022 as they were for 2021. As a result, our non-employee directors were compensated for service on our board of directors as follows in 2022:

- an annual retainer for service on the board of directors of $39,338;
- an annual retainer for service as a member of the compensation committee and nominating and governance committee of $5,305;
- an annual retainer for service as a member of the audit committee of $7,500;
- for the chairman of the compensation committee, and nominating and governance committee, an annual retainer of $10,609;
- for the chairperson of the audit committee, an annual retainer of $17,500;
- for service on the board, an annual grant of a stock option to purchase 1,300,000 ordinary shares (equivalent to 13,000 ADSs) or Annual Stock Option; the grant is made each year on the date of the Company's annual general meeting of shareholders, or AGM, on the date of the first meeting of the board held following the AGM, or on any date following such AGM as may be recommended by the compensation committee and approved by the Board, and for 2022 the Annual Stock Option was granted on June 30, 2022, the date of the 2022 AGM, vest on the date of the 2023 AGM and are exercisable at a price of $0.01 per ordinary share (equivalent to an exercise price of $1.00 per ADS);
- for continued service on the board, a one-time stock option award to purchase 3,700,000 shares (equivalent to 37,000 ADSs), or the October 2022 NED Stock Option, which grant was made on October 21, 2022, and such options vest on the date of the 2023 AGM and are exercisable at a price of $0.0048 per ordinary share (equivalent to an exercise price of $0.48 per ADS);
- for each new non-employee director that is appointed to the board of directors, an initial grant of a stock option to purchase 1,300,000 ordinary shares (equivalent to 13,000 ADSs), or Initial Stock Option Grant; if the non-employee director was not previously appointed to the board and is first elected at the Company's AGM, the grant shall be made on the date of the Company's AGM, on the date of the first meeting of the board held following the AGM, or on any date following such AGM as may be recommended by the compensation committee and approved by the board; if the non-employee director is appointed to the board in advance of the next AGM and will stand for election at that AGM, the grant shall be made at the meeting of the board at which he or she is appointed and, if not made at such meeting, shall be made promptly following such meeting by written unanimous consent of the board; and if the non-employee director is first appointed to the board in advance of the next AGM and will not stand for election at that AGM, the number of shares in the grant and the vesting schedule shall be determined by the compensation committee, taking into account the term of the appointment and the grant shall be made at the meeting of the board at which he or she is appointed and, if not made at such meeting, shall be made promptly following such meeting by written unanimous consent of the board;

- unless otherwise specified by the board or the compensation committee at the time of grant, each Annual Stock Option granted under this policy shall (i) vest in full on the date of the next AGM following the date of grant, subject to the non-employee director's continued service on the Board; (ii) have an exercise price equal to the fair market value of the Company's ordinary shares as determined in the 2014 Plan on the grant date; (iii) terminate ten years after the grant date; (iv) become fully vested immediately prior to a change of control and (v) contain such other terms and conditions as set forth in the form of option agreement approved by the board or the compensation committee prior to the grant date;

- unless otherwise specified by the board or the compensation committee at the time of grant, each Initial Stock Option Grant for newly appointed or elected directors granted under the non-employee director compensation policy shall (i) vest ratably in three equal installments with the first installment vesting on the date of the first AGM following the date of the grant, and with the second and third installments vesting, respectively, on the dates of the second and third AGMs following the date of the grant, subject to the non-employee director's continued service on the board; (ii) have an exercise price equal to the fair market value of the Company's ordinary shares as determined in the 2014 Plan on the grant date; (iii) terminate ten years after the grant date; (iv) become fully vested immediately prior to a change of control and (v) contain such other terms and conditions as set forth in the form of option agreement approved by the board or the compensation committee prior to the grant date; and

- each of these options shall be granted under our 2014 Plan, terminate ten years after the grant date and become fully vested immediately prior to a change of control.

On February 1, 2023, the Compensation Committee approved a 5% increase for our non-employee directors, effective as of January 1, 2023. All directors are eligible to receive reimbursement for reasonable out-of-pocket expenses incurred in connection with attendance at meetings of our board of directors, and our non-employee directors are also eligible to receive reimbursement, upon approval of the board of directors or a committee thereof, for reasonable out-of-pocket expenses incurred in connection with attendance at various conferences or meetings with our management.

The following table sets forth information regarding the total compensation awarded to, earned by or paid to each of our non-employee directors during the year ended December 31, 2022 for their service on our board of directors. Dr. Prudo, our former Executive Chairman, Rachelle Jacques, our President and Chief Executive Officer, and Clive Richardson, our former Chief Executive Officer and Chief Operating Officer and a former member of the Board, did not receive any additional compensation for their service as a director during 2022. Following Dr. Prudo's assumption of the role of Chairman, he became eligible to receive reimbursement for the expenses available to our other non-employee directors and, pursuant to the agreement between us and Dr. Prudo effective January 1, 2023, an annual director fee of $100,000. The compensation that we pay to the foregoing persons is discussed in the "Summary Compensation Table" above.

Name	Fees Earned or Paid in Cash ($)	Option Awards ($) [1]	Total ($)
James Hill, M.D. [2]	$ 61,502	$ 20,278	$ 81,780
Stuart Ungar [3]	49,064	20,278	69,342
David Byrne [4]	58,332	20,278	78,610
Donald Williams [5]	56,838	20,278	77,116
Peter Feldschreiber [6]	24,974	—	24,974
Michael Grissinger [7]	41,505	20,278	61,783

(1) These amounts represent the aggregate grant date fair value of options granted to each director during the year ended December 31, 2022 computed in accordance with ASC Topic 718. A discussion of the assumptions used in determining grant date fair value may be found in our Audited Financial Statements, included in our Annual Report on Form 20-F for the fiscal year ended December 31, 2022. Each of our non-executive directors received options to purchase 5,000,000 ordinary shares during the year ended December 31, 2022, consisting of (i) the Annual Stock Option granted on June 30, 2022, which options are exercisable at a price of $0.01 per ordinary share (equivalent to an exercise price of $1.00 per ADS) and (ii) the October 2022 NED Stock Option granted on October 21, 2022 and are exercisable to at price of $0.0048 per ordinary share (equivalent to an exercise price of $0.48 per ADS).

(2) As of December 31, 2022, Dr. Hill owned options to purchase an aggregate of 14,100,000 ordinary shares (equivalent to 141,000 ADSs), of which 9,100,000 ordinary shares (equivalent to 91,000 ADSs) were exercisable.

(3) As of December 31, 2022, Mr. Ungar owned options to purchase an aggregate of 14,100,000 ordinary shares (equivalent to 141,000 ADSs), of which 9,100,000 ordinary shares (equivalent to 91,000 ADSs) were exercisable.

(4) As of December 31, 2022, Mr. Byrne owned options to purchase an aggregate of 14,100,000 ordinary shares (equivalent to 141,000 ADSs), of which 9,100,000 ordinary shares (equivalent to 91,000 ADSs) were exercisable.

(5) As of December 31, 2022, Mr. Williams owned options to purchase an aggregate of 14,850,000 ordinary shares (equivalent to 148,500 ADSs), of which 9,850,000 ordinary shares (equivalent to 98,500 ADSs) were exercisable.

(6) As of December 31, 2022, Dr. Feldschreiber owned options to purchase an aggregate of 6,500,000 ordinary shares (equivalent to 65,000 ADSs), all of which were exercisable. On June 3, 2022, Dr. Feldschreiber notified the Company that he would resign from the Board, which resignation became effective as of June 3, 2022.

(7) As of December 31, 2022, Mr. Grissinger owned options to purchase an aggregate of 11,500,000 ordinary shares (equivalent to 115,000 ADSs), of which 6,500,000 ordinary shares (equivalent to 65,000 ADSs) were exercisable.

C. Board Practices

Our Articles of Association provide that our business is to be managed by the board of directors (subject to any directions made by the members of the Company by special resolution). Our board of directors is divided into three classes for purposes of election (Class A Directors, who serve a one year term before being subject to re-election at the Company's annual general meeting; Class B Directors, who serve a two year term before being subject to re-election at the annual general meeting; and Class C Directors who serve a three year term before being subject to re-election at the annual general meeting, provided also that in any two year period, a majority of the board must stand for re-election). Our board of directors currently consists of seven members: James Hill, M.D., Stuart Ungar, M.D., David Byrne, Donald Williams and Michael Grissinger currently serve as Class A directors; Rachelle Jacques currently serves as a Class B director and Ray Prudo currently serves as a Class C director. Ray Prudo served as Executive Chairman of our board of directors until December 2022 and assumed the role of Chairman of our board of directors effective January 1, 2023.

Subject to certain exceptions, the rules of Nasdaq permit a foreign private issuer to follow its home country practice in lieu of listing requirements of Nasdaq. The committees of our board of directors consist of an audit committee, a compensation committee and a nominating and corporate governance committee.

Audit Committee

Our audit committee currently consists of three members, appointed by the board of directors: Donald Williams, Michael Grissinger and David Byrne, all of whom are independent within the meaning of SEC corporate governance rules of independence for purposes of the audit committee. Mr. Williams is the chairman of our audit committee. Our board of directors has determined that Mr. Williams is the audit committee financial expert.

Compensation Committee

Our compensation committee currently consists of three members, appointed by the board of directors: James Hill, M.D., Michael Grissinger and David Byrne, all of whom are independent within the meaning of SEC corporate governance rules of independence for purposes of the compensation committee. Dr. Hill is the chairman of our compensation committee.

Nominating and Corporate Governance Committee

Our nominating and corporate governance committee currently consists of three members, appointed by our board of directors: David Byrne, James Hill, M.D., and Stuart Ungar, M.D., all of whom are independent within the meaning of SEC corporate governance rules of independence for purposes of the nominating and corporate governance committee. David Byrne is chairman of our nominating and corporate governance committee.

None of our non-employee directors have any service contracts with Akari or any of our subsidiaries that provide for benefits upon termination of employment.

D. Employees

As of December 31, 2022, we had 15 full-time employees. Seven of our employees were engaged in research and development and eight employees were engaged in management, administration and finance. Seven were located in England and eight were located in the United States.

None of our employees are members of labor unions.

E. Share Ownership

Information with respect to share ownership of members of our board of directors and executive officers is included in "Item 7. Major Shareholders and Related Party Transactions"

Option Plans

2014 Plan

Our board of directors is generally authorized to issue up to 15,000,000,000 ordinary shares of $0.0001 each until June 30, 2026, without seeking shareholder approval, subject to certain limitations. As of December 31, 2022, there were 7,444,917,123 ordinary shares outstanding, outstanding options to purchase 513,673,885 ordinary shares, outstanding RSUs that settle into 21,475,400 ordinary shares and 354,850,715 ordinary shares available for future issuance under our 2014 Equity Incentive Compensation Plan. In connection with our annual general meeting held on June 30, 2022, the amount of shares available for the grant of awards under our 2014 Equity Incentive Plan was increased to 890,000,000 ordinary shares. All of our existing issued ordinary shares are fully paid. Accordingly, no further capital may be required by us from the holders of such share. The material terms of the 2014 Plan are set forth below.

The option plan is administered by our board of directors and grants are made pursuant thereto by the compensation committee. The aggregate number of ordinary shares that may be issued upon exercise of options under the 2014 Plan is 400,000,000. Options may be granted at any time.

The per share exercise price for the shares to be issued pursuant to the exercise of an option shall be such price as determined by the board of directors and set forth in the individual option agreement, subject to any guidelines as may be determined by the board of directors from time to time, provided, however, that the exercise price shall be not less than the par value of the shares underlying the option, and subject to other conditions set forth in the 2014 Plan.

Options are exercisable pursuant to the terms under which they were awarded and subject to the terms and conditions of the 2014 Plan. In general, an option, or any part thereof, may not be exercised unless the optionee is then a service provider of our Company or any parent or subsidiary thereof (as each such term is defined in the 2014 Plan). Any tax consequences arising from the grant or exercise of any option from the payment for shares covered thereby, the sale or disposition of such shares and any other expenses are the responsibility of the optionee unless otherwise required by applicable law.

On January 23, 2017, the compensation committee approved a UK Sub-Plan of the 2014 Plan which offers UK residents the opportunity to acquire interests in us in a similar manner to that offered to US employees. The UK Sub-Plan requires that only employees may receive grants, and that all options granted under the UK Sub-Plan must be designated as “non-tax-advantaged Options” under UK law. Options granted under the UK Sub-Plan are exercisable pursuant to the terms of their award and are subject to the terms of the 2014 Plan generally, except where otherwise stated. The UK Sub-Plan differs from the 2014 Plan only in UK-specific provisions regarding a valid disposition to survivors and compliance with local UK laws regarding securities, treatment as compensation, tax matters, data privacy, and third party rights.

Grants to non-employee directors who are based in the UK or who are UK resident taxpayers are made pursuant to the 2014 Plan in accordance with the UK Appendix to the Amended and Restated Non-Employee Director Compensation Policy which was approved by the compensation committee on January 23, 2017. The UK Appendix, as with the Sub-Plan for employees, differs from the Non-Employee Director Compensation Policy by providing specific UK-specific provisions. All options granted to UK non-employee directors or resident taxpayers are, as with the Sub-Plan for employees, designated as “non-tax-advantaged options” under UK law, exercisable pursuant to the terms of the award and the 2014 Plan, and provide for UK specific provisions regarding survivorship, securities, compensation, tax, data privacy, and third party rights laws.

In addition, on January 26, 2017, our board of directors approved a CSOP Sub Plan as recommended to the board by the compensation committee. The CSOP Sub-Plan modifies the 2014 Plan to qualify as a Schedule 4 CSOP Scheme as defined under the UK's Income Tax (Earnings & Pensions) Act 2003, or ITEPA. If the statutory provisions are met, favourable tax treatment can result. CSOP options are effectuated by the execution of a deed of grant by the Company evidencing shares, option exercise price, restrictions, and other terms or conditions. Grants are limited under the CSOP Sub-Plan such that an employee cannot hold more than £30,000 (£60,000 for any new CSOP options granted from April 6, 2023) in value, measured as of grant date. In the event of, and only prior to the third anniversary of the date of grant by someone who has left work for reasons associated with: redundancy, retirement, or certain types of takeover, the recipient may exercise any CSOP option that has become exercisable but has not yet been exercised for a period of six months. A Change of Control under UK law may similarly permit option exercise.

Equity Award Grant Policy

Based on the recommendation of the compensation committee, our board of directors adopted an Equity Award Grant Policy on January 26, 2017, which sets forth policies for us to follow when we grant stock options, shares of restricted stock, restricted stock units or other equity-based awards to employees of the Company or its subsidiaries.

The grants are divided into annual grants, made on the last business day in March, new hire grants, to our new hires, and performance grants to existing employees in recognition of performance. The policy standardizes employee grants and delegates authority to the Executive Chairman and CEO to make grants other than (a) grants of more than 1,000,000 ordinary shares or share-equivalents to one individual on one date; (b) new hire or performance grants to a person who is reasonably expected to be an executive officer or director upon hire or promotion; (c) any grant which would exceed 1,000,000 ordinary shares or share equivalents to any one individual in a calendar year; or (d) any grant with an exercise price less than fair market value on the date. These non-delegated grants remain in the sole authority of the compensation committee.

Pricing will be based on the closing market price on the Nasdaq Capital Market for all such grants. All new-hire grants must be made by a writing sent to the recipient stating the terms and conditions and clarifying that the equity award is subject to approval, whether by the delegated authority pursuant to the policy or by the compensation committee or the board itself.

F. Disclosure of a Registrant's Action to Recover Erroneously Awarded Compensation

Not applicable.

Item 7. MAJOR SHAREHOLDERS AND RELATED PARTY TRANSACTIONS

A. Major Shareholders

The following table sets forth certain information with respect to the beneficial ownership of our ordinary shares as of March 31, 2023, the latest practicable date for inclusion in this annual report (except where otherwise indicated), for:

- each person, or group of affiliated persons, who are known by us to beneficially own more than 5% of our outstanding ordinary shares;
- each member of our board of directors;
- each of our other executive officers; and
- all of our directors and executive officers as a group.

The number of shares beneficially owned by each entity, person, director or executive officer is determined under the rules of the SEC and the information is not necessarily indicative of beneficial ownership for any other purpose. Under such rules, beneficial ownership includes any shares as to which the individual has the sole or shared voting power or investment power and also any shares that the individual has the right to acquire within 60 days of March 31, 2023, through the exercise of any option or other right. Unless otherwise indicated, each person has sole investment and voting power, or shares such powers with his or her spouse, with respect to the shares set forth in the following table.

Ordinary shares that may be acquired by an individual or group within 60 days of March 31, 2023, pursuant to the exercise of options or warrants, are deemed to be outstanding for the purpose of computing the percentage ownership of such individual or group, but are not deemed to be outstanding for the purpose of computing the percentage ownership of any other person shown in the table. The percentage of ownership is based on 10,111,583,823 shares of ordinary shares outstanding on March 31, 2023, adjusted as required by the rules promulgated by the SEC to determine beneficial ownership. Akari does not know of any arrangements, including any pledge by any person of securities of Akari, the operation of which may at a subsequent date result in a change of control of Akari. Unless otherwise noted, the address of each director and executive officer of Akari is: c/o Akari Therapeutics, Plc, 75/76 Wimpole Street, London W1G 9RT.

	Number of Ordinary Shares Beneficially Owned	Percentage of Ordinary Shares Beneficially Owned
Directors and Executive Officers		
Ray Prudo	2,276,483,900 (1)	21.8 %
Rachelle Jacques	155,760,675 (2)	1.5 %
James Hill, M.D.	29,100,000 (3)	*
Stuart Ungar, M.D.	29,100,020 (4)	*
Torsten Hombeck	8,375,000 (5)	*
David Byrne	29,100,000 (6)	*
Donald Williams	29,850,000 (7)	*
Michael Grissinger	26,500,000 (8)	*
Melissa Bradford-Klug	2,500,000 (9)	*
Miles Nunn	17,550,000 (10)	*
John Neylan, M.D.	2,500,000 (11)	*
All directors and officers as a group (11 persons)		24.7 %
5% or More Shareholders		
RPC Pharma Limited (12)	809,977,100	8.0 %
Praxis Trustees Limited As trustee of The Sonic Healthcare Holding Company (13)	38,709,600	*
PranaBio Investments, LLC (14)	1,026,349,100	9.9 %

* Represents beneficial ownership of less than 1% of our outstanding ordinary shares.

(1) Represents the entire holdings of RPC Pharma Limited, Dr. Ray Prudo and Praxis Trustees Limited as Trustee of The Sonic Healthcare Holding Company and includes warrants to purchase 9,210,500 ordinary shares (equivalent to 92,105 ADSs) at an exercise price of $0.03 per share (or $3.00 per ADS) which expire on July 1, 2024, warrants to purchase 7,500,000 ordinary shares (equivalent to 75,000 ADSs) at an exercise price of $0.02 per share (or $2.20 per ADS) which expire on February 21, 2025, warrants to purchase 20,229,700 ordinary shares (equivalent to 202,297 ADSs) at an exercise price of $0.0165 per share (or $1.65 per ADS) which expire on January 4, 2027, warrants to purchase 41,666,700 ordinary shares (equivalent to 416,667 ADSs) at an exercise price of $0.014 per share (or $1.40 per ADS) which expire on March 10, 2027, warrants to purchase 117,647,100 ordinary shares (equivalent to 1,176,471 ADSs) at an exercise price of $0.0085 per share (or $0.85 per ADS) which expire on September 14, 2024 and warrants to purchase 117,647,100 ordinary shares (equivalent to 1,176,471 ADSs) at an exercise price of $0.0085 per share (or $0.85 per ADS) which expire on September 14, 2029. Dr. Prudo has voting and dispositive control over the ordinary shares held by RPC Pharma Limited and owns approximately 67.8% of RPC's outstanding shares (including option grants), including 10.6% of RPC's outstanding shares held in trust for Dr. Ungar. Dr. Prudo disclaims beneficial ownership except to the extent of his actual pecuniary interest in such shares.

(2) Represents the holdings of Ms. Jacques and includes (i) options to purchase 51,908,600 ordinary shares (equivalent to 519,086 ADSs) at an exercise price of $0.0124 per share (or $1.24 per ADS), which expire on June 1, 2032, and (ii) options to purchase 7,440,575 ordinary shares (equivalent to 74,405 ADSs) at an exercise price of $0.0124 per share (or $1.24 per ADS), which expire on July 29, 2032. Does not include (i) a restricted stock award for 21,475,400 ordinary shares (equivalent to 214,754 ADSs) that vest in more than 60 days from March 31, 2023 or (ii) a restricted stock award for 189,787,200 ordinary shares (equivalent to 1,897,872 ADSs) that vest in more than 60 days from March 31, 2023.

(3) Represents the holdings of Dr. Hill and includes (i) options to purchase 231,278 ordinary shares (equivalent to 2,312 ADSs) at an exercise price of $0.3221 per share (or $32.21 per ADS), which expire on September 21, 2025, (ii) options to purchase 1,068,722 ordinary shares (equivalent to 10,687 ADSs) at an exercise price of $0.1917 per share (or $19.17 per ADS), which expire on November 25, 2025, (iii) options to purchase 1,300,000 ordinary shares (equivalent to 13,000 ADSs) at an exercise price of $0.145 per share (or $14.50 per ADS), which expire on June 29, 2026, (iv) options to purchase 1,300,000 ordinary shares (equivalent to 13,000 ADSs) at an exercise price of $0.0504 per share (or $5.04 per ADS) and which expire on June 28, 2027, (v) options to purchase 1,300,00 ordinary shares (equivalent to 13,000 ADSs) at an exercise price of $0.0208 per share (or $2.08 per ADS) and which expire on September 19, 2028, (vi) options to purchase 1,300,000 ordinary shares (equivalent to 13,000 ADSs) at an exercise price of $0.0207 per share (or $2.07 per ADS) and which expire on June 27, 2029, (vii) options to purchase 1,300,000 ordinary shares (equivalent to 13,000 ADSs) at an exercise price of $0.0218 per share (or $2.18 per ADS) and which expire on June 30, 2030 and (viii) options to purchase 1,300,000 ordinary shares (equivalent to 13,000 ADSs) at an exercise price of $0.0173 per share (or $1.73 per ADS) and which expire on June 30, 2031. Does not include (i) options to purchase 1,300,000 ordinary shares (equivalent to 13,000 ADSs) at an exercise price of $0.01 per share (or $1.00 per ADS) and which expire on June 30, 2032 that vest in more than 60 days from March 31, 2023 or (ii) options to purchase 3,700,000 ordinary shares (equivalent to 37,000 ADSs) at an exercise price of $0.0048 per share (or $0.48 per ADS) and which expire on June 30, 2032 that vest in more than 60 days from March 31, 2023. Also, does not include shares held by RPC Pharma Limited of which he has a pecuniary interest. Dr. Hill disclaims beneficial ownership of the shares held by RPC Pharma Limited.

(4) Represents the holdings of Dr. Ungar and includes (i) options to purchase 211,278 ordinary shares (equivalent to 2,112 ADSs) at an exercise price of $0.3221 per share (or $32.21 per ADS), which expire on September 21, 2025, (ii) options to purchase 1,088,722 ordinary shares (equivalent to 10,887 ADSs) at an exercise price of $0.1917 per share (or $19.17 per ADS), which expire on November 25, 2025, (iii) options to purchase 1,300,000 ordinary shares (equivalent to 13,000 ADSs) at an exercise price of $0.145 per share (or $14.50 per ADS), which expire on June 29, 2026, (iv) options to purchase 1,300,000 ordinary shares (equivalent to 13,000 ADSs) at an exercise price of $0.0504 per share (or $5.04 per ADS) and which expire on June 28, 2027, (v) options to purchase 1,300,000 ordinary shares (equivalent to 13,000 ADSs) at an exercise price of $0.0208 per share (or $2.08 per ADS) and which expire on September 19, 2028, (vi) options to purchase 1,300,000 ordinary shares (equivalent to 13,000 ADSs) at an exercise price of $0.0207 per share (or $2.07 per ADS) and which expire on June 27, 2029, (vii) options to purchase 1,300,000 ordinary shares (equivalent to 13,000 ADSs) at an exercise price of $0.0218 per share (or $2.18 per ADS) and which expire on June 30, 2030 and (viii) options to purchase 1,300,000 ordinary shares (equivalent to 13,000 ADSs) at an exercise price of $0.0173 per share (or $1.73 per ADS) and which expire on June 30, 2031. Does not include (i) options to purchase 1,300,000 ordinary shares (equivalent to 13,000 ADSs) at an exercise price of $0.01 per share (or $1.00 per ADS) and which expire on June 30, 2032 that vest in more than 60 days from March 31, 2023 or (ii) options to purchase 3,700,000 ordinary shares (equivalent to 37,000 ADSs) at an exercise price of $0.0048 per share (or $0.48 per ADS) and which expire on June 30, 2032 that vest in more than 60 days from March 31, 2023. Also, does not include shares held by RPC Pharma Limited of which he has a pecuniary interest. Dr. Ungar disclaims beneficial ownership of the shares held by RPC Pharma Limited.

(5) Consists of (i) options to purchase 4,375,000 ordinary shares (equivalent to 43,750 ADS) at an exercise price of $0.0218 per share (or $2.18 per ADS), which expire on June 30, 2030, (ii) options to purchase 1,500,000 ordinary shares (equivalent to 15,000 ADS) at an exercise price of $0.0181 per share (or $1.81 per ADS), which expire on December 31, 2030 and (iii) options to purchase 2,500,000 ordinary shares (equivalent to 25,000 ADS) at an exercise price of $0.0132 per share (or $1.32 per ADS), which expire on February 3, 2032. Does not include options to purchase 10,000,000 ordinary shares (equivalent to 100,000 ADS) at an exercise price of $0.0047 per share (or $0.47 per ADS) and which expire on October 31, 2032 that vest in more than 60 days from March 31, 2023.

(6) Represents the holdings of Mr. Byrne and includes (i) options to purchase 1,300,000 ordinary shares (equivalent to 13,000 ADSs) at an exercise price of $0.1796 per share (or $17.96 per ADS), which expire on April 22, 2026, (ii) options to purchase 1,300,000 ordinary shares (equivalent to 13,000 ADSs) at an exercise price of $0.145 per share (or $14.50 per ADS), which expire on June 29, 2026, (iii) options to purchase 1,300,000 ordinary shares (equivalent to 13,000 ADSs) at an exercise price of $0.0504 per share (or $5.04 per ADS) and which expire on June 28, 2027, (iv) options to purchase 1,300,000 ordinary shares (equivalent to 13,000 ADSs) at an exercise price of $0.0208 per share (or $2.08 per ADS) and which expire on September 19, 2028, (v) options to purchase 1,300,000 ordinary shares (equivalent to 13,000 ADSs) at an exercise price of $0.0207 per share (or $2.07 per ADS) and which expire on June 27, 2029 and (vi) options to purchase 1,300,000 ordinary shares (equivalent to 13,000 ADSs) at an exercise price of $0.0218 per share (or $2.18 per ADS) and which expire on June 30, 2030 and (vii) options to purchase 1,300,000 ordinary shares (equivalent to 13,000 ADSs) at an exercise price of $0.0173 per share (or $1.73 per ADS) and which expire on June 30, 2031. Does not include (i) options to purchase 1,300,000 ordinary shares (equivalent to 13,000 ADSs) at an exercise price of $0.0173 per share (or $1.0073 per ADS) and which expire on June 30, 2032 that vest in more than 60 days from March 31, 2023April 30, 2022 or (ii) options to purchase 3,700,000 ordinary shares (equivalent to 37,000 ADSs) at an exercise price of $0.0048 per share (or $0.48 per ADS) and which expire on June 30, 2032 that vest in more than 60 days from March 31, 2023. Also, does not include shares held by RPC Pharma Limited of which he has a pecuniary interest. Mr. Byrne disclaims beneficial ownership of the shares held by RPC Pharma Limited.

(7) Represents the holdings of Mr. Williams and includes (i) options to purchase 2,600,000 ordinary shares (equivalent to 26,000 ADSs) at an exercise price of $0.145 per share (or $14.50 per ADS), which expire on June 29, 2026, (ii) 1,300,000 ordinary shares (equivalent to 13,000 ADSs) at an exercise price of $0.0504 per share (or $5.04 per ADS) and which expire on June 28, 2027, (iii) options to purchase 1,300,00 ordinary shares (equivalent to 13,000 ADSs) at an exercise price of $0.0208 per share (or $2.08 per ADS) and which expire on September 19, 2028, (iv) options to purchase 750,000 ordinary shares (equivalent to 7,500 ADSs) at an exercise price of $0.0175 per share (or $1.75 per ADS) and which expire on November 16, 2028, (v) options to purchase 1,300,000 ordinary shares (equivalent to 13,000 ADSs) at an exercise price of $0.0207 per share (or $2.07 per ADS) and which expire on June 27, 2029, (vi) options to purchase 1,300,000 ordinary shares (equivalent to 13,000 ADSs) at an exercise price of $0.0218 per share (or $2.18 per ADS) and which expire on June 30, 2030 and (vii) options to purchase 1,300,000 ordinary shares (equivalent to 13,000 ADSs) at an exercise price of $0.0173 per share (or $1.73 per ADS) and which expire on June 30, 2031. Does not include (i) options to purchase 1,300,000 ordinary shares (equivalent to 13,000 ADSs) at an exercise price of $0.01 per share (or $1.00 per ADS) and which expire on June 30, 2032 that vest in more than 60 days from March 31, 2023 or (ii) options to purchase 3,700,000 ordinary shares (equivalent to 37,000 ADSs) at an exercise price of $0.0048 per share (or $0.48 per ADS) and which expire on June 30, 2032 that vest in more than 60 days from March 31, 2023.

(8) Represents the holdings of Mr. Grissinger and includes of (i) options to purchase 1,300,000 ordinary shares (equivalent to 13,000 ADSs) at an exercise price of $0.0347 per share (or $3.47 per ADS) and which expire on January 23, 2028, (ii) options to purchase 1,300,000 ordinary shares (equivalent to 13,000 ADSs) at an exercise price of $0.0208 per share (or $2.08 per ADS) and which expire on September 19, 2028, (iii) options to purchase 1,300,000 ordinary shares (equivalent to 13,000 ADSs) at an exercise price of $0.0207 per share (or $2.07 per ADS) and which expire on June 27, 2029, (v) options to purchase 1,300,000 ordinary shares (equivalent to 13,000 ADSs) at an exercise price of $0.0218 per share (or $2.18 per ADS) and which expire on June 30, 2030 and (vi) options to purchase 1,300,000 ordinary shares (equivalent to 13,000 ADSs) at an exercise price of $0.0173 per share (or $1.73 per ADS) and which expire on June 30, 2031. Does not include (i) options to purchase 1,300,000 ordinary shares (equivalent to 13,000 ADSs) at an exercise price of $0.01 per share (or $1.00 per ADS) and which expire on June 30, 2032 that vest in more than 60 days from March 31, 2023 or (ii) options to purchase 3,700,000 ordinary shares (equivalent to 37,000 ADSs) at an exercise price of $0.0048 per share (or $0.48 per ADS) and which expire on June 30, 2032 that vest in more than 60 days from March 31, 2023.

(9) Consists of (i) options to purchase 2,500,000 ordinary shares (equivalent to 25,000 ADSs) at an exercise price of $0.0114 per share (or $1.14 per ADS), which expire on July 29, 2032.

(10) Consists of (i) options to purchase 3,000,000 ordinary shares (equivalent to 30,000 ADS) at an exercise price of $0.141 per share (or $14.10 per ADS), which expire on March 23, 2026, (ii) options to purchase 800,000 ordinary shares (equivalent to 8,000 ADS) at an exercise price of 0.036 per share (or $3.60 per ADS), which expire on September 1, 2027, (iii) options to purchase 8,000,000 ordinary shares (equivalent to 80,000 ADS) at an exercise price of $0.0182 per share (or $1.82 per ADS), which expire on October 22, 2028, (iv) options to purchase 2,500,000 ordinary shares (equivalent to 25,000 ADS) at an exercise price of $0.0162 per share (or $1.62 per ADS), which expire on July 30, 2031 and (v) options to purchase 3,250,000 ordinary shares (equivalent to 325,000 ADSs) at an exercise price of $0.0132 per share (or $1.32 per ADS), which expire on July 30, 2031. Does not include (i) options to purchase 40,000,000 ordinary shares (equivalent to 400,000 ADSs) at an exercise price of $0.0047 per share (or $0.47 per ADS) and which expire on October 31, 2032 that vest in more than 60 days from March 31, 2023.

(11) Consists of (i) options to purchase 2,500,000 ordinary shares (equivalent to 25,000 ADSs) at an exercise price of $0.0047 per share (or $0.47 per ADS), which expire on November 8, 2032.

(12) The principal business office of RPC Pharma Limited is c/o Landmark Fiduciare (Suisse) SA, 6 Place des Eaux-Vives, P.O. Box 3461, Geneva, V8 1211, Switzerland.

(13) The principal business office of Praxis Trustees Limited As trustee of The Sonic Healthcare Holding Company is Sarina House Le Truchot, St. Peter Port, Guernsey, GY1 1GR.

(14) Represents the entire holdings of Pranabio Investments, LLC and includes warrants to purchase 32,500,000 ordinary shares (equivalent to 325,000 ADSs) at an exercise price of $0.03 per share (or $3.00 per ADS) which expire on July 1, 2024, warrants to purchase 30,000,000 ordinary shares (equivalent to 300,000 ADSs) at an exercise price of $0.02 per share (or $2.20 per ADS) which expire on February 21, 2025, warrants to purchase 12,500,000 ordinary shares (equivalent to 125,000 ADSs) at an exercise price of $0.0165 per share (or $1.65 per ADS) which expire on January 4, 2027, warrants to purchase 50,000,000 ordinary shares (equivalent to 500,000 ADSs) at an exercise price of $0.014 per share (or $1.40 per ADS) which expire on March 10, 2027, warrants to purchase 105,000,000 ordinary shares (equivalent to 1,500,000 ADSs) at an exercise price of $0.0085 per share (or $0.85 per ADS) which expire on September 14, 2024 and warrants to purchase 105,000,000 ordinary shares (equivalent to 1,500,000 ADSs) at an exercise price of $0.0085 per share (or $0.85 per ADS) which expire on September 14, 2029. Such warrants provide that at no time may Pranabio Investments, LLC or its affiliates exercise any warrant that would result in their ownership of more than 9.99% of the issued and outstanding ordinary shares on the date of exercise, and the table above reflects that options to purchase 162,181,600 ordinary shares (equivalent to 1,621,816 ADSs) are exercisable within 60 days of March 31, 2023 as a result of the restrictions on exercise imposed by this mechanism. Pranabio Investments, LLC is a Texas limited liability company. Samir R. Patel is the managing member and has sole voting and investment power with respect to the shares.

Deutsche Bank Trust Company Americas, or Deutsche Bank, is the holder of record for the Company's ADR program, pursuant to which each ADS represents 100 ordinary shares. As of March 31, 2023, Deutsche Bank held 10,107,149,700 ordinary shares representing 99.9% of the issued share capital held at that date. Certain of these ordinary shares were held by brokers or other nominees. As a result, the number of holders of record or registered holders in the United States is not representative of the number of beneficial holders or of the residence of beneficial holders.

To our knowledge, the only significant changes in the percentage ownership held by our more than 5% shareholders as reported in our annual reports during the past three years are as follows: (i) the ownership percentage of RPC Pharma Limited decreased by 5.6% to 8.0% from 13.6% as of March 31, 2023, the ownership percentage of RPC Pharma Limited decreased by 7.4% to 13.6% from 21.0% as of March 15, 2021 and decreased by 7.8% to 21.0% from 28.8% as of March 15, 2020, (ii) the ownership percentage of PranaBio Investments LLC increased by 1.2% to 9.9% from 7.7% as of March 31, 2023 and increased by 1.3% to 7.7% from 6.4% as of March 15, 2021, (iii) the ownership percentage of Aspire Capital Fund LLC decreased by 18.6% to less than 5% from as of March 31, 2023 and decreased by 0.7% to 18.6% from 19.3% as of March 15, 2021.

B. Related Party Transactions

The following discloses, since January 1, 2022, certain related party transactions involving us. The descriptions provided below are summaries of the terms of such agreements, do not purport to be complete and are qualified in their entirety by the complete agreements.

Employment and Consulting Agreements

We have or have had employment, consulting or related agreements with each member of our senior management and employee-directors. See "Item 6. Directors, Senior Management and Employees—Compensation".

Options

We have granted options to purchase our ordinary shares to certain of our officers and directors. See "Item 6.B. Compensation" and "Item 7.A.Major Shareholders". We describe our option plans under "Item 6.E. Share Ownership" and "Item 7.A. Major Shareholders".

Office Lease

We lease our UK office space from The Doctors Laboratory, or TDL, and have incurred expenses of approximately $129,000, $146,000, and $133,000 plus VAT during the years ended December 31, 2022, 2021 and 2020, respectively. David Byrne, a non-employee director of ours, is also the CEO of TDL.

Laboratory Testing Services

We received laboratory testing services for our clinical trials provided by TDL and have incurred expenses of approximately $89,000, $102,000 and $234,000 plus VAT during the years ended December 31, 2022, 2021 and 2020, respectively. The Company recorded payable balances to TDL of approximately $23,000, $32,000 and $100,000 plus VAT as of December 31, 2022, 2021 and 2020, respectively.

Consulting

Since January 2019, we have received business development consulting services from Michael Grissinger, a non-employee director of the Company. We have incurred expenses of approximately $92,000, $100,000 and $100,000 during the years ended December 31, 2022, 2021 and 2020, respectively, relating to these consulting services.

Indemnification Agreements

To the extent permitted by the U.K. Companies Act 2006, our directors and officers are entitled pursuant to our Articles of Association to be indemnified against any liability they incur by reason of their directorship or service as an officer of the Company. In addition to such indemnification, we provide our directors and executive officers with directors' and officers' liability insurance.

Financing

In connection with the financings listed below, certain shareholders and Company insiders participated.

- In March 2022, we sold to certain accredited and institutional investors, including our former Executive Chariman and current Chairman of the Board of Directors, Dr. Ray Prudo, an aggregate of (i) 7,440,833 ADSs in a registered direct offering at $1.20 per ADS and (ii) warrants to purchase up to 3,720,409 ADS at an exercise price of $1.40 per ADS, for aggregate gross proceeds of approximately $8.9 million. Dr. Prudo purchased (i) 833,334 ADSs and (ii) warrants exercisable to purchase up to 416,667 ADSs at an exercise price of $1.40 per ADS, for a total amount of approximately $1,000,001. PranaBio Investments LLC, one of our major shareholders, purchased (i) 1,000,000 ADSs and (ii) warrants exercisable to purchase up to 500,000 ADSs at an exercise amount of $1.40 per ADS, for a total amount of approximately $1,200,000.

- September 2022, we sold to certain accredited and institutional investors, including Dr. Prudo, an aggregate of 15,100,000 ADSs in a registered direct offering at $0.85 per ADS for aggregate proceeds of approximately $12.8 million. In addition, we issued to the investors in a private placement (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. Dr. Prudo purchased (i) 1,176,471 ADS and (ii) warrants excersiable to purchase up to 2,352,942 ADSs at an exercise price of $0.85 per ADS, for a total amount of approximately $1,000,000. PranaBio Investments LLC, one of our major shareholders, purchased (i) 1,500,000 ADSs and (ii) warrants to purchase up to 3,000,000 ADSs at an exercise price of $0.85 per ADS, for a total amount of approximately $1,275,000.

- In March 2023, we sold to certain accredited and institutional investors an aggregate of 26,666,667 ADSs in a registered direct offering at $0.15 per ADS for aggregate gross proceeds of approximately $4.0 million. The following existing investors and Company insiders participated in the registered direct offering:

    - Ray Prudo purchased 8,666,666 ADSs for a total amount of approximately $1,300,000;

- Rachelle Jacques purchased 964,115 ADSs for a total amount of approximately $144,617;
- Michael Grissinger purchased 200,000 ADSs for a total amount of approximately $30,000;
- Donald Williams purchased 200,000 ADSs for a total amount of approximately $30,000;
- Stuart Ungar purchased 200,000 ADSs for a total amount of approximately $30,000;
- David Byrne purchased 200,000 ADSs for a total amount of approximately $30,000;
- James Hill purchased 200,000 ADSs for a total amount of approximately $30,000; and
- PranaBio Investments LLC, one of our major shareholders, purchased 3,000,000 ADSs for a total amount of approximately $450,000.

C. Interests of Experts and Counsel.

Not applicable.

Item 8. FINANCIAL INFORMATION

A. Consolidated Statements and Other Financial Information

See “Item 18. Financial Statements,” which contains our financial statements prepared in accordance with United States GAAP.

Legal Proceedings

See “Item 4. B. Business Overview—Legal Proceedings”.

Dividend Policy

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 ordinary shares or ADSs will depend upon any future appreciation in their value. There is no guarantee that our ordinary shares or ADSs will appreciate in value or even maintain the price at which our shareholders have purchased their shares.

B. Significant Changes

A discussion of the significant changes in our business can be found under “Item 4. Information on the Company—A. History and Development of the Company.”

Item 9. THE OFFER AND LISTING

A. Offering and Listing Details

Not applicable.

B. Plan of Distribution

Not applicable.

C. Markets

Our ADSs have been listed on the Nasdaq Capital Market under the symbol “AKTX” since September 21, 2015 and under the symbol “CLTX” from January 31, 2014 until September 18, 2015. Prior to that, our ADSs were quoted on the OTCQB under the symbol “CLSXD” from January 3, 2014 to January 30, 2014 and were quoted on the OTCQB under the symbol “CLSXY” from September 16, 2013 until January 2, 2014 and under the symbol “MRRBY” from February 19, 2013 to September 15, 2013. Effective January 3, 2014, our ratio of ADSs to ordinary shares changed from one ADS per each two ordinary shares to one ADS per each ten ordinary shares and, effective as of September 17, 2015, our ratio of ADSs is to ordinary shares changed from one ADS per each ten ordinary shares to one ADS per each one hundred ordinary shares. Currently, each ADS represents one hundred ordinary shares. Effective December 8, 2020, the currency of the Company’s ordinary shares was changed from pounds sterling to US dollars and the nominal (par) value of an ordinary share was reduced to $0.0001.

D. Selling Shareholders

Not applicable.

E. Dilution

Not applicable.

F. Expenses of the Issue

Not applicable.

Item 10. ADDITIONAL INFORMATION

A. Share Capital

Not applicable.

B. Memorandum and Articles of Association

The following summarizes the material rights of holders of ordinary shares, as set out in our Articles of Association. The following summary is qualified in its entirety by reference to the Companies Act 2006 (the Companies Act) and to our Articles of Association, which are filed as an exhibit to our Form F-3/A filed with the SEC on August 30, 2021, which is incorporated by reference.

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

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

Issuance of Options and Warrants

Our Articles of Association provide that, subject to any shareholder approval requirement under any laws, regulations or the rules of any stock exchange to which we are subject, our board of directors is unconditionally authorized, from time to time, in its discretion, to grant such persons, at such times and upon such terms as it determines, options to purchase, or issue them warrants to subscribe, our shares of any class or classes or of any series of any class. The Companies Act provides that directors may issue options or warrants without shareholder approval once authorized to do so by the Articles of Association or an ordinary resolution of shareholders. Our board of directors may issue shares upon exercise of options or warrants without shareholder approval or authorization, up to the relevant authorized share capital limit.

Dividends

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

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

Rights in a Liquidation

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

Voting Rights

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

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

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

Preemptive Rights

There are no rights of pre-emption under our Articles of Association in respect of transfers of issued ordinary shares. In certain circumstances, our shareholders have preemptive rights with respect to new issuances of equity securities. However our board of directors is generally authorized to allot equity securities for cash without triggering shareholder preemptive rights, provided that this power shall (i) be limited to the allotment of equity securities up to an aggregate nominal amount of $1,500,000; and (ii) expire (unless previously revoked or varied by us), on June 30, 2026.

Transfer of Shares

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

Fiduciary Duties of Office Holders

Directors owe fiduciary duties to their companies. Chapter 2 of Part 10 of the Companies Act codifies certain of those duties. The relevant statutory duties imposed on directors under the Companies Act are:

- to act in accordance with the company's constitution, and only exercise powers for the purposes for which they are conferred;
- to act in the way he considers, in good faith, would be most likely to promote the success of the company for the benefit of its members as a whole;
- to exercise independent judgment;
- to exercise reasonable care, skill and diligence, being such as would be exercised by a reasonably diligent person with the general knowledge, skill and experience that may reasonably be expected of a person carrying out the functions carried out by the director, and the general knowledge, skill and experience that the director has;
- to avoid a situation in which he has, or can have, a direct or indirect interest that conflicts, or possibly may conflict, with the interests of the company (including in particular through exploitation of any property, information or opportunity) unless authorized by the company or its board;
- not to accept benefits from third parties; and
- to declare an interest in a proposed transaction or arrangement.

In addition, certain additional duties are imposed by the common law, such as a duty of confidentiality.

Disclosure of Personal Interests of an Officer Holder

The Companies Act requires a director to disclose to the board any direct or indirect personal interest that he or she may have in connection with any existing or proposed transaction by the company. The disclosure is required to be made promptly and, in the case of a proposed transaction, before it is entered into. All transactions in which a director has an interest must be declared, and not only those that are extraordinary transactions.

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

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

- in which he (directly or indirectly) has a material interest, other than an interest in shares or debentures or other securities of or in (or through) the Company; and
- subject to the Companies Act, which conflicts or may conflict with the interests of the Company.

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

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

- the giving of any security, guarantee or indemnity to him in respect of money lent or obligations incurred by him or by any other person at the request of or for the benefit of the Company or any of our subsidiaries, or to a third party in respect of a debt or obligation of the Company or any of our subsidiaries for which he himself has assumed responsibility in whole or in part under a guarantee or indemnity or by the giving of security;
- any proposal concerning an offer of shares or debentures or other securities of or by the Company or any of our subsidiaries for subscription or purchase in which offer he is or is to be interested as a participant as the holder of such shares, debentures or other securities or in its underwriting or sub-underwriting;
- any contract, arrangement, transaction or other proposal concerning any other company in which he (together with any person connected with him) is interested (directly or indirectly) whether as an officer, shareholder, creditor or otherwise, unless he (together with any person connected with him) holds an interest representing one per cent. or more of any class of the equity share capital (exclusive of treasury shares) of such company or of the voting rights available to members of the relevant company;
- any contract, arrangement, transaction or other proposal concerning the adoption, modification or operation of a superannuation fund or retirement, death or disability benefits scheme under which he may benefit and which has been approved by or is subject to and conditional upon approval by Her Majesty's Revenue & Customs;
- any contract, arrangement, transaction or proposal concerning the adoption, modification or operation of any scheme for enabling employees including full time executive directors of the Company and/or any subsidiary to acquire shares of the Company or any arrangement for the benefit of employees of the Company or any of our subsidiaries, which does not award him any privilege or benefit not awarded to the employees to whom such scheme relates; and
- any contract, arrangement, transaction or proposal concerning insurance which the Company proposes to maintain or purchase for the benefit of directors or for the benefit of persons including directors.

Article 27 of the Articles of Association states, that the board may authorize any matter which may otherwise involve a director breaching his duties under certain sections of the Companies Act to avoid conflicts of interest.

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

Directors' and Officers' Compensation

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

Directors' Borrowing Powers

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

Retirement of Directors

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

Share Qualification of Directors

No shareholding qualification is required by a director.

Redemption Provisions

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

Capital Calls

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

No Sinking Fund

Our ordinary shares do not have sinking fund provisions.

Modification of Rights

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

Shareholders' Meetings and Resolutions

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

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

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

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

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

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

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

- the election of directors;
- the approval of financial statements;
- the declaration of final dividends;
- the appointment of auditors; and
- the grant of authority to allot shares.

A special resolution requires the affirmative vote of not less than three-fourths of the eligible votes cast. Examples of matters that must be approved by a special resolution include changes to the Articles of Association, or our winding-up.

Limitation on Owning Securities

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

Change in Control

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

In addition, our board of directors is divided into three classes for purposes of election. One class is elected at each annual general meeting to serve for a three-year term. Because this would restrict shareholders' ability to replace the entire board at a single meeting, this provision could also have the effect of delaying, deferring or preventing a change in control of our Company.

We may be subject to the Takeover Code, if the Takeover Panel determines that we have our place of central management and control in the United Kingdom. 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 that is the case, now or in the future, then 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 the voting rights of our shares; 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.

Differences in Corporate Law between England and the State of Delaware

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

	Delaware	**England**
Number of Directors	Under Delaware law, a corporation must have at least one director and the number of directors shall be fixed by or in the manner provided in the bylaws, unless specified in the certificate of incorporation.	Under the Companies Act, a public limited company must have at least two directors and the number of directors may be fixed by or in the manner provided in a company's articles of association.

	Delaware	England
Removal of Directors	Under Delaware law, directors may be removed from office, with or without cause, by a majority shareholder vote, except (a) in the case of a corporation whose board is classified, shareholders may effect such removal only for cause, unless otherwise provided in the certificate of incorporation, and (b) in the case of a corporation having cumulative voting, if less than the entire board is to be removed, no director may be removed without cause if the votes cast against his or her removal would be sufficient to elect him or her if then cumulatively voted at an election of the entire board of directors, or, if there are classes of directors, at an election of the class of directors of which he or she is a part.	Under the Companies Act, shareholders may remove a director without cause by an ordinary resolution (which is passed by a simple majority of those voting in person or by proxy at a general meeting) irrespective of any provisions of any service contract the director has with the company, provided that 28 clear days' notice of the resolution is given to the company and certain other procedural requirements under the Companies Act are followed (such as allowing the director to make representations against his or her removal at the meeting and/or in writing).
Vacancies on the Board of Directors	Under Delaware law, vacancies and newly created directorships may be filled by a majority of the directors then in office (even though less than a quorum) or by a sole remaining director unless otherwise provided in the certificate of incorporation or bylaws of the corporation.	Under English law, the procedure by which directors (other than a company's initial directors) are appointed is generally set out in a company's articles of association, provided that where two or more persons are appointed as directors of a public limited company by resolution of the shareholders, resolutions appointing each director must be voted on individually unless a resolution of the shareholders that such resolutions do not have to be voted on individually is first agreed to by the meeting without any vote being given against it.
Annual General Meeting	Under Delaware law, the annual meeting of shareholders shall be held at such place, on such date and at such time as may be designated from time to time by the board of directors or as provided in the certificate of incorporation or by the bylaws.	Under the Companies Act, a public limited company must hold an annual general meeting each year. This meeting must be held within six months beginning with the day following the company's accounting reference date.
General Meeting	Under Delaware law, special meetings of the shareholders may be called by the board of directors or by such person or persons as may be authorized by the certificate of incorporation or by the bylaws.	Under the Companies Act, a general meeting of the shareholders of a public limited company may be called by the directors. Shareholders holding at least 5% of the paid-up capital (excluding any paid-up capital held as treasury shares) of the company carrying voting rights at general meetings can also require the directors to call a general meeting.

	Delaware	England
Notice of General Meetings	Under Delaware law, written notice of any meeting of the shareholders must be given to each shareholder entitled to vote at the meeting not less than ten nor more than 60 days before the date of the meeting and shall specify the place, date, hour and purpose or purposes of the meeting.	The Companies Act provides that a general meeting (other than an adjourned meeting) must be called by notice of: • in the case of an annual general meeting, at least 21 days; and • in any other case, at least 14 days. The company's articles of association may provide for a longer period of notice and, in addition, certain matters (such as the removal of directors or auditors) require special notice, which is 28 clear days' notice. The shareholders of a company may in all cases consent to a shorter notice period, the proportion of shareholders' consent required being 100% of those entitled to attend and vote in the case of an annual general meeting and, in the case of any other general meeting, a majority in number of the members having a right to attend and vote at the meeting, being a majority who together hold not less than 95% in nominal value of the shares giving a right to attend and vote at the meeting.
Quorum	The certificate of incorporation or bylaws may specify the number of shares, the holders of which shall be present or represented by proxy at any meeting in order to constitute a quorum, but in no event shall a quorum consist of less than $^1/_3$ of the shares entitled to vote at the meeting. In the absence of such specification in the certificate of incorporation or bylaws, a majority of the shares entitled to vote, present in person or represented by proxy, shall constitute a quorum at a meeting of shareholders.	Subject to the provisions of a company's articles of association, the Companies Act provides that two shareholders present at a meeting (in person or by proxy) shall constitute a quorum.
Proxy	Under Delaware law, at any meeting of shareholders, a shareholder may designate another person to act for such shareholder by proxy, but no such proxy shall be voted or acted upon after three years from its date, unless the proxy provides for a longer period.	Under the Companies Act, at any meeting of shareholders, a shareholder may designate another person to attend, speak and vote at the meeting on their behalf by proxy (or, in the case of a shareholder which is a corporate body, may appoint a corporate representative).

	Delaware	England
Issue of New Shares	Under Delaware law, if the company's certificate of incorporation so provides, the directors have the power to authorize additional stock. The directors may authorize capital stock to be issued for consideration consisting of cash, any tangible or intangible property or any benefit to the company or any combination thereof.	Under the Companies Act, the directors of a company must not exercise any power to allot shares or grant rights to subscribe for, or to convert any security into, shares unless they are authorized to do so by the company's articles of association or by an ordinary resolution of the shareholders. Any authorization given must state the maximum amount of shares that may be allotted under it and specify the date on which it will expire, which must be not more than five years from the date the authorization was given. The authority can be renewed by a further resolution of the shareholders.
Pre-emptive Rights	Under Delaware law, unless otherwise provided in a corporation's certificate of incorporation, a stockholder does not, by operation of law, possess pre-emptive rights to subscribe to additional issuances of the corporation's stock.	Under the Companies Act, "equity securities" (being (i) shares in the company other than shares that, with respect to dividends and capital, carry a right to participate only up to a specified amount in a distribution ("ordinary shares") or (ii) rights to subscribe for, or to convert securities into, ordinary shares) proposed to be allotted for cash must be offered first to the existing equity shareholders in the company in proportion to the respective nominal value of their holdings, unless an exception applies or a special resolution to the contrary has been passed by shareholders in a general meeting or the articles of association provide otherwise in each case in accordance with the provisions of the Companies Act.
Liability of Directors and Officers	Under Delaware law, a corporation's certificate of incorporation may include a provision eliminating or limiting the personal liability of a director to the corporation and its shareholders for monetary damages arising from a breach of fiduciary duty as a director. However, no provision can limit the liability of a director for:	Under the Companies Act, any provision (whether contained in a company's articles of association or any contract or otherwise) that purports to exempt a director of a company (to any extent) from any liability that would otherwise attach to him in connection with any negligence, default, breach of duty or breach of trust in relation to the company is void.

	Delaware	England
	• any breach of the director's duty of loyalty to the corporation or its shareholders; • acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law; • willful or negligent payment of unlawful dividends or stock purchases or redemptions; or • any transaction from which the director derives an improper personal benefit.	Any provision by which a company directly or indirectly provides an indemnity (to any extent) for a director of the company or of an associated company against any liability attaching to him in connection with any negligence, default, breach of duty or breach of trust in relation to the company of which he or she is a director is also void except as permitted by the Companies Act, which provides exceptions for the company to: (i) purchase and maintain insurance against such liability; (ii) provide a "qualifying third party indemnity" (being an indemnity against liability incurred by the director to a person other than the company or an associated company, which must not cover fines imposed in criminal proceedings, penalties imposed by regulatory bodies arising out of non-compliance with regulatory requirements, the defense costs of criminal proceedings where the director is found guilty, the defense costs of civil proceedings successfully brought against the director by the company or an associated company, or the costs of unsuccessful applications by the director for certain reliefs); and (iii) provide a "qualifying pension scheme indemnity" (being an indemnity against liability incurred in connection with the company's activities as trustee of an occupational pension plan).
Voting Rights	Delaware law provides that, unless otherwise provided in the certificate of incorporation, each shareholder of record is entitled to one vote for each share of capital stock held by such shareholder.	Under English law, unless a poll is demanded by the shareholders of a company or is required by the Chairman of the meeting or the company's articles of association, shareholders shall vote on all resolutions on a show of hands.

	Delaware	England
		Under the Companies Act, a poll may be demanded by: (i) not fewer than five shareholders having the right to vote on the resolution; (ii) any shareholder(s) representing at least 10% of the total voting rights of all the shareholders having the right to vote on the resolution (excluding any voting rights attached to treasury shares); or (iii) any shareholder (s) holding shares in the company conferring a right to vote on the resolution being shares on which an aggregate sum has been paid up equal to not less than 10% of the total sum paid up on all the shares conferring that right. A company's articles of association may provide more extensive rights for shareholders to call a poll. Under English law, an ordinary resolution is passed on a show of hands if it is approved by a simple majority (more than 50%) of the votes cast by shareholders present (in person or by proxy) and entitled to vote. If a poll is demanded, an ordinary resolution is passed if it is approved by holders representing a simple majority of the total voting rights of shareholders present (in person or by proxy) who (being entitled to vote) vote on the resolution. Special resolutions require the affirmative vote of not less than 75% of the votes cast by shareholders present (in person or by proxy) at the meeting.
Variation of Class Rights	Under Delaware law, the holders of the outstanding shares of a class shall be entitled to vote as a class upon a proposed amendment, whether or not entitled to vote thereon by the certificate of incorporation, if the amendment would increase or decrease the aggregate number of authorized shares of such class, increase or decrease the par value of the shares of such class, or alter or change the powers, preferences or special rights of the shares of such class so as to affect them adversely.	The Companies Act provides that rights attached to a class of shares may only be varied or abrogated in accordance with provision in the company's articles for the variation or abrogation of those rights or, where the company's articles contain no such provision, if the holders of shares of that class consent to the variation or abrogation. Consent for these purposes means: • consent in writing from the holders of at least 75% in nominal value of the issued shares of that class (excluding any shares held as treasury shares); or

	Delaware	England
		• a special resolution passed at a separate meeting of the holders of that class sanctioning the variation. The Companies Act provides that the quorum for a class meeting is not less than two persons holding or representing by proxy at least one-third of the nominal value of the issued shares of that class. Following a variation of class rights, shareholders who amount to not less than 15% of the shareholders of the class in question who did not approve the variation may apply to court to have the variation cancelled. Any application must be made within 21 days of the variation. The court may cancel the variation if it is satisfied having regard to all the circumstances of the case that the variation would unfairly prejudice the shareholders of the class represented by the applicant.
Shareholder Vote on Certain Transactions	Generally, under Delaware law, unless the certificate of incorporation provides for the vote of a larger portion of the stock, completion of a merger, consolidation, sale, lease or exchange of all or substantially all of a corporation's assets or dissolution requires: • the approval of the board of directors; and • approval by the vote of the holders of a majority of the outstanding stock or, if the certificate of incorporation provides for more or less than one vote per share, a majority of the votes of the outstanding stock of a corporation entitled to vote on the matter.	The Companies Act provides for schemes of arrangement, which are arrangements or compromises between a company and any class of shareholders or creditors that may be used in certain types of reconstructions, amalgamations, capital reorganizations or takeovers. These arrangements require: • the approval at a shareholders' or creditors' meeting convened by order of the court, of a majority in number of shareholders or creditors representing 75% in value of the capital held by, or debt owed to, the class of shareholders or creditors, or class thereof present and voting, either in person or by proxy; and

Delaware	England
Under Delaware law, a contract or transaction between the company and one or more of its directors or officers, or between the company and any other organization in which one or more of its directors or officers, are directors or officers, or have a financial interest, shall not be void solely for this reason, or solely because the director or officer participates in the meeting of the board which authorizes the contract or transaction, or solely because any such director's or officer's votes are counted for such purpose, if: • the material facts as to the director's or officer's relationship or interest and as to the contract or transaction are disclosed or are known to the board, and the board in good faith authorizes the contract or transaction by the affirmative votes of a majority of the disinterested directors, even though the disinterested directors be less than a quorum; • the material facts as to the director's or officer's relationship or interest and as to the contract or transaction are disclosed or are known to the shareholders entitled to vote thereon, and the contract or transaction is specifically approved in good faith by vote of the shareholders; or • the contract or transaction is fair as to the corporation as of the time it is authorized, approved or ratified, by the board of directors, a committee or the shareholders.	• the approval of the court. Once approved, sanctioned and effective, all shareholders or creditors of the relevant class and the company are bound by the terms of the scheme. In addition, the Companies Act provides for restructuring plans, which may be used by a company only for the purpose of reducing or mitigating the effects of financial difficulties it is encountering that may affect its ability to carry on business as a going concern. These plans are similar to schemes of arrangement, but: the only shareholder or creditor approval required is that of shareholders or creditors representing 75% in value of the capital held by, or debt owed to, the members present and voting of one class of shareholders or creditors that would have a genuine economic interest in the company if the plan were not approved; and if that approval is obtained, members of any other class of shareholders or creditors will be bound by the restructuring plan if they will not as a result be worse off than if the plan were not approved and the court grants its approval. The Companies Act also contains certain provisions relating to transactions between a director and the company, including transactions involving the acquisition of substantial non-cash assets from a director or the sale of substantial noncash assets to a director, and loans between a company and a director or certain connected persons of directors. If such transactions meet certain thresholds set out within the Companies Act the approval of shareholders by ordinary resolution will be required.

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

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

Other U.K. Law Considerations

Squeeze-Out

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

Sell-Out

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

Disclosure of Interest in Shares

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

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

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

Dividends

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

Purchase of Own Shares

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

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

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

Statutory Pre-Emption Rights

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

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

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

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

U.K. City Code on Takeovers and Mergers

The U.K. 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 U.K. 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.

C. Material Contracts

Set forth below are summaries of material agreements to which we are a party, other than contracts entered into in the ordinary course of business. In addition to the agreements described below, we also enter into agreements with clinical research organizations, or CROs, for the conduct of our clinical trials. The descriptions provided below do not purport to be complete and are qualified in their entirety by the complete agreements, which are attached as exhibits to this Annual Report.

Relationship Agreement

As a condition to the closing of the Acquisition, we and RPC entered into a Relationship Agreement, which provided, subject to closing of the Acquisition, the right for RPC to appoint the following number of directors to our board of directors in relation to the percentage of our Ordinary Shares held in aggregate by RPC from time to time: (i) two class A directors if RPC holds 25% or more of our Ordinary Shares; (ii) one class A director if RPC holds 10% or more but less than 25% of our Ordinary Shares; and (iii) no directors if RPC holds less than 10% of our Ordinary Shares.

Additionally, where such right to appoint a director falls away, RPC is obliged to procure the resignation of the relevant director as soon as practicably possible thereafter at no cost to us. Unless otherwise agreed by our board of directors, the directors appointed by RPC shall be class A directors.

Employment and Consulting Agreements

See "Item 6. Directors, Senior Management and Employees—Compensation—Employment and Consulting Agreements".

D. Exchange Controls

There are currently no U.K. laws, decrees or regulations that restrict the export or import of capital, including, but not limited to, foreign exchange controls, or that affect the remittance of dividends or other payments to non-U.K. residents or to U.S. holders of our securities except as otherwise set forth in "Taxation" below. There are no limitations under our Memorandum and Articles of Association restricting voting or shareholding.

E. Taxation

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

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

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

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

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

If a partnership (or any other entity treated as a partnership for U.S. federal income tax purposes) holds our ordinary shares or ADSs, the tax treatment of a partner will generally depend upon the status of the partner and upon the activities of the partnership.

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

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

United Kingdom tax considerations

Taxation of dividends

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

Taxation of Capital Gains

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

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

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

A holder of our ordinary shares or ADSs who (1) is an individual who has ceased to be resident for U.K. tax purposes in the United Kingdom, (2) was solely resident for U.K. tax purposes in the United Kingdom for either the whole or a part of at least four out of the seven U.K. tax years prior to departure, (3) only remains non-UK resident for a period of five years or less and (4) disposes of the ordinary shares or ADSs during that period may also be liable, upon returning to the United Kingdom, for U.K. tax on capital gains, subject to any available exemption or relief, even though he or she was not resident in the United Kingdom at the time of the disposal. Normally, no tax charge arises if the asset that was sold during the period of temporary non-residence was acquired during that same period. In practice, this means that only disposals of assets held prior to leaving the UK are in scope.

Inheritance Tax

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

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

- are part of the business property of a permanent establishment in the United Kingdom, or
- pertain to a fixed base in the United Kingdom used for the performance of independent personal services.

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

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

U.K. legislation provides that SDRT is chargeable at 1.5% (rounded to the nearest £5) on the issuance of a depositary receipt for U.K. shares or securities, or the issuance of such shares or securities into a clearance system. Following certain court decisions, HMRC accepted that these provisions contravened European Union law, and accordingly has not sought to enforce SDRT on issues of U.K. shares and securities to depositary receipt issuers and clearance services anywhere in the world. EU law ceased to apply in the U.K. at the end of the transition period following Brexit on December 31, 2020. Although the legislation imposing the SDRT charge has not been repealed, HMRC has stated that it remains of the view that the charge on issues remains disapplied, because the relevant EU legislation has been incorporated into domestic U.K. law under the terms of the European Union (Withdrawal) Act 2018. Accordingly, it will not seek to enforce such a charge, unless the legislation is amended. HMRC still contends that stamp duty/SDRT at 1.5% is payable on transfers (by sale or otherwise) of shares and securities to depository receipt systems or clearance services that are not an integral part of an issue of share capital or the raising of capital.

Transfers of ADSs do not attract stamp duty or SDRT.

Transfer of shares in registered form

A transfer of shares in registered form would attract ad valorem stamp duty generally at the rate of 0.5% of the purchase price of the shares (or, in certain circumstances, where a stamp duty deemed market value rules applies, the deemed consideration for the transfer). There is no charge to ad valorem stamp duty on gifts.

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

In addition, any transfers of, and unconditional agreements to transfer, unlisted shares on or after July 22, 2020 to a company that is connected with the transferor will attract a charge to stamp duty and SDRT respectively on the higher of the market value of the shares and the value of the consideration where some or all of the consideration consists of the issue of shares.

Transfer of ADSs

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

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

You are urged to consult with your own advisers regarding the UK tax consequences of the acquisition, ownership, and disposition of our ordinary shares or ADSs in the light of your particular circumstances.

United States federal income tax considerations

Ownership of ADSs

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

U.S. Taxation of Distributions

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

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

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

The additional 3.8% "net investment income tax" (described below) may apply to dividends received by certain U.S. Holders who meet certain modified adjusted gross income thresholds.

U.S. Taxation upon Sale or Other Disposition

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

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

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

The additional 3.8% "net investment income tax" (described below) may apply to gains recognized upon the sale or other taxable disposition of our ordinary shares or ADSs by certain U.S. Holders who meet certain modified adjusted gross income thresholds.

Medicare Tax

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

Passive Foreign Investment Company Rules

We may have been a PFIC for 2022, but we have not performed a detailed analysis to determine PFIC status for 2022. Because the PFIC determination is highly fact intensive, there can be no assurance that we were not a PFIC for 2022 and there can no assurance that we will not be a PFIC for 2022 or for any other taxable year. A separate determination must be made after the close of each taxable year as to whether we are a PFIC for that year. As a result, our PFIC status may change from year to year.

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

In the event we are treated as a PFIC for any taxable year, the tax consequences under the default PFIC regime described above could be avoided by either a "mark-to-market" or "qualified electing fund" election. If our ordinary shares or ADSs are considered "marketable stock," a U.S. Holder may elect to "mark-to-market" its ADSs provided the U.S. Holder completes and files IRS Form 8621 in accordance with the relevant instructions and related Treasury Regulations. A U.S. Holder making a mark-to-market election (if the eligibility requirements for such an election were satisfied) generally would not be subject to the PFIC rules discussed above, except with respect to any portion of the holder's holding period that preceded the effective date of the election. Instead, such U.S. Holder would generally include in income any excess of the fair market value of the ordinary shares or ADSs at the close of each tax year over its adjusted basis in the ordinary shares or ADSs. If the fair market value of the ordinary shares of ADSs had depreciated below the U.S. Holders adjusted basis at the close of the tax year, the U.S. Holder may generally deduct the excess of the adjusted basis of the ordinary shares or ADSs over its fair market value at that time. However, such deductions generally would be limited to the net mark-to-market gains, if any, that the U.S. Holder included in income with respect to such ordinary shares or ADSs in prior years. Income recognized and deductions allowed under the mark-to-market provisions, as well as any gain or loss on the disposition of ordinary shares or ADSs with respect to which the mark-to-market election is made, is treated as ordinary income or loss (except that loss is treated as capital loss to the extent the loss exceeds the net mark-to-market gains, if any, that a U.S. Holder included in income with respect to such ordinary share or ADSs in prior years). Gain or loss from the disposition of ordinary shares or ADSs (as to which a "mark-to-market" election was made) in a year in which we are no longer a PFIC, will be capital gain or loss. Our ordinary shares or ADSs should be considered "marketable stock" if they traded at least 15 days during each calendar quarter of the relevant calendar year in more than de minimis quantities. Any such mark to market election would not be available for a lower-tier PFIC.

Alternatively, a U.S. Holder making a valid and timely "qualified electing fund" or "QEF" election generally would not be subject to the default PFIC regime discussed above. Instead, for each PFIC year to which such an election applied, the electing U.S. Holder would be subject to U.S. federal income tax on the electing U.S. Holder's pro rata share of our net capital gain and ordinary earnings, regardless of whether such amounts were actually distributed to the electing U.S. Holder. Any gain on sale or other disposition of a U.S. Holder's ordinary shares or would be treated as capital, and the interest penalty will not be imposed. If an investor provides reasonable notice to us that it has determined to make a QEF election, we 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. Holders are urged to consult their tax advisors about the PFIC rules, including the advisability, procedure and timing of making a mark-to-market election or QEF election and the U.S. Holder's eligibility to file such elections (including, with respect to making a mark-to-market election, whether our ordinary shares or ADSs are treated as "marketable stock" for such purpose). A U.S. Holder will be required to file Internal Revenue Service Form 8621 if such U.S. Holder owns our ordinary shares or ADSs in any year in which we are classified as a PFIC.

Information reporting and backup withholding

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

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

Certain reporting requirements

Certain U.S. Holders are required to file IRS Form 926, Return by U.S. Transferor of Property to a Foreign Corporation, and certain U.S. Holders may be required to file IRS Form 5471, Information Return of U.S. Persons With Respect to Certain Foreign Corporations, reporting transfers of cash or other property to us and information relating to the U.S. Holder and us. Substantial penalties may be imposed upon a U.S. Holder that fails to comply. See also the discussion regarding Form 8621, Information Return by a Shareholder of a Passive Foreign Investment Company or Qualified Electing Fund, above.

In addition, certain U.S. Holders must report information on IRS Form 8938, Statement of Specified Foreign Financial Assets, with respect to their investments in certain "foreign financial assets," which would include an investment in our ordinary shares or ADSs, if the aggregate value of all of those assets exceeds $50,000 on the last day of the taxable year (or in some circumstances, a higher threshold). This reporting requirement applies to individuals and certain U.S. entities.

U.S. Holders who fail to report required information could become subject to substantial penalties. U.S. Holders should consult their tax advisors regarding the possible implications of these reporting requirements arising from their investment in our ordinary shares or ADSs.

F. Dividends and Paying Agents

Not applicable.

G. Statement by Experts

Not applicable.

H. Documents on Display

We are currently subject to the information and periodic reporting requirements of the Exchange Act, and file periodic reports and other information with the SEC through its electronic data gathering, analysis and retrieval (EDGAR) system. The SEC maintains an Internet website that contains reports and other information regarding issuers that file electronically with the SEC. You may read and copy this annual report, including the related exhibits and schedules, and any document we file with the SEC at http://www.sec.gov.

As a foreign private issuer, we are exempt from the rules under the Exchange Act related to the furnishing and content of proxy statements, and our officers, directors and principal shareholders are exempt from the reporting and short-swing profit recovery provisions contained in Section 16 of the Exchange Act. In addition, we are not required under the Exchange Act to file annual, quarterly and current reports and financial statements with the SEC as frequently or as promptly as United States companies whose securities are registered under the Exchange Act.

I. Subsidiary Information

Not applicable.

J. Annual Report to Security Holders.

Not applicable.

Item 11. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT RISK

You should read the following information in conjunction with Item 5, "Operating and Financial Review and Prospects;" Item 3, "Risk Factors;" and our consolidated financial statements, including the related notes thereto, including Note 2, both of which are included elsewhere in this document. The following discussion about our financial risk management activities includes "forward-looking statements" that involve risks and uncertainties. Actual results could differ materially from those projected in these forward-looking statements.

Risk Management Framework

We are exposed to a variety of risks, including changes in foreign currency exchange risk and interest rates.

Currency Exchange Rate Sensitivity

The results of our operations are subject to currency transactional risk. Operating results and financial position are reported in local currencies and then translated into United States dollars at the applicable exchange rate for preparation of our consolidated financial statements. The fluctuation of the U.S. dollar in relation to the British Pound, Euro and Swiss Franc will therefore have an impact upon profitability of our operations and may also affect the value of our assets and the amount of shareholders' equity.

Our functional currency is the United States dollar and our activities are predominantly executed using both the U.S. dollar, Euro and British Pound. We have done a limited number of financings, and we are not subject to significant operational exposures due to fluctuations in these currencies. We have not entered into any agreements, or purchased any instruments, to hedge any possible currency risks at this time.

Interest Rate Sensitivity

We currently have no short-term or long-term debt requiring interest payments. This does not require us to consider entering into any agreements or purchasing any instruments to hedge against possible interest rate risks at this time. Our interest-earning investments are short-term. Thus, any reductions in future income or carrying values due to future interest rate declines are believed to be immaterial.

Item 12. DESCRIPTION OF SECURITIES OTHER THAN EQUITY SECURITIES

A. Debt Securities

Not applicable.

B. Warrants and Rights

Not applicable.

C. Other Securities

Not applicable.

D. American Depositary Shares

Deutsche Bank Trust Company Americas, as depositary, will register and deliver the ADSs. Each ADS will represent ownership of 100 ordinary shares deposited with Deutsche Bank AG, London Branch with principal office at Winchester House, 1 Great Winchester Street, London EC2N 2DB, U.K., as custodian for the depositary. Each ADS will also represent ownership of any other securities, cash or other property which may be held by the depositary. The depositary's corporate trust office at which the ADSs will be administered is located at 60 Wall Street, New York, NY 10005, USA. The principal executive office of the depositary is located at 60 Wall Street, New York, NY 10005, USA.

The Direct Registration System, or DRS, is a system administered by The Depository Trust Company, or DTC, pursuant to which the depositary may register the ownership of uncertificated ADSs, which ownership shall be evidenced by periodic statements issued by the depositary to the ADS holders entitled thereto.

We will not treat ADS holders as our shareholders and accordingly, you, as an ADS holder, will not have shareholder rights. English law governs shareholder rights. The depositary or its custodian will be the holder of the ordinary shares underlying your ADSs. As a holder of ADSs, you will have ADS holder rights. A deposit agreement among us, the depositary and you, as an ADS holder, and the beneficial owners of ADSs sets out ADS holder rights as well as the rights and obligations of the depositary. The laws of the State of New York govern the deposit agreement and the ADSs.

Fees and Charges

As a holder of ADSs, you will be required to pay the following service fees to the depositary bank:

Service:	Fee:
Issuance of ADSs, including issuances resulting from a distribution of shares or rights or other property	Up to $0.05 per ADS issued
Cancellation of ADSs, including in the case of termination of the deposit agreement	Up to $0.05 per ADS cancelled
Distribution of cash dividends or other cash distributions	Up to $0.02 per ADS held
Distribution of ADSs pursuant to share dividends, free share distributions or exercise of rights	Up to $0.05 per ADS held
Operation and maintenance costs in administering the ADSs	An annual fee of $0.02 per ADS held
Inspections of the relevant share register maintained by the local registrar and/or performing due diligence on the central securities depository for England and Wales	An annual fee of $0.01 per ADS held (such fee to be assessed against holders of record as at the date or dates set by the depositary as it sees fit and collected at the sole discretion of the depositary by billing such holders for such fee or by deducting such fee from one or more cash dividends or other cash distributions)

As an ADS holder, you will also be responsible to pay certain fees and expenses incurred by the depositary bank and certain taxes and governmental charges such as:

- Taxes (including applicable interest and penalties) and other governmental charges.
- Such registration fees as may from time to time be in effect for the registration of ordinary shares or other deposited securities with the foreign registrar and applicable to transfers of ordinary shares or other deposited securities to or from the name of the custodian, the depositary or any nominees upon the making of deposits and withdrawals, respectively.
- Expenses for cable, telex and fax transmissions and for delivery of securities.
- Expenses and charges incurred by the Depositary in the conversion of foreign currency.
- Fees and expenses incurred in connection with the delivery or servicing of ordinary shares on deposit, including any fees of a central depository for securities in the local market, where applicable.
- Fees and expenses incurred in connection with complying with exchange control regulations and any other regulatory requirements that are not currently applicable but may arise or become applicable to ordinary shares, deposited securities, ADSs and ADRs.
- Any applicable fees and penalties thereon.

The depositary fees payable upon the issuance and cancellation of ADSs are typically paid to the depositary bank by the brokers (on behalf of their clients) receiving the newly issued ADSs from the depositary bank and by the brokers (on behalf of their clients) delivering the ADSs to the depositary bank for cancellation. The brokers in turn charge these fees to their clients. Depositary fees payable in connection with distributions of cash or securities to ADS holders and the depositary services fee are charged by the depositary bank to the holders of record of ADSs as of the applicable ADS record date.

The depositary fees payable for cash distributions are generally deducted from the cash being distributed or by selling a portion of distributable property to pay the fees. In the case of distributions other than cash (i.e., share dividends, rights, etc.), the depositary bank charges the applicable fee to the ADS record date holders concurrent with the distribution. In the case of ADSs registered in the name of the investor (whether certificated or uncertificated in direct registration), the depositary bank sends invoices to the applicable record date ADS holders. In the case of ADSs held in brokerage and custodian accounts (via DTC), the depositary bank generally collects its fees through the systems provided by DTC (whose nominee is the registered holder of the ADSs held in DTC) from the brokers and custodians holding ADSs in their DTC accounts. The brokers and custodians who hold their clients' ADSs in DTC accounts in turn charge their clients' accounts the amount of the fees paid to the depositary banks.

In the event of refusal to pay the depositary fees, the depositary bank may, under the terms of the deposit agreement, refuse the requested service until payment is received or may set off the amount of the depositary fees from any distribution to be made to the ADS holder.

The depositary may make payments to us or reimburse us for certain costs and expenses, by making available a portion of the ADS fees collected in respect of the ADR program or otherwise, upon such terms and conditions as we and the depositary bank agree from time to time.

Payment of Taxes

As an ADS holder, you will be responsible for any taxes or other governmental charges payable on your ADSs or on the deposited securities represented by any of your ADSs. The depositary may refuse to register any transfer of your ADSs or allow you to withdraw the deposited securities represented by your ADSs until such taxes or other charges are paid. It may apply payments owed to you or sell deposited securities represented by your ADSs to pay any taxes owed and you will remain liable for any deficiency. If the depositary sells deposited securities, it will, if appropriate, reduce the number of ADSs to reflect the sale and pay to you any net proceeds, or send to you any property, remaining after it has paid the taxes. You agree to indemnify us, the depositary, the custodian and each of our and their respective agents, directors, employees and affiliates for, and hold each of them harmless from, any claims with respect to taxes (including applicable interest and penalties thereon) arising from any tax benefit obtained for you.

PART II

Item 13. DEFAULTS, DIVIDEND ARREARAGES AND DELINQUENCIES

Not applicable.

Item 14. MATERIAL MODIFICATIONS TO THE RIGHTS OF SECURITY HOLDERS AND USE OF PROCEEDS

Not applicable.

Item 15. CONTROLS AND PROCEDURES

(a) Disclosure Controls and Procedures

We performed an evaluation of the effectiveness of our disclosure controls and procedures that are designed to ensure that information required to be disclosed in this annual report and filed with the SEC is recorded, processed, summarized and reported timely within the time period specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by an issuer in the reports that it files or submits under the Exchange Act, is accumulated and communicated to the issuer's management, including its principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure. There can be no assurance that our disclosure controls and procedures will detect or uncover all failures of persons within our Company to disclose information otherwise required to be set forth in our reports. Nevertheless, our disclosure controls and procedures are designed to provide reasonable assurance of achieving the desired control objectives. Based on our evaluation, our principal executive officer and principal accounting officer, have concluded that our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15(d)-15(e) of the Exchange Act) as of the end of the period covered by this annual report are effective.

(b) Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as defined in Rules 13a-15(f) and 15d-15(f) under the Securities Exchange Act of 1934, as amended. Our internal control system was designed to provide reasonable assurance to our management and board of directors regarding the reliability of financial reporting and the preparation and fair presentation of published financial statements for external purposes in accordance with generally accepted accounting principles. All internal control systems, no matter how well designed, have inherent limitations. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation and may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Our management, including the CEO and CFO, conducted an evaluation, pursuant to Rule 13a-15(c) promulgated under the Exchange Act, of the effectiveness, as of the end of the period covered by this Annual Report, of our internal control over financial reporting based on the framework in *Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013)*. Based on the results of this evaluation, our management concluded that our internal control over financial reporting was effective as of December 31, 2022.

(c) Attestation Report of Registered Public Accounting Firm

This report does not include an attestation report of our registered public accounting firm as we are not an accelerated filer or a large accelerated filer.

(d) Changes in Internal Controls over Financial Reporting

There were no changes in our internal control over financial reporting, identified in connection with the evaluation of such internal control that occurred during the current year that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 16. [RESERVED]

Item 16A. Audit Committee Financial Expert

Our board of directors has determined that Mr. Donald Williams qualifies as an audit committee financial expert pursuant to the applicable SEC rules and that Mr. Donald Williams is "independent" in accordance with the Nasdaq Capital Market corporate governance requirements. For information relating to Mr. Donald Williams' qualifications and experience, see "Item 6. Directors, Senior Management and Employees—A. Directors and Senior Management."

Item 16B. Code of Ethics

We have adopted a code of ethics that applies to all of our employees, including our chief executive officer. The text of the code of ethics is posted in the "Investor Relations" section of our website at *www.akaritx.com*. Disclosure regarding any amendments to, or waivers from, provisions of the code of conduct that apply to our directors, principal executive and financial officers will be included in a Current Report on Form 6-K within four business days following the date of the amendment or waiver, unless website posting or the issuance of a press release of such amendments or waivers is then permitted by the rules of the Nasdaq stock market.

Item 16C. Principal Accountant Fees and Services

BDO USA, LLP served as our independent registered public accounting firm and audited our consolidated financial statements for the years ended December 31, 2022 and 2021.

	2022	2021
Audit Fees [1]	$ 280,455	$ 249,146

(1) Audit fees consisted of work performed in the preparation of the consolidated financial statements, interim review procedures, and work regarding a public listing or offering, as well as work that generally only the independent registered public accounting firm can reasonably be expected to provide, such as statutory audits.

Audit Committee Pre-Approval Policies and Procedures

The audit committee reviews and pre-approves all audit and non-audit services performed by its independent registered public accounting firm, as well as the fees charged for such services. All fees incurred for the year ended 2022 for services rendered by BDO were approved in accordance with these policies. In its review of non-audit service fees, the audit committee considers, among other things, the possible impact of the performance of such services on the auditor's independence. No non-audit services were performed by BDO for the year ended December 31, 2022 and 2021.

Item 16D. Exemptions from the Listing Standards for Audit Committees

Not applicable.

Item 16E. Purchases of Equity Securities by the Issuer and Affiliated Purchasers

Not applicable.

Item 16F. Change in Registrant's Certifying Accountant

Not applicable.

Item 16G. Corporate Governance

We rely on a provision in Nasdaq's Listed Company Manual that allows us to follow English corporate law and the Companies Act 2006 with regard to certain aspects of corporate governance. This allows us to follow certain corporate governance practices that differ in significant respects from the corporate governance requirements applicable to U.S. companies listed on Nasdaq.

In accordance with English corporate law and the Companies Act 2006 and practice and subject to the exemption set forth in Rule 5615 of the Marketplace Rules of the Nasdaq Stock Market, we follow the provisions of the Companies Act, rather than the Marketplace Rules of the Nasdaq Stock Market, with respect to the following requirements:

- We do not follow Nasdaq's requirements to seek shareholder approval for all corporate actions approval in accordance with Nasdaq Stock Market Rule 5635. In particular, under this Nasdaq rule, shareholder approval is generally required for: (i) an acquisition of shares or assets of another company that involves the issuance of 20% or more of the acquirer's shares or voting rights or if a director, officer or 5% shareholder has greater than a 5% interest in the target company or the consideration to be received; (ii) the issuance of shares leading to a change of control; (iii) adoption or amendment of equity compensation arrangements; and (iv) issuances of 20% or more of the shares or voting rights (including securities convertible into, or exercisable for, equity) of a listed company via a private placement (and/or via sales by directors, officers or 5% shareholders) if such equity is issued (or sold) at below the greater of the book or market value of shares.

As a foreign private issuer, we are permitted to, and we will, follow home country practice in lieu of the above requirements.

Because we are a foreign private issuer, our directors and senior management are not subject to short-swing profit and insider trading reporting obligations under Section 16 of the U.S. Securities Exchange Act of 1934, as amended, or Exchange Act. They are, however, subject to the obligations to report changes in share ownership under Section 13 of the Exchange Act and related SEC rules.

Item 16H. Mine Safety Disclosures

Not applicable.

Item 16I. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not applicable.

PART III

Item 17. Financial Statements

We have responded to Item 18 in lieu of responding to this item.

Item 18. Financial Statements

Financial Statements are filed as part of this annual report. See page F-1.

These consolidated financial statements are not the Company's statutory accounts as defined in section 434 of the UK Companies Act 2006. Statutory accounts for the Company's financial year ended December 31, 2022 have not yet been delivered to the Registrar of Companies for England and Wales. Statutory accounts for the financial years ended December 31, 2020 and December 31, 2021 have been delivered to the Registrar in accordance with section 441 of the Companies Act 2006. An auditor's report has been made on the statutory accounts each of these two years and contained no statement under section 498(2) or (3) of the Companies Act 2006. Each of these audit reports included a statement drawing attention to circumstances indicating the existence of a material uncertainty which may cast significant doubt about the Company's ability to continue as a going concern, but was unqualified and did not include any reference to any other matters to which the auditor drew attention by way of emphasis without qualifying the report.

Item 19. Exhibits

Exhibit No.	Exhibit Description
2.1	Share Exchange Agreement, dated as of July 10, 2015, by and between Celsus Therapeutics Plc and RPC Pharma Limited (incorporated by reference to the exhibit previously filed on the Registrant's Current Report on Form 8-K filed on July 13, 2015)
2.2	A description of the rights of each class of securities that is registered under Section 12 of the Exchange Act as of the end of the period covered by this report. The information required hereby is included in Items 9, 10 and 12 hereof.*
3.1	Articles of Association of Akari Therapeutics, Plc (incorporated by reference to the exhibit previously filed with the Registrant's Report on Form F-3/A filed on August 30, 2021)
4.1	Form of Deposit Agreement among the Registrant, Deutsche Bank Trust Company Americas, as Depositary, and all Owners and Holders from time to time of American Depositary Shares issued thereunder (incorporated by reference to the exhibit previously filed with the Registrant's Registration Statement on Form F-6 (No. 333-185197) filed on November 30, 2012)
4.2	Amendment to Deposit Agreement among the Registrant, Deutsche Bank Trust Company Americas, as Depositary, and all Owners and Holders from time to time of American Depositary Shares issued thereunder (incorporated by reference to the registrant's Post-Effective Amendment No. 1 to Registration Statement on Form F-6 (No. 333-185197) filed on December 24, 2013)
4.3	Form of American Depositary Receipt; the Form is Exhibit A of the Form of Amendment to the Deposit Agreement (incorporated by reference to the exhibit previously filed with the Registrant's Registration Statement on Form F-6 (No. 333-185197) filed on November 30, 2012)
4.4	Form of Amendment No. 2 to Deposit Agreement (incorporated by reference to the exhibit previously filed with the Registrant's Post-Effective Amendment on Registration Statement Form F-6 (File No. 333-185197) filed on September 9, 2015)
4.5	Form of American Depositary Receipt; the Form is Exhibit A of the Form of Amendment to the Deposit Agreement (incorporated by reference to the exhibit previously filed with the Registrant's Post-Effective Amendment on Registration Statement Form F-6 (File No. 333-185197) filed on September 9, 2015)
10.1+	2014 Equity Incentive Plan (incorporated by reference to the exhibit previously filed with the Registrant's Report of Foreign Private Issuer on Form 6-K (No. 001-36288) filed on June 24, 2014)
10.2	Relationship Agreement, dated as of July 10, 2015, by and between Celsus Therapeutics Plc and RPC Pharma Limited. (incorporated by reference to the exhibit previously filed with the Registrant's Current Report on Form 8-K filed on July 13, 2015)

Exhibit No.	Exhibit Description
10.3	Form of Working Capital Agreement, by and between Volution Immuno Pharmaceuticals SA and the Shareholders named therein. (incorporated by reference to the exhibit previously filed with the Registrant's Current Report on Form 8-K filed on July 13, 2015)
10.4+	Amended and Restated 2014 Equity Incentive Plan (incorporated by reference to the exhibit previously filed with the Registrants Definitive Proxy Statement on Schedule 14A filed on August 3, 2015)
10.5+	Amended and Restated Non-Employee Director Compensation Policy (incorporated by reference to the exhibit previously filed with the Registrant's Current Report on Form 8-K filed on November 25, 2015)
10.6+	Amended and Restated Non-Employee Director Compensation Policy (incorporated by reference to the exhibit previously filed with the Registrant's Current Report on Form 8-K filed on June 30, 2016)
10.7	Form of Securities Purchase Agreement dated as of June 28, 2019 between Akari Therapeutics, Plc and the investors listed therein (incorporated by reference to the exhibit previously filed with the Registrant's Report on Form 6-K filed on July 2, 2019)
10.8	Form of Warrant issued by Akari Therapeutics, Plc in connection with the July 2019 Registered Direct Offering (incorporated by reference to the exhibit previously filed with the Registrant's Report on Form 6-K filed on July 2, 2019)
10.9	Form of Placement Agent Warrant issued by Akari Therapeutics, Plc in connection with the July 2019 Registered Direct Offering (incorporated by reference to the exhibit previously filed with the Registrant's Registration Statement on Form F-1 (333-233048) filed on August 6, 2019)
10.10	Form of Securities Purchase Agreement in connection with the February 2020 Private Placement (incorporated by reference to the exhibit previously filed with the Registrant's Report on Form 6-K filed on March 4, 2020)
10.11	Form of Warrant issued by Akari Therapeutics, Plc in connection with the February 2020 Private Placement (incorporated by reference to the exhibit previously filed with the Registrant's Report on Form 6-K filed on March 4, 2020)
10.12	Executive Employment Agreement, dated as of June 30, 2020, by and between the Company and Torsten Hombeck (incorporated by reference to the exhibit previously filed with the Registrant's Report on Form 6-K filed on July 1, 2020)+
10.13	Securities Purchase Agreement dated June 30, 2020 between the Company and Aspire Capital Fund, LLC (incorporated by reference to the exhibit previously filed with the Registrant's Report on Form 6-K filed on July 1, 2020)
10.14	Registration Rights Agreement dated June 30, 2020 between the Company and Aspire Capital Fund, LLC (incorporated by reference to the exhibit previously filed with the Registrant's Report on Form 6-K filed on July 1, 2020)
10.15	Form of Securities Purchase Agreement in connection with the July 2021 Private Placement (incorporated by reference to the exhibit previously filed with the Registrant's Report on Form 6-K filed on July 20, 2021)

Exhibit No.	Exhibit Description
10.16	Form of Warrant issued by Akari Therapeutics, Plc in connection with the July 2021 Private Placement (incorporated by reference to the exhibit previously filed with the Registrant's Report on Form 6-K filed on July 20, 2021)
10.17	Form of Securities Purchase Agreement dated as of December 29, 2021 between Akari Therapeutics, Plc and the investors listed therein (incorporated by reference to the exhibit previously filed with the Registrant's Report on Form 6-K filed on January 4, 2022)
10.18	Form of Warrant issued by Akari Therapeutics, Plc in connection with the December 2021 Registered Direct Offering (incorporated by reference to the exhibit previously filed with the Registrant's Report on Form 6-K filed on January 4, 2022)
10.19	Form of Securities Purchase Agreement in connection with the March 2022 Registered Direct Offering (incorporated by reference to the exhibit previously filed with the Registrant's Report on Form 6-K filed on March 10, 2022)
10.20	Form of Warrant issued by Akari Therapeutics, Plc in connection with the March 2022 Registered Direct Offering (incorporated by reference to the exhibit previously filed with the Registrant's Report on Form 6-K filed on March 10, 2022)
10.21	Form of Securities Purchase Agreement in connection with the September 2022 Registered Direct Offering and Concurrent Private Placement (incorporated by reference to the exhibit previously filed with the Registrant's Report on Form 6-K filed on September 14, 2022)
10.22	Form of Series A Warrant issued by Akari Therapeutics, Plc in connection with the September 2022 Registered Direct Offering and Concurrent Private Placement (incorporated by reference to the exhibit previously filed with the Registrant's Report on Form 6-K filed on September 14, 2022)
10.23	Form of Series B Warrant issued by Akari Therapeutics, Plc in connection with the September 2022 Registered Direct Offering and Concurrent Private Placement (incorporated by reference to the exhibit previously filed with the Registrant's Report on Form 6-K filed on September 14, 2022)
10.24	Form of Securities Purchase Agreement in connection with the March 2023 Registered Direct Offering (incorporated by reference to the exhibit previously filed with the Registrant's Report on Form 6-K filed on March 31, 2023)
10.25+	Executive Employment Agreement between the Company and Rachelle Jacques dated June 1, 2022 (incorporated by reference to the exhibit previously filed with the Registrant's Registration Statement on Form F-1 filed on October 12, 2022)
10.26+	Stock Option Agreement between the Company and Rachelle Jacques dated June 1, 2022 (incorporated by reference to the exhibit previously filed with the Registrant's Registration Statement on Form F-1 filed on October 12, 2022)
10.27+	Restricted Stock Unit Agreement between the Company and Rachelle Jacques dated June 1, 2022 (incorporated by reference to the exhibit previously filed with the Registrant's Registration Statement on Form F-1 filed on October 12, 2022)
10.28+	Executive Employment Agreement between the Company and Rachelle Jacques dated June 1, 2022 (incorporated by reference to the exhibit previously filed with the Registrant's Registration Statement on Form F-1 filed on October 12, 2022)
10.29+	Stock Option Agreement between the Company and Rachelle Jacques dated June 1, 2022 (incorporated by reference to the exhibit previously filed with the Registrant's Registration Statement on Form F-1 filed on October 12, 2022)

Exhibit No.	Exhibit Description
10.30+	Restricted Stock Unit Agreement between the Company and Rachelle Jacques dated June 1, 2022 (incorporated by reference to the exhibit previously filed with the Registrant's Registration Statement on Form F-1 filed on October 12, 2022)
21.1	List of subsidiaries (incorporated by reference to the exhibit previously filed with the Registrant's Annual Report on Form 20-F filed on April 21, 2021)
23.1	Consent of registered public accounting firm*
31.1	Certification of Chief Executive Officer*
31.2	Certification of the Chief Financial Officer*
32.1	Certification pursuant to Section 906 of the Sarbanes-Oxley Act of 2002*
32.2	Certification pursuant to Section 906 of the Sarbanes-Oxley Act of 2002*
101.INS	XBRL Instance Document*
101.SCH	XBRL Taxonomy Schema Linkbase Document*
101.CAL	XBRL Taxonomy Calculation Linkbase Document*
101.DEF	XBRL Taxonomy Definition Linkbase Document*
101.LAB	XBRL Taxonomy Labels Linkbase Document*
101.PRE	XBRL Taxonomy Presentation Linkbase Document*
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

+ Indicates management contract or compensatory plan.

* Filed herewith

SIGNATURES

The registrant hereby certifies that it meets all of the requirements for filing on Form 20-F and that it has duly caused and authorized the undersigned to sign this annual report on its behalf.

Akari Therapeutics, Plc

By: /s/ Rachelle Jacques
Name: Rachelle Jacques
Title: Chief Executive Officer

Date: April 28, 2023

AKARI THERAPEUTICS, PLC

CONSOLIDATED FINANCIAL STATEMENTS

AS OF DECEMBER 31, 2022

U.S. DOLLARS

INDEX

Report of Independent Registered Public Accounting Firm

Shareholders and Board of Directors
Akari Therapeutics, Plc
London, United Kingdom

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Akari Therapeutics, Plc (the "Company") as of December 31, 2022 and 2021, the related consolidated statements of operations and comprehensive loss, changes in shareholders' equity, and cash flows for each of the three years in the period ended December 31, 2022, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2022, in conformity with accounting principles generally accepted in the United States of America.

Going Concern Uncertainty

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the consolidated financial statements, the Company has suffered recurring losses from operations and has a net capital deficiency that raise substantial doubt about its ability to continue as a going concern. Management's plans in regard to these matters are also described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

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

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

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

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the consolidated financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the consolidated financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing separate opinions on the critical audit matter or on the accounts or disclosures to which it relates.

Classification of Warrants

As described in Note 4 to the consolidated financial statements, on December 29, 2021, the Company sold to certain accredited and institutional investors its American Depository Shares ("ADSs") in a registered direct offering, which closed on January 5, 2022. In connection with this offering, the Company also issued registered warrants to the investors and the placement agent (the "December 2021 Warrants"). On September 14, 2022, the Company sold to certain accredited and institutional investors its ADSs in a registered direct offering. In connection with this offering, the Company issued to the investors registered Series A and Series B warrants (collectively, the "September 2022 Warrants").

We identified the evaluation of the financial statement classification for the December 2021 Warrants and the September 2022 Warrants as a critical audit matter. Our principal considerations included the existence of accounting complexities related to certain provisions of the warrant agreements, including settlement provisions and derivative elements. Auditing these elements involved especially complex auditor judgment due to the terms of the applicable agreements, including the extent of specialized knowledge and skills needed.

The primary procedures we performed to address this critical audit matter included:

- Evaluating the appropriateness of management's conclusions through the review of: (i) the relevant terms of the warrant agreements, (ii) the completeness and accuracy of the Company's technical accounting analysis, and (iii) the appropriateness of application of the relevant accounting literature.

- Utilizing personnel with specialized knowledge and skills in technical accounting to assist in: (i) evaluating relevant terms of the warrant agreements in relation to the appropriate accounting literature, and (ii) assessing the appropriateness of conclusions reached by the Company.

/s/BDO USA, LLP
We have served as the Company's auditor since 2016.
New York, New York
April 28, 2023

AKARI THERAPEUTICS, Plc

CONSOLIDATED BALANCE SHEETS
As of December 31, 2022 and 2021
(in U.S. Dollars, except share data)

	December 31, 2022	December 31, 2021
Assets		
Current assets:		
Cash	$ 13,249,945	$ 9,361,270
Prepaid expenses	465,244	2,173,528
Other current assets	99,543	90,301
Total current assets	13,814,732	11,625,099
Patent acquisition costs, net	16,880	22,929
Total assets	$ 13,831,612	$ 11,648,028
Liabilities and Shareholders' Equity		
Current liabilities:		
Accounts payable	946,658	1,788,563
Accrued expenses	3,148,090	3,184,883
Warrant liability	7,852,000	—
Other liability	94,118	—
Liability related to deposits received for share subscriptions	—	1,120,000
Total liabilities	$ 12,040,866	$ 6,093,446
Commitments and contingencies (Note 7)		
Shareholders' equity:		
Share capital of $0.0001 par value		
Authorized: 15,000,000,000 ordinary shares; issued and outstanding: 7,444,917,123 and 4,759,731,923 at December 31, 2022 and December 31, 2021, respectively	744,492	475,973
Additional paid-in capital	167,076,392	153,130,813
Capital redemption reserve	52,193,811	52,193,811
Accumulated other comprehensive loss	(770,839)	(540,967)
Accumulated deficit	(217,453,110)	(199,705,048)
Total shareholders' equity	1,790,746	5,554,582
Total liabilities and shareholders' equity	$ 13,831,612	$ 11,648,028

CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
For the Years Ended December 31, 2022, 2021 and 2020
(in U.S. Dollars, except share data)

	Years Ended December 31,		
	2022	2021	2020
Operating expenses:			
Research and development expenses	$ 9,560,897	$ 9,133,455	$ 8,820,204
General and administrative expenses	13,527,311	8,080,681	9,160,770
Total operating expenses	23,088,208	17,214,136	17,980,974
Loss from operations	(23,088,208)	(17,214,136)	(17,980,974)
Other income (expense):			
Interest income	45,944	10,600	13,615
Excess fair value of warrant liability over cash proceeds	(1,963,000)	—	—
Change in fair value of warrant liability	6,946,000	—	556,810
Foreign currency exchange gains (losses)	452,664	(193,219)	350,939
Other expenses	(141,462)	(27,482)	(22,007)
Total other income (expense)	5,340,146	(210,101)	899,357
Net loss	(17,748,062)	(17,424,237)	(17,081,617)
Other comprehensive (loss) income:			
Foreign currency translation adjustment	(229,872)	107,098	(299,205)
Total comprehensive loss	$ (17,977,934)	$ (17,317,139)	$ (17,380,822)
Net loss per ordinary share, basic and diluted	$ (0.00)	$ (0.00)	$ (0.01)
Weighted average ordinary shares outstanding, basic and diluted	6,243,462,410	4,292,112,667	3,159,037,588

CONSOLIDATED STATEMENTS OF CHANGES IN SHAREHOLDERS' EQUITY
For the Years Ended December 31, 2022, 2021 and 2020
(in U.S. Dollars, except share data)

	Share Capital		Additional Paid-in Capital	Capital Redemption Reserve	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Shareholders' Equity
	Shares	Amount					
Balance at January 1, 2020	2,245,865,913	$ 31,987,016	$ 133,568,636	$ —	$ (348,860)	$ (165,199,194)	$ 7,598
Stock-based compensation	—	—	325,523	—	—	—	325,523
Issuance of ordinary shares, net of issuance costs	1,559,455,100	20,051,809	2,253,158	—	—	—	22,304,967
Issuance of share capital for entering into 2020 Purchase Agreement with Aspire Capital	40,760,900	523,778	376,222	—	—	—	900,000
Issuance of share capital upon conversion of deferred shares	10	—	—	—	—	—	—
Subdivision of ordinary shares	—	(52,193,811)	—	52,193,811	—	—	—
Reclassification of warrants to shareholders' equity	—	—	3,199,553	—	—	—	3,199,553
Exercise of warrants	1,250,000	15,941	11,559	—	—	—	27,500
Comprehensive loss	—	—	—	—	(299,205)	(17,081,617)	(17,380,822)
Balance at December 31, 2020	3,847,331,923	$ 384,733	$ 139,734,651	$52,193,811	$ (648,065)	$ (182,280,811)	$ 9,384,319
Stock-based compensation	—	—	314,650	—	—	—	314,650
Issuance of ordinary shares, net of issuance costs	912,400,000	91,240	13,081,512	—	—	—	13,172,752
Comprehensive income (loss)	—	—	—	—	107,098	(17,424,237)	(17,317,139)
Balance at December 31, 2021	4,759,731,923	$ 475,973	$ 153,130,813	$52,193,811	$ (540,967)	$ (199,705,048)	$ 5,554,582
Stock-based compensation	—	—	735,107	—	—	—	735,107
Issuance of share capital, net of issuance costs	2,685,185,200	268,519	13,210,472	—	—	—	13,478,991
Comprehensive loss	—	—	—	—	(229,872)	(17,748,062)	(17,977,934)
Balance at December 31, 2022	7,444,917,123	$ 744,492	$ 167,076,392	$52,193,811	$ (770,839)	$ (217,453,110)	$ 1,790,746

AKARI THERAPEUTICS, Plc

CONSOLIDATED STATEMENTS OF CASH FLOWS
For the Years Ended December 31, 2022, 2021 and 2020
(in U.S. Dollars)

	Years Ended December 31,		
	2022	2021	2020
Cash Flows from Operating Activities:			
Net loss	$ (17,748,062)	$ (17,424,237)	$ (17,081,617)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	3,708	4,126	8,907
Stock-based compensation	735,107	314,650	325,523
Financing expense	—	—	900,000
Excess fair value of warrant liability over cash proceeds	1,963,000	—	—
Changes in fair value of the warrant liability	(6,946,000)	—	(556,810)
Foreign currency exchange (gains) losses	(334,168)	242,503	(490,782)
Changes in operating assets and liabilities:			
Prepaid expenses and other current assets	1,698,991	(1,742,261)	192,054
Accounts payable and accrued expenses	(877,098)	(241,309)	(247,683)
Net cash used in operating activities	(21,504,522)	(18,846,528)	(16,950,408)
Cash Flows from Financing Activities:			
Proceeds from issuance of shares, net of issuance costs	25,193,991	14,292,753	25,046,461
Proceeds for future exercises of warrants to purchase shares	94,118	—	—
Proceeds from exercise of warrants to purchase shares	—	—	27,500
Net cash provided by financing activities	25,288,109	14,292,753	25,073,961
Effect of exchange rates on cash	105,088	(140,732)	200,533
Net increase (decrease) in cash	3,888,675	(4,694,507)	8,324,086
Cash, beginning of period	9,361,270	14,055,777	5,731,691
Cash, end of period	$ 13,249,945	$ 9,361,270	$ 14,055,777
Supplemental disclosures of non-cash financing activities			
Ordinary share subscription deposit	$ 1,120,000	$ —	$ —
Initial valuation of warrant liability	$ 14,798,000	$ —	$ —

AKARI THERAPEUTICS, Plc

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
December 31, 2022
(in U.S. dollars)

NOTE 1 – Nature of Business

Akari Therapeutics, Plc, (the "Company" or "Akari") is incorporated in the United Kingdom. The Company is a clinical-stage biopharmaceutical company focused on developing advanced therapies for autoimmune and inflammatory diseases involving the complement (C5) and leukotriene (LTB4) pathways. The Company's activities since inception have consisted of performing research and development activities and raising capital.

The Company is subject to a number of risks similar to those of clinical stage companies, including dependence on key individuals, uncertainty of product development and generation of revenues, dependence on outside sources of capital, risks associated with the Russian invasion of Ukraine, risks associated with clinical trials of products, dependence on third-party collaborators for research and development operations, need for marketing authorization of products, risks associated with protection of intellectual property, and competition with larger, better-capitalized companies.

To fully execute its business plan, the Company will need, among other things, to complete its research and development efforts and clinical and regulatory activities. These activities may take several years and will require significant operating and capital expenditures in the foreseeable future. There can be no assurance that these activities will be successful. If the Company is not successful in these activities it could delay, limit, reduce or terminate preclinical studies, clinical trials or other research and development activities. To fund its capital needs, the Company plans to raise funds through equity or debt financings or other sources, such as strategic partnerships and alliance and licensing arrangements, and in the long term, from the proceeds from sales of commercial products. Additional funds may not be available when the Company needs them, on terms that are acceptable to it, or at all.

Nasdaq Continued Listing Rules

On October 24, 2022, the Company received a deficiency notification letter from the Listing Qualifications Staff of the Nasdaq Stock Market (the "Nasdaq") indicating that the Company was not in compliance with Nasdaq Listing Rule 5550(a)(2) because the bid price for the Company's Common Stock had closed below $1.00 per share for the previous thirty consecutive business days. In accordance with Nasdaq Listing Rule 5810(c)(3)(A), the Company had 180 calendar days from the date of such notice, or until April 24, 2023, to regain compliance with the minimum bid price requirement. To regain compliance, the bid price for the Company's Common Stock must have closed at $1.00 per share or more for a minimum of ten consecutive business days. On April 25, 2023, Nasdaq granted the Company an additional 180 calendar day period, or until October 23, 2023, in which to regain compliance with the minimum $1.00 bid price requirement. While the Company is exercising diligent efforts to maintain the listing of its ADSs on Nasdaq, there can be no assurance that the Company will be able to maintain compliance with the Nasdaq listing standards.

Liquidity

As of December 31, 2022, the Company had $13.2 million of cash. To date, the Company has primarily financed its operations through the sale of share capital. The Company has experienced significant negative cash flows from operations since inception including net losses of $17.7 million, $17.4 million and $17.1 million for the years ended December 31, 2022, 2021 and 2020, respectively. The Company expects to incur substantial operating losses and negative cash flows from operations for the foreseeable future.

As of April 28, 2023, the Company expects its existing cash, which includes net proceeds of $3.7 million received from the issuance of share capital in its March 2023 registered direct offering (See Note 11), will be sufficient to fund its operations through October 2023. To fund its future capital needs, the Company plans to raise additional funds through equity or debt financings or other sources, such as strategic partnerships, alliance and/or licensing arrangements, government grants and in the long term, proceeds from sales of commercial product.

Based on its recurring losses from operations incurred since inception, the Company's expectation of continuing operating losses for the foreseeable future, negative operating cash flows for the foreseeable future, and the need to raise additional capital to finance its future operations, the Company has concluded that there is substantial doubt regarding its ability to continue as a going concern within one year after the date that these consolidated financial statements are issued. The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business. As such, the accompanying consolidated financial statements do not reflect any adjustments relating to the recoverability and classification of recorded assets and liabilities that might be necessary if the Company is unable to continue as a going concern.

NOTE 2 – Summary of Significant Accounting Policies

Basis of Presentation – The accompanying consolidated financial statements have been prepared in accordance with U.S. GAAP and the rules and regulations of the SEC, assuming that the Company will continue to operate as a going concern.

Principles of Consolidation – The consolidated financial statements include the accounts of the Company, Volution Immuno Pharmaceuticals SA, a private Swiss company, and Akari Malta Limited, a private Maltese company, both wholly-owned subsidiaries. All intercompany transactions have been eliminated.

Foreign Currency – The functional currency of the Company is U.S. dollars, as that is the primary economic environment in which the Company operates as well as the currency in which it has been financed.

The reporting currency of the Company is U.S. dollars. The Company translates its non-U.S. operations' assets and liabilities denominated in foreign currencies into U.S. dollars at current rates of exchange as of the balance sheet date and income and expense items at the average exchange rate for the reporting period. Translation adjustments resulting from exchange rate fluctuations are recorded as foreign currency translation adjustments, a component of accumulated other comprehensive loss. Gains or losses from foreign currency transactions are included in foreign currency exchange gains/(losses).

Use of Estimates – The preparation of the Company's consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities and the reported amounts of expenses during the reporting periods. Significant estimates and assumptions reflected in these consolidated financial statements include, but are not limited to, the valuation of share-based awards, the valuation of warrant liabilities, the evaluation of impairment and useful lives of intangible assets (patents), accrued liabilities and the valuation allowance for deferred income taxes. The Company bases its estimates on historical experience, known trends and other market-specific or other relevant factors that it believes to be reasonable under the circumstances. Estimates are periodically reviewed in light of changes in circumstances, facts and experience. Changes in estimates are recorded in the period in which they become known. Actual results may differ from those estimates or assumptions.

Fair Value Measurements – Certain assets and liabilities are carried at fair value under U.S. GAAP. Fair value is an exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or a liability. As a basis for considering such assumptions, ASC 820, *Fair Value Measurements and Disclosures* ("ASC 820") establishes a three-tier value hierarchy, which prioritizes the inputs used in the valuation methodologies in measuring fair value:

Level 1 – quoted prices in active markets for identical assets or liabilities.

Level 2 – inputs other than Level 1 that are observable, either directly or indirectly, such as quoted prices in active markets for similar assets or liabilities, quoted prices for identical or similar assets or liabilities in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

(in U.S. dollars)

Level 3 – unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

The fair value hierarchy also requires the Company to maximize the use of observable inputs and minimize the use of unobservable inputs when measuring fair value.

The Company accounted for unregistered warrants issued to investors and a placement agent in connection with the 2019 registered direct offering and the 2020 private placements as a warrant liability and were carried at fair value and remeasured at each reporting period, with changes in fair value recorded as a separate line item in the Consolidated Statements of Operations and Comprehensive Loss. On December 8, 2020, the Company changed the nominal currency of its ordinary shares from pounds sterling to U.S. dollars and reclassified its warrants from liabilities to shareholders' equity (See Note 4).

The September 2022 Warrants (as defined below) met the definition of a freestanding instrument as such warrants are legally detachable and separately exercisable, and these warrants met the criteria of a derivative. The fair value of these warrants is classified as a liability and recorded at fair value (See Note 4). Such warrants are remeasured to fair value at each reporting date until the warrant is exercised or expires. Changes in the fair value of the warrant liability are recognized in the Consolidated Statements of Operations and Comprehensive Loss (See Note 3).

The carrying values of the Company's cash, prepaid expenses and other current assets, accounts payable and accrued expenses approximate their fair values due to the short-term nature of these assets and liabilities.

Cash – The Company considers all highly-liquid investments with original maturities of 90 days or less at the time of acquisition to be cash equivalents. The Company had no cash equivalents as of December 31, 2022 and December 31, 2021.

Prepaid Expenses – Payments made prior to the receipt of goods or services are capitalized until the goods or services are received.

Other Current Assets – Other current assets consist principally of VAT receivables.

Property and Equipment, net - Property and equipment are stated at cost, net of accumulated depreciation. Depreciation is calculated using the straight-line method over the estimated useful lives of the assets at the following annual rates:

	Years
Computers, peripheral, and scientific equipment	3
Office furniture and equipment	3

Property and equipment, consists of the following:

	December 31, 2022	December 31, 2021
Computers, peripheral, and scientific equipment	$ 85,489	$ 85,489
Office furniture and equipment	79,449	79,449
Total property and equipment	164,938	164,938
Less: Accumulated depreciation	(164,938)	(164,938)
Property and equipment, net	$ —	$ —

Depreciation expense for the years ended December 31, 2022, 2021 and 2020 was $0, $0 and $5,013, respectively, and was recorded in both research and development expenses and general and administrative expenses in the Consolidated Statements of Operations and Comprehensive Loss.

Long-Lived Assets – The Company reviews all long-lived assets for impairment whenever events or circumstances indicate the carrying amount of such assets may not be recoverable. Recoverability of assets to be held or used is measured by comparison of the carrying value of the asset to the future undiscounted net cash flows expected to be generated by the asset. If such asset is considered to be impaired, the impairment recognized is measured by the amount by which the carrying value of the asset exceeds the discounted future cash flows expected to be generated by the asset.

Patent Acquisition Costs – Patent acquisition costs and related capitalized legal fees are amortized on a straight-line basis over the shorter of the legal or economic life. The estimated useful life is 22 years. The Company expenses costs associated with maintaining and defending patents subsequent to their issuance in the period incurred. Amortization of patent acquisition costs for the years ended December 31, 2022, 2021 and 2020 was $3,708, $4,126 and $3,894, respectively.

Accrued Expenses – As part of the process of preparing the consolidated financial statements, the Company estimates accrued expenses. This process involves identifying services that third parties have performed on the Company's behalf and estimating the level of service performed and the associated cost incurred on these services as of each balance sheet date in the Company's consolidated financial statements. Examples of estimated accrued expenses include contract service fees in conjunction with pre-clinical and clinical trials, professional service fees and contingent liabilities. In connection with these service fees, the Company's estimates are most affected by its understanding of the status and timing of services provided relative to the actual services incurred by the service providers. In the event that the Company does not identify certain costs that have been incurred or it under or over-estimates the level of services or costs of such services, the Company's reported expenses for a reporting period could be understated or overstated. The date on which certain services commence, the level of services performed on or before a given date, and the cost of services are often subject to the Company's estimation and judgment. The Company makes these judgments based upon the facts and circumstances known to it in accordance with U.S. GAAP.

Research and Development Expenses – Costs associated with research and development are expensed as incurred unless there is an alternative future use in other research and development projects. Research and development expenses include, among other costs, salaries and personnel-related expenses, fees paid for contract research services, fees paid to clinical research organizations, costs incurred by outside laboratories, manufacturers' and other accredited facilities in connection with clinical trials and preclinical studies.

Payments made prior to the receipt of goods or services to be used in research and development are capitalized until the goods or services are received. The Company records expenses related to clinical studies and manufacturing development activities based on its estimates of the services received and efforts expended pursuant to contracts with multiple contract research organizations (CROs) and manufacturing vendors that conduct and manage these activities on its behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract, and may result in uneven payment flows. There may be instances in which payments made to the Company's vendors will exceed the level of services provided and result in a prepayment of the expense. Payments under some of these contracts depend on factors such as the successful enrollment of subjects and the completion of clinical study milestones. In amortizing or accruing service fees, the Company estimates the time period over which services will be performed, enrollment of subjects, number of sites activated and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the Company's estimate, the Company will adjust the accrued or prepaid expense balance accordingly.

Research and development expenses for the years ended December 31, 2022, 2021 and 2020 were $9,560,897, $9,133,455 and $8,820,204, respectively. The Company accounts for research and development tax credits at the time its realization becomes probable as a credit to research and development expenses in the consolidated statements of operations and comprehensive loss (See Note 7). The Company realized $2,318,385 of research and development tax credits in 2022 related to the 2021 tax year, $3,066,875 of research and development tax credits in 2021 related to the 2020 tax year and $3,372,093 of research and development tax credits in 2020 related to the 2019 tax year.

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Stock-Based Compensation – The Company measures all stock-based awards granted to employees, directors and non-employees based on the estimated fair value on the date of grant and recognizes compensation expense of those awards over the requisite service period, which is generally the vesting period of the respective awards. Forfeitures are accounted for as they occur. The Company classifies stock-based compensation expense in its consolidated statements of operations and comprehensive loss in the same manner in which the award recipient's payroll costs are classified or in which the award recipient's service payments are classified.

The fair value of each restricted ordinary share award is estimated on the date of grant based on the fair value of the Company's ordinary shares on that same date. The fair value of each option grant is estimated on the date of grant using the Black-Scholes option pricing model, which requires inputs based on certain subjective assumptions, including the expected stock price volatility, the expected term of the award, the risk-free interest rate, and expected dividends (See Note 5). The Company estimates its expected stock price volatility based on the historical volatility of publicly traded peer companies. The expected term of the Company's options has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is based on the fact that the Company has never paid cash dividends on ordinary shares and does not expect to pay any cash dividends in the foreseeable future.

Leases – The Company accounts for its leases in accordance with Accounting Standards Updates (ASU) No. 2016-02, Leases ("ASU 2016-2"). ASU 2016-02 establishes a right-of-use (ROU) model that requires a lessee to record a ROU asset and a lease liability on the balance sheet for all leases with terms longer than 12 months. Leases will be classified as either finance or operating, with classification affecting the pattern of expense recognition in the consolidated statements of operations and comprehensive loss. The Company determines if an arrangement is a lease at inception. This determination generally depends on whether the arrangement conveys to the Company the right to control the use of an explicitly or implicitly identified fixed asset for a period of time in exchange for consideration. Control of an underlying asset is conveyed to the Company if the Company obtains the rights to direct the use of and to obtain substantially all of the economic benefits from using the underlying asset. Operating leases are classified as right of use ("ROU") assets, short term lease liabilities, and long-term lease liabilities. Operating lease ROU assets and lease liabilities are recognized at the commencement date based on the present value of lease payments over the lease term. ROU assets are amortized and lease liabilities accrete to yield straight-line expense over the term of the lease. Lease payments included in the measurement of the lease liability are comprised of fixed payments. Leases with an initial term of twelve months or less are not recorded on the consolidated balance sheet and the Company recognizes lease expense for these leases on a straight-line basis over the lease term. The Company applies this policy to all underlying asset categories. Leasehold improvements are capitalized and depreciated over the lesser of useful life or lease term. As of December 31, 2022, the Company did not have a lease with a term longer than twelve months.

Concentration of Credit Risk – Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash. The Company generally maintains balances in various operating accounts at financial institutions in amounts that may exceed federally insured limits. The Company has not experienced any losses related to its cash and does not believe that it is subject to unusual credit risk beyond the normal credit risk associated with commercial banking relationships.

Income Taxes – On March 27, 2020, the United States enacted the Coronavirus Aid, Relief, and Economic Security Act, referred to herein as the CARES Act, as a response to the economic uncertainty resulting from COVID-19. The CARES Act includes modifications for net operating loss carryovers and carrybacks, limitations of business interest expense for tax, immediate refund of alternative minimum tax (AMT) credit carryovers. Tax provisions of the Act also include the deferral of certain payroll taxes, relief for retaining employees, and other provisions. The Company determined that these provisions did not have a material impact on the consolidated financial statements.

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The Company accounts for income taxes in accordance with the accounting rules that require an asset and liability approach to accounting for income taxes based upon the future expected values of the related assets and liabilities. Deferred income tax assets and liabilities are determined based on the differences between the financial reporting and tax bases of assets and liabilities and for tax loss and credit carry forwards and are measured using the expected tax rates estimated to be in effect when such basis differences reverse. Valuation allowances are established, if necessary, to reduce the deferred tax asset to the amount that will, more likely than not, be realized. The Company has recorded a full valuation allowance on its deferred tax assets as of December 31, 2022 and December 31, 2021.

Uncertain Tax Positions – The Company follows the provisions of ASC 740 "*Accounting for Uncertainty in Income Taxes*", which prescribes recognition thresholds that must be met before a tax position is recognized in the financial statements and provides guidance on de-recognition, classification, interest and penalties, accounting in interim periods, disclosure, and transition. Under ASC 740 "*Accounting for Uncertainty in Income Taxes*," an entity may only recognize or continue to recognize tax positions that meet a "more-likely-than-not" threshold. Interest and penalties related to uncertain tax positions are recognized as general and administrative expense. At December 31, 2022 and 2021, the Company had no uncertain tax positions.

Earnings (Loss) Per Share – Basic earnings (loss) per ordinary share is computed by dividing net income (loss) available to ordinary shareholders by the weighted-average number of ordinary shares outstanding during the period. Diluted earnings (loss) per ordinary share is computed by dividing net income (loss) available to ordinary shareholders by the sum of (1) the weighted-average number of ordinary shares outstanding during the period, (2) the dilutive effect of the assumed exercise of options and warrants using the treasury stock method and (3) the dilutive effect of other potentially dilutive securities. For purposes of the diluted net loss per share calculation, share options and warrants are considered to be potentially dilutive securities and are excluded from the calculation of diluted net loss per share because their effect would be anti-dilutive. Therefore, basic and diluted net loss per share was the same for the periods presented due to the Company's net loss position.

Comprehensive Income (Loss) – Comprehensive loss is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources. The Company's other comprehensive loss is comprised of foreign currency translation adjustments.

The following table provides details with respect to changes in accumulated other comprehensive loss, which is comprised of foreign currency translation adjustments, as presented in the balance sheets at December 31, 2022, 2021 and 2020:

Balance January 1, 2020	$ (348,860)
Net current period other comprehensive loss	(299,205)
Balance December 31, 2020	$ (648,065)
Net current period other comprehensive income	107,098
Balance December 31, 2021	$ (540,967)
Net current period other comprehensive loss	(229,872)
Balance December 31, 2022	$ (770,839)

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Recent Accounting Pronouncements

Adopted during the year

In August 2020, the FASB issued ASU 2020-06, Debt—Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging—Contracts in Entity's Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity's Own Equity (ASU 2020-06), which simplifies the accounting for certain financial instruments with characteristics of liabilities and equity, including convertible instruments and contracts on an entity's own equity. Specifically, ASU 2020-06 simplifies accounting for convertible instruments by removing major separation models in ASC 470-20 that require separate accounting for embedded conversion features. ASU 2020-06 also removes certain settlement conditions in ASC 815-40 that are required for equity contracts to qualify for the derivative scope exception, which will permit more equity contracts to qualify for the scope exception and simplifies the diluted earnings per share calculation in certain areas. ASU 2020-06 is effective for interim and annual periods beginning after December 15, 2021, with early adoption permitted. Adoption of ASU 2020-06 can either be on a modified retrospective or full retrospective basis. The Company adopted this guidance effective January 1, 2022. The adoption of the guidance did not have a material impact on the consolidated financial statements and related disclosures.

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NOTE 3 – Fair Value Measurements

The following table presents information about the Company's financial liabilities measured at fair value on a recurring basis and indicate the level of the fair value hierarchy used to determine such values:

December 31, 2022	Level 1	Level 2	Level 3	Total
Liabilities				
Warrant liability - Series A	$ —	$ —	$ 1,812,000	$ 1,812,000
Warrant liability - Series B	—	—	6,040,000	6,040,000
	$ —	$ —	$ 7,852,000	$ 7,852,000

There were no transfers between Level 1, Level 2 and Level 3 during the year ended December 31, 2022.

Series A and Series B Warrants

The fair value of the warrant liability is based on significant inputs not observable in the market, which represents a Level 3 measurement within the fair value hierarchy.

On September 14, 2022, the Company's sale of ADSs to accredited and institutional investors (See Note 4) also included the issuance of series A and series B warrants. The series A warrants allow the investors to purchase an aggregate of 15,100,000 ADSs at $0.85 per ADS ("Series A warrants"). The Series A warrants are immediately exercisable and expire two years from issuance (September 14, 2024). The series B warrants allow the investors to purchase an aggregate of 15,100,000 ADSs at $0.85 per ADS ("Series B warrants"). The Series B warrants are immediately exercisable and expire seven years from issuance (September 14, 2029). The Series A warrants and the Series B warrants may be exercised on a cashless basis if six months after issuance there is no effective registration statement registering the ADSs underlying the warrants. Pursuant to the cashless exercise provision, the warrant holder must make an additional payment to the Company equal to the nominal value of an ADS (i.e., $0.0001) per warrant ADS to be issued pursuant to the cashless exercise.

The fair value of the Series A and Series B warrants was determined using the Black-Scholes Option Pricing Model, which uses various assumptions, including (i) fair value of the Company's ADSs, (ii) exercise price of the warrant, (iii) expected term of the warrant, (iv) expected volatility and (v) expected risk-free interest rate.

Below are the assumptions used for the fair value calculations of warrants issued on September 14, 2022:

	September 14, 2022		December 31, 2022	
	Series A	Series B	Series A	Series B
Stock price	$ 0.71	$ 0.71	$ 0.47	$ 0.47
Exercise price	$ 0.85	$ 0.85	$ 0.85	$ 0.85
Expected term (in years)	2.0	7.0	1.7	6.7
Volatility	100.0 %	120.0 %	80.0 %	120.0 %
Risk-free rate	3.78 %	3.52 %	4.37 %	3.96 %

The following table summarizes the activity in the warrant liability during the year ended December 31, 2022:

	Series A	Series B	Total
Fair value at January 1, 2022	$ —	$ —	$ —
Issuance of warrant	5,285,000	9,513,000	14,798,000
Change in fair value	(3,473,000)	(3,473,000)	(6,946,000)
Fair value at December 31, 2022	**$ 1,812,000**	**$ 6,040,000**	**$ 7,852,000**

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NOTE 4 – Shareholders' Equity

September 2022 Registered Direct Offering

On September 14, 2022, the Company sold to certain accredited and institutional investors, led by existing investors of the Company, including Dr. Ray Prudo, the Company's Chairman, an aggregate of 15,100,000 ADSs in a registered direct offering ("September 2022 Registered Direct Offering") at $0.85 per ADS for aggregate gross proceeds of approximately $12.8 million. The Company also entered into a letter agreement with A.G.P./Alliance Global Partners (the "September 2022 Placement Agent") to serve as the placement agent for the Company in connection with this offering. In connection with the sale of the ADSs in the September 2022 Registered Direct Offering, the Company issued to the investors registered Series A warrants to purchase an aggregate of 15,100,000 ADSs at $0.85 per ADS and registered Series B warrants to purchase an aggregate of 15,100,000 ADSs at $0.85 per ADS (See Note 3).

The Company determined that the Series A and Series B warrants (collectively, the "September 2022 Warrants") represent freestanding financial instruments because based on the warrant term their volatility input would preclude an option contract from being considered indexed to an entity's own stock. For this reason, the September 2022 Warrants should be recorded as liability-classified instruments in accordance with ASC 815-40-25, *Accounting for Derivative Financial Instruments Indexed to, and Potentially Settled in, a Company's Own Stock* and ASC 815-40-15, *Determining Whether an Instrument (or Embedded Feature) Is Indexed to an Entity's Own Stock*.

In accordance with ASC 820, *Fair Value Measurement*, the Company measured the September 2022 Warrants at grant date fair value. The fair value related to warrants are classified within the Level 3 value hierarchy because it is based on external valuation models that contain certain unobservable inputs (See Note 3). The grant date fair value of the September 2022 Warrants totaled $14,798,000, which exceeded the $12,835,000 proceeds received from the sale of ADSs. The Company concluded that the September 2022 Registered Direct Offering was conducted on an arm's length basis and it used an external subject matter valuation expert to determine the fair value of the warrants. The excess fair value over the proceeds received of $1,963,000 at grant date was recognized as a non-operating expense in the consolidated statement of operations and comprehensive loss.

In connection with the September 2022 Registered Direct Offering, the Company expensed $1.7 million of issuance costs associated with the September 2022 Warrants during the year ended December 31, 2022, which have been recognized as general and administrative expense in the consolidated statement of operations and comprehensive loss.

At December 31, 2022, the fair value of the September 2022 Warrants was $7,852,000.

March 2022 Registered Direct Offering

On March 10, 2022, the Company sold to certain accredited and institutional investors, led by existing investors of the Company, including Dr. Ray Prudo, the Company's Chairman, an aggregate of 7,440,833 ADSs in a registered direct offering ("March 2022 Registered Direct Offering") at $1.20 per ADS for aggregate gross proceeds of approximately $8.9 million. The Company also entered into a letter agreement with Paulson Investment Company, LLC (the "March 2022 Placement Agent") to serve as the placement agent for the Company in connection with this offering. In connection with the sale of the ADSs in the March 2022 Registered Direct Offering, the Company issued to the investors registered warrants to purchase an aggregate of 3,720,409 ADSs at $1.40 per ADS ("March 2022 Investor Warrants"). The March 2022 Investor Warrants are immediately exercisable and will expire five years from issuance, subject to adjustment as set forth therein. The Company paid to the March 2022 Placement Agent an aggregate of $774,320 in placement agent fees and expenses and issued registered warrants to the March 2022 Placement Agent to purchase an aggregate of 297,633 ADS ("March 2022 Placement Agent Warrants") on the same terms as the March 2022 Investor Warrants, except that the March 2022 Placement Agent Warrants are exercisable at $1.50 per ADS. Both the March 2022 Investor Warrants and the March 2022 Placement Agent Warrants (together the "March 2022 Warrants") may be exercised on a cashless basis if six months after issuance there is no effective registration statement registering the ADSs underlying the warrants. Pursuant to the cashless exercise provision, the warrant holder must make an additional payment to the Company equal to the nominal value of an ADS (i.e., $0.0001) per warrant ADS actually to be issued pursuant to the cashless exercise. The total amount of March 2022 Warrants issued in connection with this registered direct offering amounted to 4,018,042, all of which were outstanding as of December 31, 2022.

December 2021 Registered Direct Offering

On December 29, 2021, the Company sold to certain accredited and institutional investors, led by existing investors of the Company, including Dr. Ray Prudo, the Company's Chairman, an aggregate of 4,311,019 ADSs in a registered direct offering ("December 2021 Registered Direct Offering") at $1.40 per ADS for aggregate gross proceeds of approximately $6.0 million, which closed on January 5, 2022, of which approximately $1.1 million was received on December 31, 2021. The Company also entered into a letter agreement with Paulson Investment Company, LLC (the "December 2021 Placement Agent") to serve as the placement agent for the Company in connection with this offering. In connection with the sale of the ADSs in the December 2021 Registered Direct Offering, the Company issued to the investors registered warrants to purchase an aggregate of 2,155,507 ADSs at $1.65 per ADS ("December 2021 Investor Warrants"). The December 2021 Investor Warrants are immediately exercisable and will expire five years from issuance, subject to adjustment as set forth therein. The Company paid to the December 2021 Placement Agent an aggregate of $542,834 in placement agent fees and expenses and issued registered warrants to the December 2021 Placement Agent to purchase an aggregate of 172,441 ADS ("December 2021 Placement Agent Warrants") on the same terms as the December 2021 Investor Warrants, except that the December 2021 Placement Agent Warrants are exercisable at $1.75 per ADS. Both the December 2021 Investor Warrants and the December 2021 Placement Agent Warrants (together the "December 2021 Warrants") may be exercised on a cashless basis if six months after issuance there is no effective registration statement registering the ADSs underlying the warrants. Pursuant to the cashless exercise provision, the warrant holder must make an additional payment to the Company equal to the nominal value of an ADS (i.e., $0.0001) per warrant ADS actually to be issued pursuant to the cashless exercise. The total amount of December 2021 Warrants issued in connection with this registered direct offering amounted to 2,327,948, all of which were outstanding as of December 31, 2022.

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2021 Private Placements

On July 7, 2021, the Company entered into securities purchase agreements with certain accredited and institutional investors, including Praxis Trustees Limited as trustee of Sonic Healthcare Holding Company EFRBS which is beneficially owned by Dr. Ray Prudo, the Company's Chairman, providing for the issuance of an aggregate of 7,947,529 ADSs in a private placement at $1.55 per ADS for aggregate gross proceeds of approximately $12.3 million, which subsequently closed (the "2021 Private Placements"). The Company also entered into a letter agreement with Paulson Investment Company to serve as the placement agent for the Company in connection with this offering (the "July 2021 Placement Agent"). In connection with the offering, on July 16, 2021, the Company issued to the July 2021 Placement Agent unregistered warrants to purchase a total of 398,384 ADSs at $2.32 per ADS ("July 2021 Warrants"). The July 2021 Warrants will expire five years from issuance and are immediately exercisable, subject to adjustment as set forth therein. Subject to certain conditions, the Company has the option to "call" the exercise of the warrants from time to time after any 10-consecutive trading day period during which the daily volume-weighted average price of the ADSs exceeds $3.00. The Company paid to the July 2021 Placement Agent an aggregate of $993,000 in placement agent fees and expenses. The July 2021 Warrants may be exercised on a cashless basis if nine months after issuance there is no effective registration statement registering the ADSs underlying the warrants. Pursuant to the cashless exercise provision, the warrant holder must make an additional payment to the Company equal to the nominal value of an ADS (i.e., $0.0001) per warrant ADS actually to be issued pursuant to the cashless exercise. The total amount of the July 2021 Warrants issued in connection with the 2021 Private Placements amounted to 398,384, all of which were outstanding as of December 31, 2022.

2020 Purchase Agreement and Registration Rights Agreement with Aspire Capital

On June 30, 2020, the Company entered into a Purchase Agreement ("2020 Purchase Agreement") with Aspire Capital which expired after the contractual 30-month commitment period lapsed on January 27, 2023. Prior to expiration, Aspire Capital invested an aggregate of $8.0 million of the original purchase commitment out of $30.0 million available under the facility.

The 2020 Purchase Agreement provided that, upon the terms and subject to the conditions and limitations set forth therein, Aspire Capital was committed to purchase up to an aggregate of $30.0 million of the Company's ADSs, with each ADS representing one hundred (100) ordinary shares, during a 30-month period beginning on the effective date of a registration statement related to the transaction. Concurrently with entering into the 2020 Purchase Agreement, the Company also entered into a registration rights agreement with Aspire Capital, in which the Company agreed to file one or more registration statements, as permissible and necessary to register under the Securities Act of 1933, as amended (the "Securities Act"), the sale of the Company's securities that have been issued to Aspire Capital under the 2020 Purchase Agreement.

Under the 2020 Purchase Agreement, after the SEC declared effective the registration statement referred to above (which occurred in July 2020), on any trading day selected by the Company, the Company has the right, in its sole discretion, to present Aspire Capital with a purchase notice (each, a "Purchase Notice"), directing Aspire Capital (as principal) to purchase up to 150,000 ADSs per business day and up to $30.0 million of the Company's ADSs in the aggregate at a per share price (the "Purchase Price") equal to the lesser of:

- the lowest sale price of the Company's ADSs on the purchase date; or
- the arithmetic average of the three (3) lowest closing sale prices for the ADSs during the ten (10) consecutive business days ending on the business day immediately preceding such Purchase Date (to be appropriately adjusted for any reorganization, recapitalization, non-cash dividend, stock split, reverse stock split or other similar transaction).

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In addition, on any date on which the Company submitted a Purchase Notice to Aspire Capital in an amount of 150,000 ADSs, the Company also had the right, in its sole discretion, to present Aspire Capital with a volume-weighted average price purchase notice (each, a "VWAP Purchase Notice") directing Aspire Capital to purchase an amount of ADSs equal to up to 30% of the aggregate shares of the Company's ADSs traded on its principal market on the next trading day (the "VWAP Purchase Date"), subject to a maximum number of 250,000 ADSs. The purchase price per share pursuant to such VWAP Purchase Notice was generally 97% of the volume-weighted average price for the Company's ADSs traded on its principal market on the VWAP Purchase Date.

The 2020 Purchase Agreement provided that the Company and Aspire Capital shall not effect any sales under the Purchase Agreement on any purchase date where the closing sale price of the Company's ADSs is less than $0.25. Additionally, governing law in the United Kingdom, where the Company is incorporated, requires a minimum payment per ADS to be issued pursuant to a purchase notice equal to the nominal value of an ADS (i.e., $0.0001). There are no trading volume requirements or restrictions under the Purchase Agreement, and the Company controlled the timing and number of sales of the Company's ADSs to Aspire Capital. Aspire Capital had no right to require any sales by the Company but was obligated to make purchases from the Company as directed by the Company in accordance with the Purchase Agreement. There are no limitations on use of proceeds, financial or business covenants, restrictions on future fundings, rights of first refusal, participation rights, penalties or liquidated damages in the Purchase Agreement.

In accordance with ASC 815-40-15, *Determining Whether an Instrument (or Embedded Feature) Is Indexed to an Entity's Own Stock*, since the ultimate floor price, which was effectively the nominal value of the ADS which was denominated in GBP at the time of entering into the 2018 Purchase agreement as well as the 2020 Purchase Agreement (together "the Purchase Agreements") prior to the 2020 Redenomination, the number of shares issuable under the contract was impacted by foreign currency, therefore ASC 815-40-15-7 precluded the Purchase Agreements from being indexed to the Company's own stock. The Company determined that the right to sell shares to Aspire Capital under the Purchase Agreements represents a freestanding put option that met the criteria of a derivative pursuant to ASC 815 *Derivatives and Hedging.* Since the purchase price per share pursuant to the Purchase Agreements was at the market, the Company concluded that the put option had a fair value of zero, and therefore no additional accounting related to the put option was required.

In consideration for entering into the 2020 Purchase Agreement, the Company agreed to issue to Aspire Capital 40,760,900 ordinary shares of the Company (the "2020 Commitment Shares") which had a fair value of approximately $900,000. Since the Company has determined that the 2020 Purchase Agreement was considered a freestanding put option derivative in accordance with ASC 815 *Derivatives and Hedging* when entering into the agreement, the Company recorded the value of the 2020 Commitment Shares in General and administrative expenses in the Consolidated Statements of Operations and Comprehensive Loss. The 2020 Purchase Agreement could have been terminated by the Company at any time, at its discretion, without any cost to the Company. Aspire Capital had agreed that neither it nor any of its agents, representatives and affiliates shall engage in any direct or indirect short-selling or hedging of the Company's securities during any time prior to the termination of the 2020 Purchase Agreement. Any proceeds the Company received under the 2020 Purchase Agreement were expected to be used for working capital and general corporate purposes.

During the year ended December 31, 2020, the Company sold to Aspire Capital 460,758,800 ordinary shares of the Company for gross proceeds of approximately $6,000,000. During the year ended December 31, 2021, the Company sold to Aspire Capital 117,647,100 ordinary shares of the Company for gross proceeds of approximately $2,000,001. No ordinary shares were sold to Aspire Capital during the year ended December 31, 2022.

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Reclassification of Warrants to Shareholders' Equity

Warrants issued prior to December 8, 2020 were originally determined to represent freestanding financial instruments whose foreign currency considerations pursuant to cash and cashless exercise required liability classification and should be recorded as liability-classified awards in accordance with ASC 815-40-25, *Accounting for Derivative Financial Instruments Indexed to, and Potentially Settled in, a Company's Own Stock* and ASC 815-40-15, *Determining Whether an Instrument (or Embedded Feature) Is Indexed to an Entity's Own Stock*. These warrants were measured at their grant date fair value and subsequently remeasured at each reporting period with changes being recorded as a separate line item in the consolidated statements of operations and comprehensive loss. On December 8, 2020, the Company held a general meeting ("2020 General Meeting") and changed the currency of its ordinary shares from pounds sterling to U.S. dollars ("2020 Redenomination"). Because of the 2020 Redenomination, the Company reassessed whether its financial instruments or other contracts that previously required derivative accounting within the scope of ASC 815 *Financial Instruments* either (a) no longer met the definition of a derivative or (b) met a scope exception to the derivative guidance due to a change in facts and circumstances. The Company concluded that due to the 2020 Redenomination, these warrants now met the requirements for classification as equity under ASC 815-40-25 as of December 8, 2020, the date of the 2020 General Meeting. The Company updated the carrying amount of the warrant liability to its fair value on December 8, 2020, with changes recorded in the consolidated statements of operations and comprehensive Loss and then reclassified the warrant liability balance to additional paid in capital within shareholders' equity:

	Fair value of warrants liabilities
Balance at December 31, 2019	$ 1,014,868
Issuance of 2020 Warrants	2,749,369
Reclassification of warrant liability to shareholders' equity upon exercise of 12,500 warrant ADSs	(7,874)
Change in fair value of liabilities related to warrants	(556,810)
Balance at December 8, 2020	3,199,553
Reclassification to additional-paid-in capital with in shareholders' equity	(3,199,553)
Balance at December 31, 2020	$ —

Warrants Issued in 2021 and 2022

Except for warrants issued in September 2022 (Note 3), the Company accounts for warrants issued to investors and a placement agent after December 8, 2020 as equity classified instruments, recorded to additional paid-in capital within shareholders' equity on the consolidated balance sheets. The fair values were measured at their grant date with no subsequent remeasurement.

The Company determined that, at the time of their issuance, the July 2021 Warrants, the December 2021 Warrants and the March 2022 Warrants met the requirements for classification as equity under ASC 815-40-25. The costs directly attributable to realizing proceeds of issuing ADSs such as placement agent fees, commissions, legal and accounting fees pertaining to the financing and other external, incremental fees and expenses paid to advisors were recognized in additional paid-in capital within shareholders' equity on the consolidated balance sheets. At July 16, 2021, the fair value of the July 2021 Warrants was $231,063 and was recorded within additional paid-in capital of shareholders' equity. At January 4, 2022, the fair value of the December 2021 Warrants was $2,605,577 and was recorded within additional paid-in capital of shareholders' equity. At March 10, 2022, the fair value of the March 2022 Warrants was $3,693,622 and was recorded within additional paid-in capital of shareholders' equity.

AKARI THERAPEUTICS, Plc

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
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Below are the assumptions used for the fair value calculations of the warrants issued in 2021:

	July 16, 2021
Standard deviation	110.00 %
Annual risk-free interest rate	0.79 %
Required return on equity	17.00 %
Expected life in years	4.98
Annual turnover rate	0.00 %
Period risk-free rate	0.07 %

Below are the assumptions used for the fair value calculations of warrants issued in 2022 (except the September 2022 Warrants):

	January 4, 2022	March 10, 2022
Expected dividend yield	0 %	0 %
Expected volatility	110 %	110 %
Risk-free interest	1.4 %	1.9 %
Expected life in years	5.0	5.0

The following table summarizes the Company's outstanding warrants as of December 31, 2022, 2021 and 2020:

Description	Exercise Price	Balance December 31, 2020	Warrants Issued in 2021	Balance December 31, 2021	Warrants Issued in 2022	Balance December 31, 2022
2019 Investor Warrants	$ 3.00	1,184,213	—	1,184,213	—	1,184,213
2019 Placement Warrants	$ 2.85	177,629	—	177,629	—	177,629
2020 Investor Warrants	$ 2.20	2,797,636	—	2,797,636	—	2,797,636
2020 Placement Warrants	$ 2.55	449,623	—	449,623	—	449,623
July 2021 Placement Agent Warrants	$ 2.32	—	398,384	398,384	—	398,384
December 2021 Investor Warrants	$ 1.65	—	—	—	2,155,507	2,155,507
December 2021 Placement Agent Warrants	$ 1.75	—	—	—	172,441	172,441
March 2022 Investor Warrants	$ 1.40	—	—	—	3,720,409	3,720,409
March 2022 Placement Agent Warrants	$ 1.50	—	—	—	297,633	297,633
September 2022 Series A Investor Warrants	$ 0.85	—	—	—	15,100,000	15,100,000
September 2022 Series B Investor Warrants	$ 0.85	—	—	—	15,100,000	15,100,000
		4,609,101	398,384	5,007,485	36,545,990	41,553,475

NOTE 5 – Equity Incentive Plan

In accordance with the Company's 2014 Equity Incentive Plan (the "2014 Plan"), the number of shares that may be issued upon exercise of options under the Plan shall not exceed 890,000,000 ordinary shares. At December 31, 2022, 354,850,715 ordinary shares were available for future issuance under the Plan. The option plan is administered by the Company's Board of Directors and grants are made pursuant thereto by the compensation committee. The per share exercise price for the shares to be issued pursuant to the exercise of an option shall be such price equal to the fair market value of the Company's ordinary shares on the grant date and set forth in the individual option agreement. Options expire ten years after the grant date and typically vest over one to four years.

Shares that are expired, terminated or canceled are returned to the 2014 Plan and made available for future awards.

AKARI THERAPEUTICS, Plc

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Options

The following is a summary of the Company's option activity under the 2014 Plan for the years ended December 31, 2022, 2021 and 2020:

	Number of shares	Weighted average exercise price	Weighted average grant date fair value	Weighted average remaining contractual term (in years)	Aggregate intrinsic value
Options outstanding as of January 1, 2020	94,349,035	$ 0.10	—	7.6	$ —
Granted	208,000,000	$ 0.02	$ 0.01	—	—
Forfeited	(2,500,000)	$ 0.02	$ 0.02	—	—
Options outstanding at December 31, 2020	112,649,035	$ 0.09	—	7.1	$ —
Granted	30,300,000	$ 0.02	$ 0.01	—	—
Options outstanding at December 31, 2021	142,949,035	$ 0.07	—	6.8	$ —
Granted	409,396,700	$ 0.01	$ 0.01	—	—
Forfeited	(38,671,850)	$ 0.15	$ 0.10	—	—
Options outstanding at December 31, 2022	513,673,885	$ 0.02	—	8.7	$ —
Exercisable options at December 31, 2022	128,451,772	$ 0.04	—	6.6	$ —

The aggregate intrinsic value of options is calculated as the difference between the exercise price of the options and the fair value of the Company's common stock for those options that had exercise prices lower than the fair value of the Company's common stock.

No stock option awards were exercised during the years ended December 31, 2022, 2021 and 2020.

Option Valuation

Below are the assumptions used to determine the fair value of stock awards granted during the years ended December 31, 2022, 2021 and 2020:

	December 31,		
	2022	2021	2020
Expected dividend yield	0 %	0 %	0 %
Expected volatility	72.8-90.4 %	70.7-83.2 %	83.9-86.9 %
Risk-free interest	1.46-4.34 %	0.64-1.25 %	0.38-0.49 %
Expected life	5.5-6.25 years	5.5-6.25 years	5.5-6.25 years

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The following is a summary of the Company's share options granted separated into ranges of exercise price as of December 31, 2022:

Exercise price (range) ($)	Options outstanding	Weighted average remaining contractual life (years)	Weighted average exercise price ($)	Options exercisable	Remaining contractual life for exercisable options (years)	Weighted average exercise price for exercisable options ($)
<0.01	106,500,000	9.8	0.01	—	—	—
0.01	286,896,700	9.3	0.01	29,674,587	9.2	0.01
0.02-0.05	102,000,000	6.8	0.02	80,500,000	6.3	0.02
0.12-0.32	18,277,185	3.3	0.16	18,277,185	3.3	0.16
	513,673,885			**128,451,772**		

Restricted Stock Units

The Company began awarding restricted stock units ("RSUs") during the year ended December 31, 2022. RSUs are stock-based awards granted to recipients with specified vesting provisions. In the case of RSUs, ordinary shares are generally delivered on or following satisfaction of vesting conditions. The Company issues RSUs to management that vest solely based on the recipient's continued service over time, primarily with a two-year vesting ("Time-Based RSUs"). For these RSUs, the Company recognizes the cost as compensation expense on a straight-line basis.

The Company estimates the fair value of its Time-Based RSUs on the date of grant based on the Company's closing stock price at the time of grant.

The following table summarizes the Company's restricted stock activity for the year ended December 31, 2022:

	Shares/ Units	Weighted average grant date fair value per share
Unvested as of January 1, 2022	—	—
Granted	21,475,400	$ 0.01
Vested	—	—
Forfeited	—	—
Unvested as of December 31, 2022	21,475,400	$ 0.01

Stock-Based Compensation Expense

The Company recorded stock-based compensation expense in the following expense categories of its consolidated statements of operations and comprehensive loss:

	Years Ended December 31,		
	2022	2021	2020
Research and development	$ 120,191	$ 55,028	$ 82,192
General and administrative	614,916	259,622	243,331
Total stock-based compensation expense	$ 735,107	$ 314,650	$ 325,523

As of December 31, 2022, total unrecognized compensation cost related to unvested share-based payment awards was $2,739,097, which is expected to be recognized over a weighted average period of 3.1 years.

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NOTE 6 – Related Party Transactions

London Office Lease - The Company leases its offices in London from The Doctors Laboratory ("TDL") and has incurred expenses of approximately $129,000, $146,000 and $133,000 plus VAT during the years ended December 31, 2022, 2021 and 2020, respectively. David Byrne, a non-employee director of the Company, is the Chief Executive Officer of TDL and Dr. Ray Prudo, the Company's former Executive Chairman, is the non-Executive Chairman of the Board of Directors of TDL.

Laboratory Testing Services - The Company received laboratory testing services for its clinical trials provided by TDL, including certain administrative services, and has incurred expenses of approximately $89,000, $102,000 and $234,000 plus VAT during the years ended December 31, 2022, 2021 and 2020, respectively. The Company recorded payable balances to TDL of approximately $23,000, $32,000 and $100,000 plus VAT as of December 31, 2022, 2021 and 2020, respectively.

Consulting - A non-employee director of the Company began providing business development consulting services in January 2018. The consulting agreement was terminated in November 2022. The Company incurred expenses of approximately $92,000, $100,000 and $100,000 during the years ended December 31, 2022, 2021 and 2020, respectively, relating to these consulting services.

NOTE 7 – Commitments and Contingencies

Lease commitment – The Company currently leases its offices in London and New York on a month-to-month basis.

For the years ended December 31, 2022, 2021 and 2020, the Company incurred total rental expense in the amount of approximately $169,000, $183,000 and $173,000, respectively.

NOTE 8 – Loss Per Share

Basic loss per ordinary share is computed by dividing net loss available to ordinary shareholders by the weighted-average number of ordinary shares outstanding during the period. Diluted loss per ordinary share is computed by dividing net loss available to ordinary shareholders by the sum of (1) the weighted-average number of ordinary shares outstanding during the period, (2) the dilutive effect of the assumed exercise of share options using the treasury stock method, and (3) the dilutive effect of other potentially dilutive securities.

The following is the calculation of the basic and diluted weighted average shares outstanding for the years ended December 31,2022, 2021 and 2020, respectively:

	Years Ended December 31,		
	2022	2021	2020
Company posted	Net loss	Net loss	Net loss
Basic weighted average shares outstanding	6,243,462,410	4,292,112,667	3,159,037,588
Dilutive effect of Ordinary Share equivalents	None	None	None
Dilutive weighted average shares outstanding	6,243,462,410	4,292,112,667	3,159,037,588

(in U.S. dollars)

The Company's potentially dilutive securities, which include options, warrants to purchase ordinary shares and unvested restricted stock, have been excluded from the computation of diluted net loss per share as the effect would be to reduce the net loss per share attributable to common stockholders. Therefore, the weighted average number of ordinary shares outstanding used to calculate both basic and diluted net loss per share is the same. The Company excluded the following potential ordinary shares, presented based on amounts outstanding at each period end, from the computation of diluted net loss per share for the periods indicated because including them would have had an anti-dilutive effect (in ordinary equivalent shares):

	Years Ended December 31,		
	2022	2021	2020
Share options	513,673,885	142,949,035	112,649,035
Warrants	4,155,347,500	500,748,500	460,910,100
Restricted stock units	21,475,400	—	—
Total anti-dilutive share equivalents	4,690,496,785	6,436,975,355	573,559,135

NOTE 9 – Income Taxes

Tax rates

The Company is incorporated in England. The effective corporate tax rate applying to a company that is incorporated in England on December 31, 2022 is 19%, which is consistent with the rate from December 31, 2021 and 2020.

Tax assessment

The periods open to inquiry by the United Kingdom ("UK") tax authorities are 2022, 2021 and 2020. The Company has not been issued final tax assessments since its establishment in Switzerland.

Deferred taxes

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Management currently believes that since the Company has a history of losses, it is more likely than not that the deferred tax assets relating to the loss carryforwards and other temporary differences will not be realized in the foreseeable future. Therefore, the Company provided a full valuation allowance to reduce the deferred tax assets.

The main reconciling item between the statutory tax rate of the Company and the effective tax rate is the recognition of valuation allowances in respect of deferred taxes relating to accumulated net operating losses carried forward due to the uncertainty of the realization of such deferred taxes.

At December 31, 2022 and 2021, there were no known uncertain tax positions. The Company has not identified any tax positions for which it is reasonably possible that a significant change will occur during the next 12 months.

The components of net loss before income tax are as follows:

	Years Ended December 31,		
	2022	2021	2020
Domestic (UK)	$ (18,017,916)	$ (17,308,782)	$ (17,394,074)
Foreign	269,854	(115,455)	312,457
Net loss before income tax	$ (17,748,062)	$ (17,424,237)	$ (17,081,617)

AKARI THERAPEUTICS, Plc

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Income tax expense relating to the Company's operations are as follows:

	Years Ended December 31,		
	2022	2021	2020
Current income taxes			
Domestic (UK)	$ —	$ —	$ —
U.S.	—		
Foreign	—	—	—
Deferred income taxes	—	—	—
Domestic (UK)	—	—	—
Foreign	—	—	—
Income tax expense	$ —	$ —	$ —

The following is a reconciliation of income tax expense computed at the UK statutory rate compared to the Company's income tax expense as reported in its consolidated statements of operations and comprehensive loss:

	Years Ended December 31,		
	2022	2021	2020
Net loss before income tax	$ (17,748,062)	$ (17,424,237)	$ (17,081,617)
Statutory rate	19.00 %	19.00 %	19.00 %
Expected income tax recovery	(3,372,132)	(3,310,605)	(3,245,507)
Impact on income tax expense/recovery from			
Change in valuation allowance	4,327,206	3,958,517	4,287,778
Permanent differences	408,400	39,572	81
U.S. state taxes (net of FBOS)	(1,114,279)	(534,862)	(655,877)
Tax rate difference in foreign jurisdictions	(248,042)	(122,064)	(136,343)
Change of tax rate due to U.S. tax reform	4,200	60,369	—
Change in equity compensation	751,989	—	—
Change in operating losses	(132,989)	—	—
Change of tax rate from prior year	(624,353)	(90,927)	—
Deferred tax adjustments	—	—	250,132
Income tax expense	$ —	$ —	$ —

The tax effects of temporary differences that gave rise to significant portions of the Company's deferred tax assets were as follows:

	December 31, 2022	December 31, 2021
Deferred tax assets		
Stock-based compensation	$ 954,821	$ 1,426,602
PP&E and other accrued liabilities	641,935	571,006
Intangibles	1,658,731	1,588,365
Warrant revaluation	(946,770)	—
Tax loss carry forward	32,307,419	26,736,219
Valuation allowance	(34,616,136)	(30,322,192)
Net deferred tax assets	$ —	$ —

The Company has reviewed its tax positions for its past domestic and foreign tax filings and has not identified any uncertain income tax positions. The Company's position is to record penalties and interest on any uncertain tax position, if any, and record such items to general and administrative expense.

(in U.S. dollars)

At December 31, 2022, the Company had approximately $108.7 million of UK operating loss carryforwards to reduce future UK taxable income. These carryforwards do not expire. At December 31, 2022, the Company had approximately $106.3 million of foreign operating loss carryforwards in the US (including federal, state and local jurisdictions) and Switzerland. Carryforwards in the US totaling approximately $1.1 million expire in 2032, $14.8 million expire in 2034, $3.7 million expire in 2036, $10.4 million expire in 2037, $50.8 million expire after 2037, and $24.8 million do not expire. The carryforwards in Switzerland totaling approximately $0.7 million expire in 2023. In general, an ownership change, as defined by Section 382 of the Internal Revenue Code, results from transactions increasing the ownership of certain shareholders or public groups in the stock of a corporation by more than 50% over a three-year period. In fiscal 2023, the Company conducted a study to assess whether a change of control has occurred. The Company concluded that it had experienced a change of control, as defined by Section 382, and utilization of certain net operating loss carryforwards would be subject to an annual limitation under Section 382. The Company determined that the limitation was immaterial to its consolidated financial statements.

Research and development credits

The Company carries out extensive research and development activities and may benefit from the UK research and development tax relief regime, whereby the Company can receive an enhanced UK tax deduction on its research and development activities. Qualifying expenditures comprise of chemistry and manufacturing consumables, employment costs for research staff, clinical trials management, and other subcontracted research expenditures. Where the Company is loss making for the period it can elect to surrender taxable losses for a refundable tax credit. The losses available to surrender are equal to the lower of the sum of the research and development qualifying expenditure and enhanced tax deduction and the Company's taxable losses for the period with the tax credit for December 31, 2022 available at a rate of 14.5%. The credit therefore gives a cash flow advantage to Company at a lower rate than would be available if the enhanced losses were carried forward and relieved against future taxable profits.

The Company accounts for research and development tax credits at the time its realization becomes probable (Note 2). Due to the uncertainty of the approval of these tax credit claims and the potential that an election for a tax credit in the form of cash is not made, the Company did not record a receivable for the 2022 tax year at December 31, 2022.

NOTE 10 – Segment Information

The chief operating decision maker ("CODM") is the Company's Chief Executive Officer (CEO). Neither the CODM nor the Company's directors receive disaggregated financial information about the locations in which research and development is occurring. Therefore, the Company considers that it has only one reporting segment.

The following table presents the Company's tangible fixed assets by geographic region:

	December 31, 2022	December 31, 2021
United Kingdom	$ —	$ —
United States	—	—
Total	$ —	$ —

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NOTE 11 – Subsequent Events

Registered Direct Offering

On March 31, 2023, the Company entered into securities purchase agreements with certain accredited and institutional investors, including Dr. Ray Prudo, the Company's Chairman, providing for the issuance of an aggregate of 26,666,667 ADSs in a registered direct offering at $0.15 per ADS, resulting in gross proceeds of approximately $4.0 million. The Company paid an aggregate of approximately $0.3 million in placement agent fees and expenses.

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

Akari Therapeutics, Plc
London, United Kingdom

We hereby consent to the incorporation by reference in the Registration Statements on Form S-8 (No. 333-230998, 333-198109 and No. 333-207444) and on Form F-3 (No. 333-237389, 333-251673 and 333-258918) of Akari Therapeutics, Plc of our report dated April 28, 2023, relating to the consolidated financial statements which appear in this Annual Report on Form 20-F. Our report contains an explanatory paragraph regarding the Company's ability to continue as a going concern.

/s/ BDO USA, LLP
New York, New York

April 28, 2023

Exhibit 31.1

CERTIFICATION OF THE PRINCIPAL EXECUTIVE OFFICER UNDER SECTION 302 OF THE

SARBANES-OXLEY ACT

I, Rachelle Jacques, certify that:

1. I have reviewed this annual report on Form 20-F of Akari Therapeutics, Plc;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the company as of, and for, the periods presented in this report;

4. The company's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the company and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the company's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the company's internal control over financial reporting that occurred during the period covered by the annual report that has materially affected, or is reasonably likely to materially affect, the company's internal control over financial reporting; and

5. The company's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the company's auditors and the audit committee of the company's board of directors (or persons performing the equivalent functions):

a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the company's ability to record, process, summarize and report financial information; and

b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the company's internal control over financial reporting.

Date: April 28, 2023

/s/ Rachelle Jacques

Rachelle Jacques
Chief Executive Officer

Exhibit 31.2

CERTIFICATION OF THE PRINCIPAL ACCOUNTING OFFICER UNDER SECTION 302 OF THE

SARBANES-OXLEY ACT

I, Dr. Torsten Hombeck, certify that:

1. I have reviewed this annual report on Form 20-F of Akari Therapeutics, Plc;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the company as of, and for, the periods presented in this report;

4. The company's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the company and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the company's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the company's internal control over financial reporting that occurred during the period covered by the annual report that has materially affected, or is reasonably likely to materially affect, the company's internal control over financial reporting; and

5. The company's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the company's auditors and the audit committee of the company's board of directors (or persons performing the equivalent functions):

a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the company's ability to record, process, summarize and report financial information; and

b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the company's internal control over financial reporting.

Date: April 28, 2023

/s/ Dr. Torsten Hombeck

Dr. Torsten Hombeck
Chief Financial Officer and Principal Accounting Officer

Exhibit 32.1

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER UNDER SECTION 906 OF THE

SARBANES-OXLEY ACT

Pursuant to 18 U.S.C. Section 1350, as created by Section 906 of the Sarbanes-Oxley Act of 2002, the undersigned officer of Akari Therapeutics, Plc (the "Company") hereby certifies, to such officer's knowledge that:

(i) the accompanying Annual Report on Form 20-F of the Company for the year ended December 31, 2022 (the "Report") fully complies with the requirements of Section 13(a) or Section 15(d), as applicable, of the Securities Exchange Act of 1934, as amended; and

(ii) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: April 28, 2023

/s/ Rachelle Jacques

Rachelle Jacques
Chief Executive Officer

The foregoing certification is being furnished solely to accompany the Report pursuant to 18 U.S.C. Section 1350, and is not being filed for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and is not to be incorporated by reference to any filing of the Company, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

Exhibit 32.2

CERTIFICATION OF PRINCIPAL ACCOUNTING OFFICER UNDER SECTION 906 OF THE

SARBANES-OXLEY ACT

Pursuant to 18 U.S.C. Section 1350, as created by Section 906 of the Sarbanes-Oxley Act of 2002, the undersigned officer of Akari Therapeutics, Plc (the "Company") hereby certifies, to such officer's knowledge that:

(i) the accompanying Annual Report on Form 20-F of the Company for the year ended December 31, 2022 (the "Report") fully complies with the requirements of Section 13(a) or Section 15(d), as applicable, of the Securities Exchange Act of 1934, as amended; and

(ii) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: April 28, 2023

/s/ Dr. Torsten Hombeck

Dr. Torsten Hombeck
Chief Financial Officer and Principal Accounting Officer

The foregoing certification is being furnished solely to accompany the Report pursuant to 18 U.S.C. Section 1350, and is not being filed for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and is not to be incorporated by reference to any filing of the Company, whether made before or after the date hereof, regardless of any general incorporation language in such filing.