Table of Contents

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**

For the transition period from _____to _____.

OR

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

Date of event requiring this shell company report _____

Commission file number: 001-38452

MEREO BIOPHARMA GROUP PLC
(Exact name of Registrant as specified in its charter)

England and Wales
(Jurisdiction of incorporation or organization)

One Cavendish Place
4th Floor
London, W1G 0QF
United Kingdom
Tel: +44-333-023-7300
(Address of principal executive offices)

Charles Sermon, General Counsel
Tel: +44-333-023-7300
Email: cs@mereobiopharma.com
1 Cavendish Place

4th Floor
London, W1G 0QF
United Kingdom
(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	Name of each exchange on which registered

American Depositary Shares, each representing five ordinary shares, nominal value of £0.003 per share	**MREO**	**The Nasdaq Stock Market LLC**
Ordinary Shares, nominal value of £0.003 per share		**The Nasdaq Stock Market LLC***

* Not for trading, but only in connection with the registration of American Depositary Shares representing such Ordinary Shares pursuant to the requirements of the U.S. 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

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

The number of outstanding shares as of December 31, 2022 was:

Title of each class	Number of Shares Outstanding at December 31, 2022
Ordinary shares, nominal value of £0.003 per share	624,928,519

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 (as defined 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 statements. ☐

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 ☒

TABLE OF CONTENTS

PART ONE		5
Item 1.	Identity of Directors, Senior Management And Advisers	5
Item 2.	Offer Statistics and Expected Timetable	5
Item 3.	Key Information	5
Item 4.	Information On The Company	59
Item 4A.	Unresolved Staff Comments	98
Item 5.	Operating And Financial Review And Prospects	98
Item 6.	Directors, Senior Management And Employees	109
Item 7.	Major Shareholders And Related Party Transactions	127
Item 8.	Financial Information	129
Item 9.	The Offer And Listing	129
Item 10.	Additional Information	130
Item 11.	Quantitative And Qualitative Disclosures About Market Risk	136
Item 12.	Description of Securities Other Than Equity Securities	137
PART TWO		139
Item 13.	Defaults, Dividend Arrearages And Delinquencies	139
Item 14.	Material Modifications To The Rights Of Security Holders And Use Of Proceeds	139
Item 15.	Controls And Procedures	139
Item 16.	Reserved	139
Item 16A.	Audit Committee Financial Expert	140
Item 16B.	Code of Ethics	140
Item 16C.	Principal Accountant Fees and Services	140
Item 16D.	Exemptions From The Listing Standards For Audit Committees	141
Item 16E.	Purchases of Equity Securities By The Issuer And Affiliated Purchasers	141
Item 16F.	Change In Registrant's Certifying Accountant	141
Item 16G.	Corporate Governance	141
Item 16H.	Mine Safety Disclosure	145
Item 16I.	Disclosure Regarding Foreign Jurisdictions that Prevent Inspections	145
PART THREE		146
Item 17.	Financial Statements	146
Item 18.	Financial Statements	146
Item 19.	Exhibits	146

CERTAIN DEFINITIONS

Unless otherwise indicated and except where the context otherwise requires, references in this annual report on Form 20-F to:

- "AATD" are to alpha-1-antitrypsin deficiency, a lack of alpha 1 anti-trypsin protein, a protein made by the liver that's released into the bloodstream to protect the body from neutrophil serine proteases damaging the lungs;
- "Acumapimod" are to an oral p38 MAP kinase inhibitor for potential treatment of AECOPD;
- "Alvelestat" are to an oral neutrophil elastase inhibitor for potential treatment of AATD;
- "ADSs" are to our American Depositary Shares, each of which represents five ordinary shares of Mereo BioPharma Group plc;
- "ADRs" are to the American Depositary Receipts that evidence our ADSs;
- "AECOPD" are to acute exacerbation of chronic obstructive pulmonary disease;
- "BLA" are to Biologics License Application;
- "CMA" are to Conditional Marketing Authorization;
- "CMO" are to contract manufacturing organization;
- "COPD" are to chronic obstructive pulmonary disease, the name for a group of lung conditions that cause breathing difficulties;
- "CRO" are to contract research organization;
- "DTC" are to Depository Trust Company;
- "EMA" are to European Medicines Agency;
- "Etigilimab" are to an anti-TIGIT therapeutic candidate designed to activate the immune system through multiple mechanisms and enable anti-tumor activity;
- "FDA" are to the United States Food and Drug Administration;
- "HH" are to hypogonadotropic hypogonadism, a condition in which the male testes or the female ovaries produce little or no sex hormones;
- "Leflutrozole" are to an oral aromatase inhibitor for potential treatment of male infertility associated with HH;
- "MAA" are to Marketing Authorization Application;
- "Mereo," the "Company," the "Group," "we," "our," "ours," "us" or similar terms are to Mereo BioPharma Group plc, together with its subsidiaries;
- the "Merger" are to the merger of Mereo MergerCo One Inc. and OncoMed Pharmaceuticals, Inc. ("OncoMed"), with OncoMed surviving as a wholly-owned subsidiary of Mereo US Holdings Inc., and as an indirect wholly-owned subsidiary of Mereo BioPharma Group plc, and in 2020 OncoMed was renamed as Mereo BioPharma 5, Inc. ("Mereo BioPharma 5");
- the "Merger Agreement" are to the Agreement and Plan of Merger and Reorganization, dated December 5, 2018, by and among Mereo BioPharma Group plc, Mereo US Holdings Inc., Mereo MergerCo One Inc. and OncoMed;
- "Navi" are to Navicixizumab;
- "NDA" are to New Drug Application;

- "NE" neutrophil elastase, a serine protease and a major constituent of lung elastoytic activity;
- "OI" are to osteogenesis imperfecta a rare genetic bone disorder characterized by fragile bones that break easily, also known as brittle bone disease;
- "OncXerna" are to OncXerna Therapeutics, Inc.
- "ordinary shares" are to our ordinary shares, each of £0.003 nominal value;
- "SEC" are to the United States Securities and Exchange Commission;
- "Setrusumab" are to a fully human monoclonal antibody for potential treatment of OI;
- "$," "USD," "US$" and "U.S. dollar" are to the United States dollar;
- "TIGIT" are to T-cell immunoreceptor with Ig and ITIM domains;
- "Ultragenyx" are to Ultragenyx Pharmaceutical, Inc.;

and

- "£," "GBP," "pound sterling," "pence" and "p" are to the British pound sterling (or units thereof).

PRESENTATION OF FINANCIAL INFORMATION

This annual report contains our audited consolidated financial statements as of December 31, 2022 and 2021 and for the years ended December 31, 2022, 2021 and 2020 (our "audited consolidated financial statements"), prepared in accordance with International Financial Reporting Standards ("IFRS"), as issued by the International Accounting Standards Board ("IASB"). Our financial information is presented in pound sterling. None of our financial statements were prepared in accordance with generally accepted accounting principles in the United States ("U.S.").

This annual report contains translations of certain pound sterling amounts into U.S. dollars at specified rates solely for the convenience of the reader. These translations should not be construed as representations that the pound sterling amounts actually represent such U.S. dollar amounts or could be converted into U.S. dollars at the rate indicated. Unless otherwise indicated, such U.S. dollar amounts have been translated from pound sterling at an exchange rate of £0.8262 to US$1.00, the exchange rate for pound sterling on December 31, 2022.

USE OF TRADEMARKS, SERVICE MARKS AND TRADENAMES

"Mereo," the Mereo logo and other trademarks, trade names or service marks of Mereo appearing in this annual report are the property of Mereo. This Form 20-F also contains trade names, trademarks and service marks of others, which are the property of their respective owners. We do not intend our use or display of other companies' trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, these other companies.

This annual report contains additional trademarks, service marks, and trade names of others, which are the property of their respective owners. All trademarks, service marks, and trade names appearing in this annual report are, to Mereo's knowledge, the property of their respective owners. Mereo does not intend its use or display of other companies' trademarks, service marks, copyrights or trade names to imply a relationship with, or endorsement or sponsorship of Mereo by, any other companies.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This annual report contains statements that constitute forward-looking statements within the meaning of Section 27A of the U.S. Securities Act of 1933, as amended (the "Securities Act"), Section 21E of the U.S. Securities Exchange Act of 1934, as amended (the "Exchange Act") and the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. The forward-looking statements in this annual report that are subject to risks and uncertainties. These forward-looking statements include information about possible or assumed future results of our business, financial condition, results of operations, liquidity, plans and objectives. In some cases, you can identify forward-looking statements by terminology such as "anticipate," "believe," "could," "expect," "foresee," "should," "plan," "intend," "estimate," "would," "may," "outlook," and potential," among others. The absence of these words, however, does not mean that the statements are not forward-looking. The statements we make regarding the following matters are forward-looking by their nature:

Forward-looking statements appear in a number of places in this annual report and include, but are not limited to, statements regarding intent, belief or current expectations. Forward-looking statements are based on the current beliefs and assumptions of the management of Mereo and on information currently available to such management. While the management of Mereo believes that these forward-looking statements are reasonable as and when made, there can be no assurance that future developments will be as anticipated. Such statements are subject to risks and uncertainties, and actual results may differ materially from those expressed or implied in the forward-looking statements due to of various factors, including, but not limited to, those identified under the section "Item 3. Key Information—D. Risk Factors" in this annual report. These risks and uncertainties include factors relating to:

- the development of our product candidates, including statements regarding the expected initiation, timing, progress, and availability of data from our clinical trials;
- the potential attributes and benefits of our product candidates and their competitive position;
- our ability to partner or sell our non-core product candidates, acumapimod for the treatment of AECOPD and leflutrozole for the treatment of male infertility associated with HH on attractive terms or at all;
- our ability to successfully commercialize, or enter into strategic relationships with third parties to commercialize, our product candidates, if approved;
- our estimates regarding expenses, future revenues, capital requirements, and our need for additional financing;
- our being subject to ongoing regulatory obligations if our products secure regulatory approval;
- our reliance on third parties to conduct our clinical trials and on third-party suppliers to supply or produce our product candidates;
- the patient market size of any diseases and market adoption of our products by physicians and patients;
- our ability to obtain and maintain adequate intellectual property rights and adequately protect and enforce such rights;
- the duration of our patent portfolio;
- the COVID-19 pandemic, or any other similar pandemic, and the associated disruptions during and after such pandemics that could materially impact our business, including, delays to enrollment of patients in clinical trials for our product candidates, delays to clinical trial supplies, planned clinical developments and our ongoing or future clinical studies;
- the United Kingdom's withdrawal from the European Union could increase our cost of doing business or otherwise negatively impact our business, results of operations and financial condition;
- our ability to retain key personnel and recruit additional qualified personnel;
- our ability to manage growth; and
- our ability to successfully integrate and realize the benefits of our past or future strategic acquisitions or investments.

You should refer to the section titled "Item 3.D Risk Factors" for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements in this annual report will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this annual report.

SUMMARY RISK FACTORS

You should carefully consider the risks and uncertainties described below, together with the other information contained in this annual report, before making any investment decision. Any of the following risks and uncertainties could have a material adverse effect on our business, prospects, results of operations and financial condition. The market price of our ADSs could decline due to any of these risks and uncertainties, and you could lose all or part of your investment. The risks described below are those that we currently believe may materially affect us. We may face additional risks and uncertainties not currently known to us or that we currently deem to be immaterial.

- We have a limited operating history and have never generated any revenue from product sales.
- We will need additional funding to complete the development of our current product candidates; to license, acquire, and develop future product candidates; and to commercialize our product candidates, if approved. If we are unable to raise capital when needed, we could be forced to delay, reduce, or eliminate research and development programs, any future commercialization efforts or acquisitions of potential product candidates.
- We depend heavily on the success of setrusumab, alvelestat and etigilimab. We cannot give any assurance that any of these product candidates or therapeutic candidates will receive regulatory approval, which is necessary before they can be commercialized. If we are unable to commercialize setrusumab, alvelestat and etigilimab, whether on our own or through agreements with third parties, or experience significant delays in doing so, our ability to generate revenue and our financial condition will be adversely affected.
- The COVID-19 pandemic impacted and may continue to impact our business or any other similar pandemic may materially impact our business, including, delays to enrollment of patients in clinical trials for our product candidates, delays in engagement with or responses from regulatory authorities, delays to clinical trial supplies, planned clinical developments and our ongoing or future clinical studies.
- We depend on enrollment of patients in our clinical trials for our product candidates. If we are unable to enroll patients in our clinical trials, or enrollment is slower than anticipated, in particular for our product candidates with rare disease indications, our research and development efforts could be adversely affected.
- We may become exposed to costly and damaging liability claims, either when testing our product candidates in the clinic or at the commercial stage, and our product liability insurance may not cover all damages from such claims.
- Enacted and future healthcare legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and may affect the prices we may set.
- We operate in a highly competitive and rapidly changing industry, which may result in others acquiring, developing, or commercializing competing product candidates before or more successfully than we do.
- We intend to directly commercialize or co-commercialize our product candidates for rare diseases and to out-license or sell our other product candidates for further development and/or commercialization. If we are unable to develop our own sales, marketing, and distribution capabilities or enter into business arrangements, we may not be successful in commercializing our product candidates.
- The successful commercialization of our product candidates will depend in part on the extent to which governmental authorities and health insurers establish adequate coverage, reimbursement levels, and pricing policies. Failure to obtain or maintain coverage and adequate reimbursement for our product candidates, if approved, could limit our ability to market those product candidates and decrease our ability to generate revenue.
- Our existing and future product candidates may not gain market acceptance, in which case our ability to generate revenues from product sales will be compromised.
- We rely, and expect to continue to rely, on our partners to develop and commercialize our licensed or partnered product candidates. If our partners do not secure adequate funding or satisfy their obligations under our agreements with them, or if they terminate our licenses, partnerships or collaborations with them, we may not be able to develop or commercialize our licensed or partnered product candidates as planned.
- We rely, and expect to continue to rely, on third parties, including independent investigators and CROs, to conduct our clinical trials. If these CROs do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates, or such approval or commercialization may be delayed, and our business could be substantially harmed.
- We currently rely on third-party CMOs for the production of clinical supply of our product candidates and intend to rely on CMOs for the production of commercial supply of our product candidates, if approved. Our dependence on CMOs may impair the development of our product candidates and may impair the commercialization of our product candidates, which would adversely impact our business and financial position.

- We rely on patents and other intellectual property rights to protect our product candidates, the obtainment, enforcement, defense and maintenance of which may be challenging and costly. Failure to enforce or protect these rights adequately could harm our ability to compete and impair our business.
- We may become subject to third parties' claims alleging infringement of third-party patents and proprietary rights, or we may be involved in lawsuits to protect or enforce our patents and other proprietary rights, which could be costly and time consuming, delay or prevent the development and commercialization of our product candidates, or put our patents and other proprietary rights at risk.
- Our business and operations may suffer, and proprietary information may be lost, in the event of information technology system failures, cyberattacks or deficiencies in our cybersecurity.
- Our future growth and ability to compete depends on retaining our key personnel and recruiting additional qualified personnel.
- We may not satisfy Nasdaq's requirements for continued listing. If we cannot satisfy these requirements, Nasdaq could delist our ADSs which could have an adverse impact on the liquidity and market price of our ADSs.
- Failure to establish and maintain effective internal controls could have a material adverse effect on our business and stock price.

PART ONE

Item 1. Identity of Directors, Senior Management And Advisers

Not applicable.

Item 2. Offer Statistics and Expected Timetable

Not applicable.

Item 3. Key Information

3.A. [Reserved]

3.B. Capitalization and Indebtedness

Not applicable.

3.C. Reasons For the Offer and Use of Proceeds

Not applicable.

3.D. Risk Factors

You should carefully consider the risks and uncertainties described below, together with the other information contained in this annual report, before making any investment decision. Any of the following risks and uncertainties could have a material adverse effect on our business, prospects, results of operations and financial condition. The market price of our ADSs could decline due to any of these risks and uncertainties, and you could lose all or part of your investment. The risks described below are those that we currently believe may materially affect us. We may face additional risks and uncertainties not currently known to us or that we currently deem to be immaterial.

Risks Related to Our Business and Industry

We have a limited operating history and have never generated any revenue from product sales.

We are a multi-asset, clinical-stage biopharmaceutical company with a limited operating history, and have incurred significant operating losses since our formation. For the year-ended December 31, 2022 we had a net loss of £34.2 million, and we had a net profit of £12.7 million and a net loss of £163.6 million, for the years ended December 31, 2021 and 2020, respectively. As of December 31, 2022, we had an accumulated net loss of £331.2 million (£297.0 million as of December 31, 2021). Our losses have resulted principally from expenses incurred from the research and development of our product candidates and from general and administrative costs that we have incurred while building and operating our business

infrastructure. We expect to continue to incur significant operating losses for the foreseeable future as we invest in our research and development efforts, and seek to obtain regulatory approval and potentially commercialize our product candidates. We anticipate that our expenses will increase substantially as we:

- seek to secure a partnership and prepare for a potential Phase 3 clinical trial of alvelestat for the treatment of severe AATD, support the ongoing investigator-led Phase 2 study in AATD and support the expansion of the investigator-sponsored study in Bronchiolitis Obliterans Syndrome ("BOS") into Phase 2;
- undertake the activities required as part of our collaboration with Ultragenyx and potential commercialization of setrusumab, if approved in the European Union ("EU") and the United Kingdom ("U.K.");
- undertake development of our product candidates in any additional potential indications;
- seek regulatory approvals for our product candidates;
- potentially establish a commercial infrastructure to commercialize or co-commercialize selected product candidates, if approved;
- work with CMOs to develop manufacturing processes and scale-up for Phase 3 studies and potential commercialization;
- maintain, expand, and protect our intellectual property portfolio;
- secure, maintain, or obtain freedom to operate for our technologies and product candidates;
- add clinical, scientific, operational, financial, legal and management personnel, including personnel to support the development of our product candidates and potential future commercialization or co-commercialization efforts and support our operations as a U.S. public company listed on Nasdaq;
- expand our operations and potentially hire additional employees in the United Kingdom, United States and in Europe, territories where we anticipate direct commercialization or commercialization with a partner; and
- seek to acquire additional novel product candidates to treat rare diseases in the future.

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

We have devoted substantially all of our financial resources and efforts to the acquisition and clinical development of our product candidates. We have not completed the clinical development of any product through approval and have never generated any revenue from product sales.

To become and remain profitable, we must succeed in developing and commercializing product candidates that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing clinical trials of our current or any future product candidates, obtaining regulatory approval for our product candidates that successfully complete clinical trials, establishing manufacturing supplies and marketing capabilities, and ultimately commercializing, if approved, or entering into strategic relationships for our current and future product candidates. We are only in the preliminary stages of many of these activities. We may never succeed in these activities and, even if we do, we may never generate revenue that is significant enough to achieve profitability.

Because of the numerous risks and uncertainties associated with biopharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. We may be subject to different or contradictory regulatory requirements in different countries, and different regulatory authorities may not be aligned on the clinical trials necessary to support approval of our product candidates. If we are required by the FDA, the EMA, or other regulatory authorities to perform studies in addition to those we currently anticipate, or if there are any delays in completing our clinical trials or the development of our current product candidates, our expenses could increase and our ability to generate revenue could be further delayed. In addition, we may not be able to acquire new product candidates or may encounter unexpected difficulties or delays in such acquisitions, which would impair our business.

Furthermore, adoption by the medical community of our product candidates, if approved, may be limited if third-party payors offer inadequate reimbursement coverage. Cost control initiatives may decrease coverage and payment levels for our product candidates, which in turn would negatively affect the price that we will be able to charge for such product candidates. We are unable to predict the coverage that will be provided by private or government payors for any product we have in development. Any denial of private or government payor coverage, inadequate reimbursement for our product candidates, or delay in receipt of reimbursement payments could harm our business and, even if we do generate product royalties or product sales, we may never achieve or sustain profitability. Our failure to sustain profitability would depress the market price of our ADSs and could impair our ability to raise capital, acquire new product candidates, expand our business, or continue our operations. A decline in the market price of our ADSs also could cause you to lose all or a part of your investment.

We will need additional funding to complete the development of our current product candidates; to license, acquire, and develop future product candidates; and to commercialize our product candidates, if approved. If we are unable to raise capital when needed, we could be forced to delay, reduce, or eliminate research and development programs, any future commercialization efforts or acquisitions of potential product candidates.

While we raised $183 million (£137.9 million) in private placements of ordinary shares and convertible loan notes in 2020 and in a public offering of ADSs in February 2021, we expect our expenses to increase substantially in connection with our ongoing activities, particularly as we continue to advance our rare disease portfolio. In addition, if we obtain marketing approval for product candidates where we retain commercial rights, we expect to incur significant commercialization expenses related to product sales, marketing, distribution and manufacturing. Furthermore, we expect to continue to incur additional costs associated with operating as a publicly traded company in the United States and maintaining a listing on Nasdaq. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

We believe that our existing cash and cash equivalents will be sufficient to enable us to fund our operating expenses and capital expenditure requirements into 2026 at which point we will require additional capital. Our failure to obtain sufficient funds on acceptable terms when needed could have a material adverse effect on our business, results of operations and financial condition.

We have based our liquidity and capital resources estimates on assumptions that may prove to be wrong. As a result, we could use our capital resources sooner than we currently expect, or our operating plan may change as a result of many factors unknown to us. These factors, among others, may necessitate that we seek additional capital sooner than currently planned.

Our future capital requirements will depend on many factors, including:

- The costs, timing and results of our Phase 1b/2 study for etigilimab, and ongoing investigator-sponsored clinical trials for alvelestat in AATD and in patients with BOS; and the costs for our activities related to our ongoing collaboration with Ultragenyx for setrusumab for the treatment of adults and children with OI and the costs for our preparation for eventual commercialization of setrusumab in Europe and the U.K.;
- the costs and timing of manufacturing clinical supplies of our product candidates;
- the costs, timing, and outcome of regulatory review of our product candidates, including post-marketing studies that could be required by regulatory authorities;
- the costs, timing, and outcome of potential future commercialization activities, including manufacturing, marketing, sales, life cycle management and distribution, for our product candidates that we commercialize directly;
- the timing and amount of revenue, if any, received from commercial sales of our product candidates;
- the costs and timing of preparing, filing, and prosecuting patent applications; maintaining and enforcing our intellectual property rights; and defending any intellectual property-related claims, including any claims by third parties that we are infringing, misappropriating or otherwise violating the third party's intellectual property rights;
- the sales price and availability of adequate third-party coverage and reimbursement for our product candidates;
- the effect of competitors and market developments;
- the performance of our collaborators and partners under the existing agreements on setrusumab and navicixizumab;

- the extent to which we are able to acquire new product candidates or enter into licensing or collaboration arrangements for our product candidates;
- milestone and deferred payments under our license and option agreement with AstraZeneca; and
- tax liabilities or other assessments and our ability to claim R&D tax credits or other reliefs.

Fundraising and business development efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect our business, the holdings or the rights of our shareholders, or the value of our ADSs.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay, or discontinue our research and development programs or any commercialization efforts; be unable to expand our operations or acquire product candidates; or be unable to otherwise capitalize on our business opportunities, as desired, which could harm our business.

Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

Since our formation, we have devoted substantially all of our resources to acquiring our product candidates and developing setrusumab, alvelestat, etigilimab, acumapimod and leflutrozole; building our intellectual property portfolio; developing our supply chain; planning our business; raising capital; and providing general and administrative support for these operations. Additionally, prior to our acquisition of etigilimab and navicixizumab in the Merger, Mereo BioPharma 5 (formerly OncoMed) had invested significant resources to developing both product candidates. We have not yet demonstrated our ability to successfully complete any Phase 3 or other pivotal clinical trials, obtain regulatory approval, arrange for third parties to manufacture commercial-scale product candidates, or conduct or partner with others to conduct sales and marketing activities necessary for successful product commercialization. Additionally, although we have acquired product candidates from two large pharmaceutical companies, we have not demonstrated the sustainability of our business model of acquiring and developing product candidates from, and becoming a partner of choice for, pharmaceutical and biotechnology companies, nor have we demonstrated our ability to obtain approvals for or to commercialize or co-commercialize these product candidates. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

We may not be successful in our efforts to identify and acquire additional product candidates.

Part of our strategy involves identifying and acquiring novel product candidates that have received significant investment from large pharmaceutical and biotechnology companies and that have substantial pre-clinical, clinical, and manufacturing data packages. The process by which we identify product candidates may fail to yield product candidates for clinical development for a number of reasons, including those discussed in these risk factors and also:

- any product candidates we acquire that have generated positive clinical data for our target indication or in diseases other than our target indications may not prove to be effective in treating our target indications;
- potential product candidates may, with further studies, be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be product candidates that will receive marketing approval and achieve market acceptance;
- the regulatory pathway for a potential product may be too complex and difficult to navigate successfully or economically; and
- there may be competitive bids for potential product candidates which we do not seek to or are unable to match.

In addition, we may choose to focus our efforts and resources on a potential product that ultimately proves to be unsuccessful. Further, time and resources spent searching for, identifying, acquiring, and developing potential product candidates may distract our management’s attention from our primary business or other development programs. If we are unable to identify and acquire additional suitable product candidates for clinical development, this would adversely impact our business strategy and our financial position and share price.

Raising additional capital may cause dilution to, or adversely affect the rights of, our security holders, restrict our operations; or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, as we can generate substantial product revenues, we may seek to finance our cash needs through securities offerings, debt financings, license and collaboration agreements, or other capital raising transactions. If we raise capital through securities offerings, your ownership interest will be diluted, and the terms of the securities we issue in such transactions may include liquidation or other preferences that adversely affect your rights as a holder of our ADSs. Debt financing, if available, could result in fixed payment obligations, and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, to acquire, sell or license intellectual property rights, to make capital expenditures, to declare dividends, or other operating restrictions. If we raise additional funds through collaboration or licensing agreements, we may have to relinquish valuable rights to our technologies, future revenue streams, or product candidates or grant licenses on terms that may not be favorable to us. In addition, we could also be required to seek funds through arrangements with collaborators or others at an earlier stage than otherwise would be desirable. Raising additional capital through any of these or other means could adversely affect our business and the holdings or rights of our security holders, and may cause the market price of our ADSs to decline.

We depend heavily on the success of setrusumab, alvelestat and etigilimab. We cannot give any assurance that any of these product candidates or therapeutic candidates will receive regulatory approval, which is necessary before they can be commercialized. If we are unable to commercialize setrusumab, alvelestat and etigilimab, whether on our own or through agreements with third parties, or experience significant delays in doing so, our ability to generate revenue and our financial condition will be adversely affected.

We do not currently generate any revenue from sales of any product candidates, and we may never be able to develop or commercialize a marketable product. We have invested substantially all of our efforts and financial resources in the acquisition and development of setrusumab, alvelestat and etigilimab, among other product candidates in our portfolio. Our ability to generate royalty and product revenues, which we do not expect will occur for at least the next several years, if ever, will depend heavily on the successful development and eventual commercialization of our current product candidates, if approved, which may never occur. Our current product candidates will require additional clinical development, management of clinical and manufacturing activities, regulatory approval in multiple jurisdictions, procurement of manufacturing supply, commercialization, substantial additional investment by us or our partners, and significant marketing efforts before we generate any revenue from product sales or royalties.

We are not permitted to market or promote any product candidates in the United States, United Kingdom, Europe, or other countries before we receive regulatory approval from the FDA, the EMA, or comparable U.K. or foreign regulatory authorities, and we may never receive such regulatory approval for our current product candidates. We have not submitted a BLA or a NDA to the FDA, an MAA or CMA to the EMA, or comparable applications to other regulatory authorities. The success of our current product candidates will depend on many factors, including the following:

- successful initiation and completion of preclinical studies with favorable results, including toxicology and other studies designed to be compliant with good laboratory practices (“GLP”);
- allowance to proceed with clinical trials under Investigational New Drug applications (“INDs”), by the FDA, or of similar regulatory submissions by comparable foreign regulatory authorities for the conduct of clinical trials of our product candidates;
- successful initiation, enrollment and completion of clinical studies in accordance with Good Clinical Practice (“GCP”) requirements and other applicable rules and regulations;
- the frequency and severity of adverse events observed in clinical trials;
- maintaining and establishing relationships with contract research organizations (“CROs”) and clinical sites for the clinical development of our product candidates;

- demonstrating the safety, purity, and potency, or efficacy of our product candidates to the satisfaction of the FDA and other applicable regulatory authorities;
- receipt of regulatory approvals from applicable regulatory authorities, including approvals of NDAs or BLAs from the FDA, or MAAs from the EMA and maintaining any such approvals;
- making arrangements with our third-party manufacturers for, or establishing, clinical or commercial manufacturing capabilities;
- establishing sales, marketing and distribution capabilities and launching commercial sales of our product candidates, if and when approved, whether alone or in collaboration with others;
- obtaining, establishing and maintaining patent and trade secret protection or regulatory exclusivity for our product candidates;
- maintaining an acceptable safety profile for our product candidates following regulatory approval, if any;
- maintaining and growing an organization of people who can develop and, if approved, commercialize, market and sell our product candidates, if approved; and
- if approved, acceptance of our current product candidates by patients, the medical community, and third-party payors; our ability to compete with other therapies to treat OI, AATD, BOS or certain oncology indications; continued acceptable safety profiles following approval of our current product candidates; and our ability to qualify for, maintain, enforce, and defend our intellectual property rights and claims.

If we do not successfully manage one or more of these factors in a timely manner or at all, we could experience significant delays or may not be able to successfully commercialize our current product candidates.

We cannot be certain that our current product candidates will be successful in clinical trials or receive regulatory approval. Further, our current product candidates may not receive regulatory approval even if they are successful in clinical trials. If we do not receive regulatory approvals for our current product candidates, we may not be able to continue our operations. Even if we successfully obtain regulatory approvals to manufacture and market our current product candidates, our revenues will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval and have commercial rights. If the markets for patient subsets that we are targeting are not as significant as we estimate, we may not generate significant revenues from sales of such product candidates, if approved.

We plan to seek regulatory approval to commercialize, or co-commercialize, our current rare disease product candidates in the United States, U.K and the EU, and potentially in additional countries. While the scope of regulatory approval is similar in many countries, to obtain separate regulatory approval in multiple countries requires us to comply with the numerous and varying regulatory requirements of such countries regarding safety and efficacy and governing, among other things, clinical trials and commercial sales, pricing and distribution, and we cannot predict success in these jurisdictions.

Exchange rate fluctuations may materially affect our results of operations and financial condition.

Owing to the international scope of our operations, fluctuations in exchange rates, particularly between the pound sterling and the U.S. dollar, the Euro, or the Swiss Franc, may adversely affect us. Further, potential future revenue may be derived from multiple jurisdictions and in multiple currencies. As a result, our business and the price of our ADSs may be affected by fluctuations in foreign exchange rates not only between the pound sterling and the U.S. dollar, but also the currencies of other countries, which may have a significant impact on our results of operations and cash flows from period to period. Currently, we do not have any exchange rate hedging arrangements in place.

The COVID-19 pandemic impacted and may continue to materially impact our business including planned clinical developments.

Our business could be adversely affected by health epidemics in regions where we and/or our partners conducted clinical trials have concentrations of clinical trial sites or other business operations, and could cause significant disruption in the operations of third-parties upon whom we rely. The COVID-19 pandemic and its related variants resulted in delays in our ability to enroll and treat patients and obtain data from clinical trials, particularly in patients with severe AATD.

The continued effects of the COVID-19 pandemic may also cause us to experience disruptions that would significantly impact our business including:

- A delay or interruption in our ability to enroll and treat patients and to obtain data from ongoing clinical trials;
- A delay in our timelines for the initiation of new clinical trials;
- A delay in our ability to recruit patients to our clinical trials and to screen patients for eligibility for our clinical trials;
- Interruption to key clinical trial activities including monitoring of clinical sites, patient visits, inability to follow patients after they have received treatment and patient assessments and patients dropping out from trials early reduce the numbers impacting efficacy analysis;
- A delay in availability of additional drug product for setrusumab, alvelestat or etigilimab due to lack of manufacturing capacity and/or raw materials at our third-party CMOs;
- A delay in our ability to close and negotiate third-party partnerships or collaborations or to progress third-party collaborations already in place;
- Limitations on employee resources as a result of increased sickness, requirement for employees to care for family members or requirement for employees to self-isolate themselves;
- Interruptions and delays in our development programs as a result of any government required “stay-at-home” guidelines;
- Delay in responses from regulatory authorities in relation to approvals, amendments or other regulatory engagements required for our ongoing development activities;
- Supply chain interruptions; or
- Diversion of CMO activities and raw materials to COVID-19 products, including restrictions imposed by various governments, causing delays to clinical trial supplies.

The extent to which the ultimate impact of the COVID-19 pandemic, or any other health epidemic, may impact our future business is highly uncertain and difficult to predict. We do not yet know the full extent of potential delays or impacts on our business, our clinical trials, our research programs, healthcare systems or the global economy as a whole. However, these effects could have a material adverse effect on our business, financial condition and results of operations. To the extent the COVID-19 pandemic materially adversely affects our business and financial results, it may also have the effect of significantly heightening many of the other risks described in this Risk Factors section.

The U.K.’s withdrawal from the EU, commonly referred to as Brexit, could increase our cost of doing business or otherwise negatively impact our business, results of operations and financial condition.

Brexit could increase our cost of doing business or otherwise negatively impact our business, results of operations and financial condition. Brexit continues to create uncertainty concerning the future relationship between the U.K. and the EU, following the U.K.’s withdrawal from the EU in January 2020. Our principal office is located in the U.K. and together with our partners we conduct clinical trials in the EU. Since a significant portion of the regulatory framework in the U.K. is derived from EU laws, Brexit materially impacts the regulatory regime with respect to the development, manufacture, importation, approval and commercialization of our product candidates in the U.K. or the EU.

Since the end of the Brexit transition period on January 1, 2021, Great Britain (England, Scotland and Wales) has not been directly subject to EU laws, however under the terms of the Ireland/Northern Ireland Protocol, EU laws generally apply to Northern Ireland. It is currently unclear to what extent the U.K. Government will seek to align its regulations with the EU. The EU laws that have been transposed into U.K. law through secondary legislation remain applicable in Great Britain.

However, under the Retained EU Law (Revocation and Reform) Bill 2022, which is currently before the U.K. parliament, any retained EU law not expressly preserved and "assimilated" into domestic law or extended by ministerial regulations (to no later than June 23, 2026) will automatically expire and be revoked by December 31, 2023. In addition, new legislation such as the EU Clinical Trials Regulation ("CTR") is not applicable in Great Britain. While the EU- U.K. Trade and Cooperation Agreement ("TCA") includes the mutual recognition of Good Manufacturing Practice ("GMP") inspections of manufacturing facilities for medicinal products and GMP documents issued, it does not contain wholesale mutual recognition of U.K. and EU pharmaceutical regulations and product standards. There may be divergent local requirements in Great Britain from the EU in the future, which may impact clinical and development activities that occur in the U.K. in the future. Similarly, clinical trial submissions in the U.K. will not be able to be bundled with those of EU countries within the EMA Clinical Trial Information System ("CTIS"), adding further complexity, cost and potential risk to future clinical and development activity in the U.K. Significant political and economic uncertainty remains about how much the relationship between the U.K. and EU will differ as a result of the U.K.'s withdrawal.

Such a withdrawal from the EU is unprecedented, and it is unclear how the U.K.'s access to the European single market for goods, capital, services and labor within the EU, or single market, and the wider commercial, legal and regulatory environment, will impact our current and future operations, including activities conducted by third parties and contract manufacturers on our behalf. In addition to the foregoing, our U.K. operations support our current and future operations and clinical activities in other countries in the EU and EEA and these operations and clinical activities could be disrupted by the ongoing effects of Brexit.

Since the regulatory framework in the U.K. covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization ("MA"), commercial sales and distribution of pharmaceutical products is derived from EU directives and regulations, Brexit could materially impact the future regulatory regime with respect to the potential commercialization of our products in the U.K. Under the Medicines and Medical Devices Act 2021, the Secretary of State or an 'appropriate authority' has delegated powers to amend or supplement existing regulations in the area of medicinal products and medical devices. This allows new rules to be introduced in the future by way of secondary legislation, which aims to allow flexibility in addressing regulatory gaps and future changes in the fields of human medicines, clinical trials and medical devices. Any delay in commercializing our products in the U.K. and/or the EU could restrict our ability to generate revenue. The uncertainty around the U.K.'s future relationship with the EU continues to cause economic uncertainty which could adversely affect our business, financial condition and results of operations and could adversely affect the market price of our ADSs.

Following the licensing agreement for navicixizumab and the completion of a strategic partnership for setrusumab, and if we out-license or sell our non-core product candidates or out-license any of our core rare disease product candidates for any territories, we could be exposed to future liabilities.

In January 2021, we completed a strategic partnership for setrusumab and completed the out-license of navicixizumab in January 2020. We plan to partner or sell or out-license our non-core product candidates acumapimod for the treatment of AECOPD and leflutrozole for the treatment of male infertility associated with HH, recognizing the need for a larger sales infrastructure and greater resources to take these product candidates to market.

We may be exposed to future liabilities and/or obligations with respect to any such out-licensing or sale arrangements or partnerships. We may be required to set aside provisions for warranty claims or contingent liabilities in respect of such sales or out-licensing arrangements. We may be required to pay damages (including, but not limited to, litigation costs) to a purchaser or licensee to the extent that any representations or warranties that we had given to that purchaser or licensee prove to be inaccurate or to the extent that we have breached any of our covenants or obligations contained in the disposal documentation. In certain circumstances, it is possible that any incorrect representations and warranties could give rise to a right by the purchaser or licensee to unwind the contract in addition to receiving damages. Furthermore, we may become involved in disputes or litigation in connection with such product candidates. Certain obligations and liabilities associated with our prior management of the development of any disposed product candidate can also continue to exist notwithstanding any sale, such as liabilities arising from the infringement of intellectual property rights of others.

As a result of the above, the total amount of costs and expenses that may be incurred with respect to liabilities associated with an out-license or sale may exceed our expectations, and we may experience other unanticipated adverse effects, all of which could adversely affect our business, financial condition, results of operations, and prospects.

Our business is subject to economic, political, regulatory and other risks associated with international operations and business disruptions could seriously harm our financial condition and increase costs.

Our business is subject to risks associated with conducting business internationally. We source research and development, manufacturing, consulting, and other services from companies based throughout the United States, the EU, and Switzerland, and we conduct our clinical trials in the United States, Canada, certain European countries, and other countries. Accordingly, our future results could be harmed by a variety of factors, including:

- economic weakness, including inflation, or political instability in particular non-U.K. economies and markets;
- differing regulatory requirements for drug approvals in non-U.K. countries;
- differing jurisdictions could present different issues for securing, maintaining, or obtaining freedom to operate for our intellectual property in such jurisdictions;
- potentially reduced protection for intellectual property rights;
- difficulties in compliance with non-U.K. laws and regulations;
- changes in non-U.K. regulations and customs, tariffs, and trade barriers;
- changes in non-U.K. currency exchange rates of the pound sterling and currency controls;
- changes in a specific country's or region's political or economic environment, including the implications of the United Kingdom's withdrawal from the EU;
- trade protection measures, import or export licensing requirements or other restrictive actions by U.K. or non-U.K. governments;
- differing reimbursement regimes and price controls in certain non-U.K. markets;
- negative consequences from changes in tax laws;
- compliance with tax, employment, immigration, and labor laws for employees living or traveling outside of the United Kingdom;
- workforce uncertainty in countries where labor unrest is more common than in the United Kingdom;
- difficulties associated with staffing and managing international operations, including differing labor relations;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad;
- business interruptions resulting from geo-political actions, including war and terrorism, health epidemics and other widespread outbreaks of contagious disease, or natural disasters, including earthquakes, typhoons, hurricanes, floods and fires; and
- business interruptions resulting from the COVID-19 pandemic or any other health epidemics.

For example, the COVID-19 pandemic resulted in delays in our ability to enroll and treat patients, obtaining data from our clinical trials, our ability to recruit additional patients to our clinical trials and to screen new patients for eligibility for our clinical trials. Additionally, the after-effects of supply chains disruptions may impact our development activities. Moreover, in February 2022, tensions between the United States and Russia escalated when Russia invaded Ukraine. In response, The North Atlantic Treaty Organization, or NATO, has deployed additional military forces to Eastern Europe and the United States, United Kingdom and the EU, among others, have significantly expanded their Trade Controls against Russia. The invasion of Ukraine and the retaliatory measures that have been taken, or could be taken in the future, by the United States, NATO, and other countries have created global security concerns that could result in a regional conflict and otherwise have a lasting impact on regional and global economies, any or all of which could disrupt our supply chain, adversely affect the cost of raw materials and other services, adversely affect our ability to conduct ongoing and future clinical trials of our product candidates, and adversely affect our ability to commercialize our products (subject to regulatory approval) in this region.

Our future growth and ability to compete depends on retaining our key personnel and recruiting additional qualified personnel.

Our success depends upon the continued contributions of our key management, including all of our senior management team, and scientific and technical personnel, many of whom have been instrumental for us and have substantial experience with rare diseases and the biopharmaceutical and pharmaceutical industries. The loss of key managers and senior physicians or

scientists could delay our acquisition and development activities. In addition, the competition for qualified personnel in the biopharmaceutical and pharmaceutical fields is intense, and our future success depends upon our ability to attract, retain and motivate highly skilled scientific, technical, and managerial employees. We face competition for personnel from other companies and organizations. If our recruitment and retention efforts are unsuccessful in the future, it may be difficult for us to achieve our development objectives, raise additional capital, and implement our business strategy.

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

To manage our planned future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities or acquire new facilities, and continue to retain, recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such planned growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Changes in our tax rates, unavailability of certain tax credits or reliefs, or exposure to additional tax liabilities or assessments could adversely affect our results of operations and financial condition.

As a U.K. resident trading entity, we are subject to U.K. corporate taxation. Due to the nature of our business, we have generated operating losses since formation. As at December 31, 2022, 2021 and 2020, we had cumulative carry-forward tax losses of 125.8 million, 122.6 million and 136.9 million, respectively. The availability to carry forward and offset these tax loss carry-forwards against future operating profits is subject to certain restrictions.

As a company that carries out extensive research and development (“R&D”) activities, we benefit from the U.K. HM Revenue and Customs (“HMRC”) small and medium sized enterprises research and development relief, or SME R&D Relief, which provides relief against U.K. Corporation Tax and enables us to surrender some of our trading losses that arise from our research and development activities for a cash rebate. To date, a cash rebate of up to 33.35% of eligible R&D expenditure has been available, but the cash rebate will reduce to a maximum of 27% for R&D intensive companies where at least 40% of their total expenditure in on qualifying R&D, or to 18.6% of eligible R&D expenditure for other companies, with effect from April 1, 2023 pursuant to changes made by the Finance Act 2023. Certain subcontracted qualifying research expenditures are eligible for a cash rebate though the rate of the cash rebate will reduce with effect from April 1, 2023, from up to 21.67% of the subcontracted expenditures to 17.53% for R&D intensive companies or 12.09% for other companies. In addition, we may not be able to continue to claim payable R&D tax credits in the future because we may no longer qualify as a small or mediumsized company. In that case, we would expect to benefit from the taxable credit for qualifying R&D expenditure under the R&D Expenditure Credit (RDEC) scheme available to large companies which may be either offset against corporation tax liabilities or paid net of tax as a cash credit where there is no liability in the future.. Subcontracted expenditure is not however a qualifying cost under the RDEC scheme. In the event we generate revenues in the future, we may also benefit from the U.K. “patent box” regime that allows profits attributable to revenues from patents or patented product candidates to be taxed at an effective rate of 10%. This relief applies to profits earned following election into the regime.. When taken in combination with the enhanced relief available on our R&D expenditures, we expect a long-term lower rate of corporation tax to apply to us. If, however, there are unexpected adverse changes to the U.K. R&D tax credit regime or the “patent box” regime, or for any reason we are unable to qualify for such advantageous tax legislation, or we are unable to use net operating loss and tax credit carry forwards and certain built-in losses to reduce future tax payments, our business, results of operations, and financial condition may be adversely affected. In particular, HM Treasury and HMRC launched a consultation in January 2023 entitled “R&D Tax Reliefs Review, Consultation on a single scheme” which seeks views on the possible merger of the SME R&D Relief scheme and the RDEC scheme applicable to large companies, the outcome of which may be further changes to the reliefs available to us. If it is decided to merge the schemes, any new regime is expected to apply with effect from April 1, 2024.

New rules were introduced, effective for accounting periods starting after April 1, 2021, whereby the amount of SME payable R&D tax credit that a business can receive in any one year will be capped at £20,000 plus three times the company’s total Pay As You Earn (PAYE) and National Insurance contributions (NIC) liability. Exemptions to the cap have been introduced which are available to companies that meet certain conditions. We do not believe these changes could have an impact on our tax credit for the year ending December 31, 2022, which would be payable in 2023. If tax authorities challenge our determinations and/or audit prior periods there could be adverse tax consequences to us that could adversely affect our results of operations and financial condition.

Risks Related to Development, Clinical Testing, Manufacturing and Regulatory Approval

Prior to our acquisition of setrusumab, alvelestat, etigilimab, acumapimod, leflutrozole and navicixizumab, we were not involved in the development of these product candidates and, as a result, we are dependent on Novartis, AstraZeneca and Mereo BioPharma 5 (formerly OncoMed) having accurately reported the results and correctly collected and interpreted the data from all clinical trials conducted prior to our acquisition.

We were not involved in the development of our current product candidates prior to our acquisition of such product candidates from Novartis, AstraZeneca and Mereo BioPharma 5. For all of our current product candidates, we have had no involvement with or control over their manufacturing or pre-clinical and clinical development prior to our acquisition of them. We are dependent on Novartis, AstraZeneca and Mereo BioPharma 5 having conducted their research and development in accordance with the applicable protocols and legal, regulatory, and scientific standards; having accurately reported the results of all clinical trials conducted prior to our acquisition; and having correctly collected and interpreted the data from these trials. To the extent Novartis, AstraZeneca or Mereo BioPharma 5 has not done this, the clinical development, regulatory approval, or commercialization of our product candidates may be adversely affected.

Clinical and preclinical development involves a lengthy and expensive process with an uncertain outcome. Any difficulties or delays in the commencement or completion, or the termination or suspension, of our or our partners current or planned clinical trials could result in increased costs to us, delay or limit our ability to generate revenue or adversely affect our commercial prospects.

Before obtaining approval from regulatory authorities for the commercialization of any of our product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidate, or with respect to product candidates regulated as biologics, safety, purity and potency, in humans. Before we can initiate clinical trials for any product candidates, we must submit the results of preclinical studies to the FDA or comparable foreign regulatory authorities along with other information, including information about product candidate chemistry, manufacturing and controls and our proposed clinical trial protocol, as part of an IND or similar regulatory submission. The FDA or comparable foreign regulatory authorities may require us to conduct additional preclinical studies for any product candidate before it allows us to initiate clinical trials under any IND or similar regulatory submission, which may lead to delays and increase the costs of our preclinical development programs. Moreover, even if we commence clinical trials, issues may arise that could cause regulatory authorities to suspend or terminate such clinical trials. Any such delays in the commencement or completion of our ongoing and planned clinical trials for our product candidates could significantly affect our product development timelines and product development costs and harm our financial position.

The results from preclinical studies or early clinical trials of a product candidate may not predict the results of later clinical trials of the product candidate, and interim results of a clinical trial are not necessarily indicative of final results. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy characteristics despite having progressed through preclinical studies and initial clinical trials. It is not uncommon to observe results in clinical trials that are unexpected based on preclinical studies and early clinical trials, and many product candidates fail in clinical trials despite very promising early results. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical development even after achieving promising results in earlier studies.

We do not know whether our planned clinical trials will begin on time or be completed on schedule, if at all. The commencement, data readouts and completion of clinical trials can be delayed for a number of reasons, including delays related to:

- inability to generate sufficient preclinical, toxicology, or other *in vivo* or *in vitro* data to support the initiation or continuation of clinical trials;
- Obtaining allowance or approval from regulatory authorities to commence a trial or reaching a consensus with regulatory authorities on trial design;
- the FDA, EMA or comparable foreign regulatory authorities disagreeing as to the design or implementation of our clinical trials;

- any failure or delay in reaching an agreement with CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- delays in identifying, recruiting and training suitable clinical investigators;
- obtaining approval or positive opinion from one or more institutional review boards ("IRBs"), or ethics committees at clinical trial sites;
- IRBs refusing to approve, suspending or terminating the trial at an investigational site, precluding enrollment of additional subjects, or withdrawing their approval of the trial;
- changes or amendments to the clinical trial protocol;
- clinical sites deviating from the trial protocol or dropping out of a trial;
- failure by our CROs to perform in accordance with GCP requirements or applicable regulatory rules and guidelines in other countries;
- manufacturing sufficient quantities of our product candidates, or obtaining sufficient quantities of combination therapies for use in clinical trials;
- subjects failing to enroll or remain in our trials at the rate we expect, or failing to return for post-treatment follow-up, including subjects failing to remain in our trials;
- patients choosing an alternative product for the indications for which we are developing our product candidates, or participating in competing clinical trials;
- lack of adequate funding to continue a clinical trial, or costs being greater than we anticipate;
- subjects experiencing severe or serious unexpected drug-related adverse effects;
- occurrence of serious adverse events in trials of the same class of agents conducted by other companies that could be considered similar to our product candidates;
- selection of clinical endpoints that require prolonged periods of clinical observation or extended analysis of the resulting data;
- transfer of manufacturing processes to larger-scale facilities operated by a CMO delays or failure by our CMOs or us to make any necessary changes to such manufacturing process, or failure of our CMOs to produce clinical trial materials in accordance with current Good Manufacturing Practice ("cGMP") or similar foreign requirements, regulations or other applicable requirements; and
- third parties being unwilling or unable to satisfy their contractual obligations to us in a timely manner.

In addition, disruptions caused by the COVID-19 pandemic, or any other similar pandemic, may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting or completing our planned and ongoing clinical trials.

Clinical trials must be conducted in accordance with the FDA and other applicable regulatory authorities' legal requirements, regulations and guidelines, and remain subject to oversight by these governmental agencies and ethics committees or IRBs at the medical institutions where such clinical trials are conducted. We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by a Data Safety Monitoring Board for such trial or by the FDA or comparable foreign regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory

requirements or applicable clinical trial protocols, adverse findings from inspections of clinical trial sites by the FDA, EMA or comparable foreign regulatory authorities, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. In addition, changes in regulatory requirements and policies may occur, and we may need to amend clinical trial protocols to comply with these changes. Amendments may require us to resubmit our clinical trial protocols to regulators or to IRBs for reexamination, which may impact the costs, timing or successful completion of a clinical trial.

In addition, the FDA's and other regulatory authorities' policies with respect to clinical trials may change and additional government regulations may be enacted. For instance, the regulatory landscape related to clinical trials in the EU recently evolved. The EU Clinical Trials Regulation ("CTR") which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. While the Clinical Trials Directive required a separate clinical trial application ("CTA") to be submitted in each member state in which the clinical trial takes place, to both the competent national health authority and an independent ethics committee, the CTR introduces a centralized process and only requires the submission of a single application for multi-center trials. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed. The CTR foresees a three-year transition period. The extent to which ongoing and new clinical trials will be governed by the CTR varies. Clinical trials for which an application was submitted (i) prior to January 31, 2022 under the Clinical Trials Directive, or (ii) between January 31, 2022 and January 31, 2023 and for which the sponsor has opted for the application of the Clinical Trials Directive remain governed by said Directive until January 31, 2025. After this date, all clinical trials (including those which are ongoing) will become subject to the provisions of the CTR. Compliance with the CTR requirements by us, and our third-party service providers, such as CROs, may impact our developments plans.

If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may be impacted.

It is currently unclear to what extent the U.K., will seek to align its clinical trials legislation with the EU. The U.K. regulatory framework in relation to clinical trials is derived from EU clinical trials legislation which pre-dated the CTR (as implemented into U.K. law, through secondary legislation). On January 17, 2022, the U.K. Medicines and Healthcare products Regulatory Agency ("MHRA") launched an eight-week consultation on reframing the U.K. legislation for clinical trials. The outcome of the consultation has not yet been published, but will be closely watched as it will determine whether the U.K. chooses to align with the CTR or diverge from it to maintain regulatory flexibility. A decision by the U.K. Government not to closely align its regulations with the new approach that has been adopted in the EU may have an effect on the cost of conducting clinical trials in the U.K. as opposed to other countries. If there are divergent local requirements in Great Britain from the EU in the future, this may impact clinical and development activities that occur in the U.K. in the future. Similarly, clinical trial submissions in the U.K. will not be able to be bundled with those of EU countries within the EMA Clinical Trial Information System ("CTIS"), adding further complexity, cost and potential risk to future clinical and development activity in the U.K.

Further, conducting clinical trials in foreign countries, as we may do for our product candidates, presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled subjects in foreign countries to adhere to clinical protocols as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with foreign regulatory schemes, and political and economic risks, including war, relevant to such foreign countries.

Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our product candidates.

In addition, many of the factors that cause, or lead to, the termination suspension of, or a delay in the commencement or completion of, clinical trials may also ultimately lead to the denial of regulatory approval of a product candidate. Any resulting delays to our clinical trials could shorten any period during which we may have the exclusive right to commercialize our product candidates. In such cases, our competitors may be able to bring products to market before we do, and the commercial viability of our product candidates could be significantly reduced. Any of these occurrences may harm our business, financial condition and prospects.

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

From time to time, we may publicly disclose interim, top-line, or preliminary data from our clinical trials and preclinical studies, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the interim, top-line, or preliminary results that we report may differ from future results of the same studies or trials, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Top-line and preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the topline or preliminary data we previously published. As a result, topline and preliminary data should be viewed with caution until the final data are available.

Interim data from clinical trials that we may complete are further subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between interim, top-line, or preliminary data and final data could significantly harm our business prospects. Further, disclosure of such data by us or by our competitors could result in volatility in the price of our common stock.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our Company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product candidate or our business. If the interim, top-line, or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

Our product candidates may have serious adverse, undesirable, or unacceptable side effects which may delay or prevent marketing approval or lead to the withdrawal of approval after it has been granted. If such side effects are identified during the development of these product candidates or following approval, if any, we may need to abandon our development of these product candidates, the commercial profile of any approved label may be limited, or we may be subject to other significant negative consequences following marketing approval, if any.

Undesirable side effects that may be caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials, and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA, or other foreign authorities, or, if such product candidates are approved, result in a more restrictive label and other post-approval requirements. Any treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete the trial, or could result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly. If our product candidates are associated with undesirable side effects or have unexpected characteristics in preclinical studies or clinical trials, we may need to interrupt, delay or abandon their development or limit development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective.

Results of our ongoing and future clinical trials, or results from clinical trials for other similar product candidates, could reveal a high and unacceptable severity and prevalence of adverse side effects. In such an event, development efforts of that product candidate altogether. We, our partners, the FDA, other comparable foreign regulatory authorities or an IRB may suspend clinical trials of a product candidate at any time for various reasons, including a belief that subjects in such trials are being exposed to unacceptable health risks or adverse side effects. Even if the side effects do not preclude the product candidate from obtaining or maintaining regulatory approval, undesirable side effects may inhibit market acceptance due to tolerability concerns as compared to other available therapies. Any of these developments could materially harm our business, financial condition and prospects.

Drug-related side effects could also affect patient recruitment or the ability of enrolled patients to complete a trial or result in potential product liability claims. Additionally, if any of our product candidates receives marketing approval and we or others later identify undesirable or unacceptable side effects caused by these product candidates, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw or modify approvals of any such product and require us to take it off the market;
- regulatory authorities may require the addition of labeling statements, specific warnings, a contraindication or field alerts to physicians and pharmacies;
- regulatory authorities may require a medication guide outlining the risks of such side effects for distribution to patients, or that we implement a Risk Evaluation and Mitigation Strategy (“REMS”) plan to ensure that the benefits of the product outweigh its risks;
- we may be required to change the way a product is administered, conduct additional clinical trials or change the labeling of a product;
- we may be subject to limitations on how we may promote the product;
- sales of the product may decrease significantly;
- third-party private or government payors may not offer, or may offer inadequate, reimbursement coverage for our product candidates, or reimbursement payments may be delayed or impossible to recover;
- we may be subject to litigation or product liability claims; and
- our reputation may suffer.

Any of these events could prevent us or any collaborators from achieving or maintaining market acceptance of our product candidates or could substantially increase commercialization costs and expenses, which in turn could delay or prevent us from generating significant revenue from the sale of our product candidates.

Manufacturing tests of setrusumab have shown that it may cause an opalescence appearance to the liquid antibody formulation.

Our product candidate for treating OI, setrusumab, is of the IgG2 type subclass monoclonal antibody. The IgG2 subclass is known for having a tendency to reversibly self-associate and this can cause an opalescence appearance to the liquid antibody formulation that can be mediated by protein concentration, pH and temperature. The presence of an opalescence solution does not have an impact on product potency and effectiveness and does not generally correlate with the formation of aggregates or particles. We have conducted several large-scale manufacturing runs of drug substance and drug product at third-party CMOs without observing any opalescence and we have further conducted formulation studies in order to minimize any risk of significant opalescence or of aggregate formation. We have also conducted product stability studies and excipient optimization, resulting in a change in the methodology for product reconstitution; however, there can be no assurances that this opalescence will not occur in future manufacturing runs.

We depend on enrollment of patients in our clinical trials for our product candidates. If we are unable to enroll patients in our clinical trials, or enrollment is slower than anticipated, in particular for our product candidates with rare disease indications, our research and development efforts could be adversely affected.

Successful and timely completion of clinical trials for our product candidates will require that we enroll a sufficient number of patient candidates. Trials may be subject to delays as a result of the limited number of patients with the diseases that these product candidates target, patient enrollment taking longer than anticipated or patient withdrawal. We will compete with other companies in enrolling the same limited population of patients, which may further challenge our ability to timely enroll patients in our clinical trials as there are a significant number of studies ongoing in oncology in the United States and Europe. Due to the small number of patients for any rare disease or tumor type, it may be difficult for us to enroll a sufficient number of patients in our clinical trials for our product candidates with indications in rare diseases or enrollment for these product candidates may take significantly longer than we anticipate. There are an estimated 50,000 and 60,000 persons in North America and Europe, respectively, with the genotypes that we intend to enroll in our clinical trials for AATD, the target indication for alvelestat. However, due to underdiagnosis, there are estimated to be approximately 10,000 patients diagnosed in North America. Patient enrollment depends on many factors, including:

- size and nature of the targeted patient population;
- severity of the disease or condition under investigation;
- availability and efficacy of approved therapies for the disease or condition under investigation;
- patient eligibility criteria for the trial in question as defined in the protocol;
- perceived risks and benefits of the product candidate under study;
- clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any products that may be approved for, or any product candidates under investigation for, the indications we are investigating;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment;
- proximity and availability of clinical trial sites for prospective patients;
- continued enrollment of prospective patients by clinical trial sites;
- the risk that patients enrolled in clinical trials will drop out of such trials before completion; and
- delays or difficulties in enrollment and completion of studies due to the COVID-19 pandemic or any other similar pandemic.

These factors may make it difficult for us to enroll enough patients to complete our clinical trials in a timely and cost-effective manner. For example, we experienced significant delays in recruitment for our Phase 2 alvelestat trial in individuals with severe alpha-1 antitrypsin deficiency-related lung disease, who are at greater risk from COVID-19 given that the condition is a respiratory and lung condition. Due to the effects of the COVID-19 pandemic on this vulnerable population and the impact on enrollment timelines, we closed the study to enrollment at 99 patients at the end of 2021. This was lower than the protocol defined number of patients in the original study design. We also rely on, and will continue to rely on, CROs and clinical trial sites to ensure proper and timely conduct of our clinical trials and preclinical studies. Though we have entered into agreements governing their services, we will have limited influence over their actual performance. Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates and jeopardize our ability to obtain regulatory approval for the sale of our product candidates. Furthermore, even if we are able to enroll a sufficient number of patients for our clinical trials, we may have difficulty maintaining enrollment of such patients in our clinical trials.

We may become exposed to costly and damaging liability claims, either when testing our product candidates in the clinic or at the commercial stage, and our product liability insurance may not cover all damages from such claims.

We are exposed to potential product liability and professional indemnity risks that are inherent in the development, manufacturing, marketing, and use of pharmaceutical product candidates. Currently, we have no product candidates that have been approved for commercial sale; however, the current and future use of our product candidates by us and any collaborators, in clinical trials, and the sale of these product candidates, if approved, in the future, may expose us to liability claims. These claims might be made by patients that use the product, healthcare providers, pharmaceutical companies, our collaborators, or others selling these product candidates. Any claims against us, regardless of their merit, could be difficult and costly to defend and could adversely affect the market for our product candidates or any prospects for commercialization of our product candidates. In addition, regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our product candidates;

- injury to our reputation;
- withdrawal of clinical trial participants;
- costs to defend related litigation;
- diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- regulatory investigation, product recalls or withdrawals, or labeling, marketing or promotional restrictions;
- loss of revenue; and
- the inability to commercialize, co-commercialize or promote our product candidates.

Although the clinical trial process is designed to identify and assess potential side effects, it is always possible that a drug, even after regulatory approval, may exhibit unforeseen side effects. If our product candidates were to cause adverse side effects during clinical trials or after approval, we may be exposed to substantial liabilities. Physicians and patients may not comply with any warnings that identify known potential adverse effects and patients who should not use our product candidates.

Although we maintain product liability insurance for our product candidates, it is possible that our liabilities could exceed our insurance coverage. We intend to expand our coverage to include the sale of commercial product candidates if we obtain marketing approval for any of our product candidates. However, we may not be able to maintain insurance coverage at a reasonable cost or obtain insurance coverage that will be adequate to satisfy any liability that may arise. If a successful product liability claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, our assets may not be sufficient to cover such claims and our business operations could be impaired.

The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our product candidates, our business will be substantially harmed.

The clinical development, manufacturing, labeling, storage, record-keeping, advertising, promotion, import, export, marketing and distribution of our product candidates are subject to extensive regulation by the FDA in the U.S. and by comparable foreign regulatory authorities in foreign markets, such as the EMA. In the U.S., we are not permitted to market our product candidates in the U.S. until we receive regulatory approval of a BLA or NDA from the FDA. The process of obtaining such regulatory approval is expensive, often takes many years following the commencement of clinical trials and can vary substantially based upon the type, complexity and novelty of the product candidates involved, as well as the target indications and patient population. Approval policies or regulations may change, and the FDA, EMA and comparable foreign regulatory authorities have substantial discretion in the approval process, including the ability to delay, limit or deny approval of a product candidate for many reasons. Despite the time and expense invested in clinical development of product candidates, regulatory approval of a product candidate is never guaranteed. Of the large number of drugs in development, only a small percentage successfully complete the FDA or foreign regulatory approval processes and are commercialized.

Prior to obtaining approval to commercialize a product candidate in the U.S. or abroad, we must demonstrate with substantial evidence from adequate and well-controlled clinical trials, and to the satisfaction of the FDA or comparable foreign regulatory authorities, that such product candidates are safe and effective for their intended uses, and in the case of biological products, that such product candidates are safe, pure and potent. Results from nonclinical studies and clinical trials can be interpreted in different ways. Even if we believe available nonclinical or clinical data support the safety purity, potency, or efficacy, of our product candidates, such data may not be sufficient to obtain approval from the FDA and comparable foreign regulatory authorities. The FDA, EMA or comparable foreign regulatory authorities, as the case may be, may also require us to conduct additional preclinical studies or clinical trials for our product candidates either prior to or post-approval, or may object to elements of our clinical development program.

The FDA, EMA or comparable foreign regulatory authorities can delay, limit or deny approval of a product candidate for many reasons, including:

- such authorities may disagree with the design or execution of our clinical trials;
- negative or ambiguous results from our clinical trials or results may not meet the level of statistical significance required by the FDA, EMA or comparable foreign regulatory agencies for approval;
- serious and unexpected drug-related side effects may be experienced by participants in our clinical trials or by individuals using drugs similar to our product candidates;
- the population studied in the clinical trial may not be sufficiently broad or representative to assure safety in the full population for which we seek approval;
- such authorities may not accept clinical data from trials that are conducted at clinical facilities or in countries where the standard of care is potentially different from that of their own country;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- such authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- such authorities may not agree that the data collected from clinical trials of our product candidates are acceptable or sufficient to support the submission of a BLA, NDA, MAA or other submission or to obtain regulatory approval in the U.S. or elsewhere, and such authorities may impose requirements for additional preclinical studies or clinical trials;
- such authorities may disagree with us regarding the formulation, labeling and/or the product specifications of our product candidates;
- approval may be granted only for indications that are significantly more limited than those sought by us, and/or may include significant restrictions on distribution and use;
- such authorities may find deficiencies in the manufacturing processes or facilities of the third-party manufacturers with which we contract for clinical and commercial supplies; or
- such authorities may not accept a submission due to, among other reasons, the content or formatting of the submission.

With respect to foreign markets, approval procedures vary among countries and, in addition to the foregoing risks, may involve additional product testing, administrative review periods and agreements with pricing authorities.

Even if we eventually complete clinical trials and receive approval of a BLA, NDA, MAA or comparable marketing application for our product candidates, the FDA or a comparable regulatory authority may grant approval contingent on the performance of costly additional clinical trials and/or the implementation of a REMS, which may be required because the FDA believes it is necessary to ensure safe use of the product after approval. Any delay in obtaining, or inability to obtain, applicable regulatory approval would delay or prevent commercialization of that product candidate and would materially adversely impact our business and prospects.

In addition, FDA and foreign regulatory authorities may change their approval policies and new regulations may be enacted. For instance, the EU pharmaceutical legislation is currently undergoing a complete review process, in the context of the Pharmaceutical Strategy for Europe initiative, launched by the European Commission in November 2020. The European Commission's proposal for revision of several legislative instruments related to medicinal products (potentially revising the duration of regulatory exclusivity, eligibility for expedited pathways, etc.) is currently expected during the first half of 2023. The proposed revisions, once they are agreed and adopted by the European Parliament and European Council (not expected before the end of 2024 or early 2025) may have a significant impact on the biopharmaceutical industry in the long term.

We may attempt to secure approval from the FDA or comparable foreign regulatory authorities through the use of accelerated approval pathways. If we are unable to obtain such approval, we may be required to conduct additional preclinical studies or clinical trials beyond those that we contemplate, which could increase the expense of obtaining, and delay the receipt of, necessary marketing approvals. Even if we receive accelerated approval from the FDA, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous post-marketing requirements, the FDA may seek to withdraw any accelerated approval we have obtained.

We may in the future seek accelerated approval for our one or more of our product candidates. Under the accelerated approval program, the FDA may grant accelerated approval to a product candidate designed to treat a serious or life-threatening condition that provides meaningful therapeutic benefit over available therapies upon a determination that the product candidate has an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease, such as irreversible morbidity or mortality. For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit.

The accelerated approval pathway may be used in cases in which the advantage of a new drug over available therapy may not be a direct therapeutic advantage, but is a clinically important improvement from a patient and public health perspective. If granted, accelerated approval is usually contingent on the sponsor's agreement to conduct, in a diligent manner, additional confirmatory studies to verity and describe the drug's clinical benefit. If such post-approval studies fail to confirm the drug's clinical benefit or are not completed in a timely manner, the FDA may withdraw its approval of the drug on an expedited basis. In addition, in December 2022, President Biden signed an omnibus appropriations bill to fund the U.S. government through fiscal year 2023. Included in the omnibus bill is the Food and Drug Omnibus Reform Act of 2022, which among other things, introduced reforms intended to expand the FDA's ability to regulate products receiving accelerated approval, including by increasing the FDA's oversight over the conduct of confirmatory trials; however, the ultimate impact of these reforms remains unclear.

Prior to seeking accelerated approval for any of our product candidates, we intend to seek feedback from the FDA and will otherwise evaluate our ability to seek and receive accelerated approval. There can be no assurance that after our evaluation of the feedback and other factors we will decide to pursue or submit an NDA or BLA for accelerated approval or any other form of expedited development, review or approval. Furthermore, if we decide to submit an application for accelerated approval for our product candidates, there can be no assurance that such application will be accepted or that any expedited development, review or approval will be granted on a timely basis, or at all. The FDA or other comparable foreign regulatory authorities could also require us to conduct further studies prior to considering our application or granting approval of any type. A failure to obtain accelerated approval or any other form of expedited development, review or approval for our product candidate would result in a longer time period to commercialization of such product candidate, if any, could increase the cost of development of such product candidate and could harm our competitive position in the marketplace.

Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire, retain or deploy key leadership and other personnel, prevent new or modified products from being developed, review, approved or commercialized in a timely manner or at all, which could negatively impact our business.

The ability of the FDA and foreign regulatory authorities to review and approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, the FDA's or foreign regulatory authorities' ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's or foreign regulatory authorities' ability to perform routine functions. Average review times at the FDA and foreign regulatory authorities have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies, such as the EMA following its relocation to Amsterdam and resulting staff changes, may also slow the time necessary for new drugs, and biologics or modifications to approved drugs and biologics to

be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities.

Separately, in response to the global COVID-19 pandemic, the FDA postponed most inspections of domestic and foreign manufacturing facilities at various points. Even though the FDA has since resumed standard inspection operations of domestic facilities where feasible, the FDA has continued to monitor and implement changes to its inspectional activities to ensure the safety of its employees and those of the firms it regulates as it adapts to the evolving COVID-19 pandemic, and any resurgence of the virus or emergence of new variants may lead to further inspectional delays. Regulatory authorities outside the United States have adopted similar policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Even if any of our product candidates obtains regulatory approval, we will be subject to ongoing obligations and continued regulatory review, which may result in significant additional expense. Additionally, any of our product candidates, if approved, could be subject to labeling and other restrictions and market withdrawal and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with such product.

If the FDA or a comparable foreign regulatory authority approves any of our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, and recordkeeping for such product will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, facility registration, and drug listing, as well as continued compliance with cGMP or similar foreign requirements for manufacturing, good distribution practice, requirements for product distribution, and GCP requirements for any clinical trials that we conduct post-approval, all of which may result in significant expense and limit our ability to commercialize, or co-commercialize, a product. We and our contract manufacturers will also be subject to user fees and periodic inspection by the FDA, and other comparable foreign regulatory authorities to monitor compliance with these requirements and the terms of any product approval we may obtain. In addition, any regulatory approvals that we receive for a product may also be subject to limitations on the approved indicated uses for which such product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of such product.

If there are changes in the application of legislation or regulatory policies, or if problems are discovered with a product or the manufacture of a product, or if we or one of our distributors, licensees, or co-marketers fails to comply with regulatory requirements, the regulatory authorities could take various actions. These include if we or a regulatory agency discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facilities where the product is manufactured, a regulatory agency may impose restrictions on that product, the manufacturing facility or us, including requiring recall or withdrawal of the product from the market or suspension of manufacturing. In addition, failure to comply with FDA and other comparable foreign regulatory requirements may subject our company to administrative or judicially imposed sanctions, including:

- restrictions on the marketing or manufacturing of our products, withdrawal of the product from the market or voluntary or mandatory product recalls;
- restrictions on product distribution or use, or requirements to conduct post-marketing studies or clinical trials;
- fines, restitutions, disgorgement of profits or revenues, warning letters, untitled letters or holds on clinical trials;
- refusal by the FDA or comparable foreign regulatory authority to approve pending applications or supplements to approved applications submitted by us or suspension or revocation of approvals;
- product seizure or detention, or refusal to permit the import or export of our products; and
- injunctions or the imposition of civil or criminal penalties.

The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and generate revenue and could require us to expend significant time and resources in response and could generate negative publicity.

The policies of the FDA, the EMA, and other regulatory authorities may change and additional government regulations may be enacted that could prevent, limit, or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature, or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States, the U.K., EU, or other jurisdictions. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may be subject to enforcement action and we may not achieve or sustain profitability.

Even if we obtain marketing approval of any of our product candidates in a major pharmaceutical market such as the United States or the EU, we may not be able to obtain approval or commercialize that product in other markets, which would limit our ability to realize our full market potential.

In order to market any product candidates in a country or territory, we must establish and comply with numerous and varying regulatory requirements of such country or territory regarding safety and efficacy. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval procedures vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking regulatory approvals in multiple markets may require additional pre-clinical studies or clinical trials, which would be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our product candidates in those countries. Satisfying these and other regulatory requirements is costly, time consuming, uncertain, and may be subject to unanticipated delays. In addition, our failure to obtain regulatory approval in any country may delay or have negative effects on the process for regulatory approval in other countries. We currently do not have any product candidates approved for sale in the United States, the EU, the U.K. or any other markets, and our management team does not have experience in obtaining regulatory approval in markets outside of the United States, the EU and the U.K. If we seek regulatory approval in other markets and fail to obtain marketing approval in those markets or, if our product candidates are approved in such markets but we fail to maintain such approvals, our ability to realize the full market potential of our product candidates will be compromised.

Our employees and independent contractors, including principal investigators, CROs, CMOs, consultants, vendors, and any other third parties we may engage in connection with the development and commercialization of our product candidates may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could adversely affect our business.

Misconduct by our employees and independent contractors, including principal investigators, CROs, CMOs, consultants, vendors, and any other third parties we may engage in connection with the development and commercialization of our product candidates, could include intentional, reckless, or negligent conduct or unauthorized activities that violate: (i) the laws and regulations of the FDA and other similar regulatory authorities, including those laws that require the reporting of true, complete and accurate information to such authorities; (ii) manufacturing standards; (iii) data privacy, security, fraud and abuse, and other healthcare laws and regulations; or (iv) laws that require the reporting of true, complete, and accurate financial information and data. Specifically, sales, marketing, and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing, and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs, and other business arrangements. Activities subject to these laws could also involve the improper use or misrepresentation of information obtained in the course of clinical trials, creation of fraudulent data in pre-clinical studies or clinical trials, or illegal misappropriation of drug product, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with such laws or regulations. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant civil, criminal and administrative penalties, damages,

monetary fines, disgorgements, possible exclusion from participation in Medicare, Medicaid, other U.S. federal healthcare programs or healthcare programs in other jurisdictions, individual imprisonment, other sanctions, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations. We are also subject to the data privacy regime in the EU and U.K., which imposes obligations and restrictions on the collection and use of personal data relating to individuals located in the EU and U.K., respectively, and includes the EU and U.K. General Data Protection Regulation (the "GDPR") and, in the EU, any national laws implementing or supplementing the GDPR. If we do not comply with our obligations under these privacy regimes, we could be exposed to significant fines and may be the subject of litigation and/or adverse publicity, which could have a material adverse effect on our reputation and business.

Risks Related to Healthcare Laws and Other Legal Compliance Matters

Enacted and future healthcare legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and may affect the prices we may set.

In the United States, EU, the U.K. and other jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes and proposed changes to the healthcare system that could affect our future results of operations. In particular, there have been and continue to be a number of initiatives at the U.S. federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (as so amended, the "ACA") was enacted, which substantially changed the way healthcare is financed by both governmental and private insurers. Among the provisions of the ACA, those of greatest importance to the pharmaceutical and biotechnology industries include the following:

- an annual, non-deductible fee payable by any entity that manufactures or imports certain branded prescription drugs and biologic agents (other than those designated as orphan drugs), which is apportioned among these entities according to their market share in certain government healthcare programs;
- a Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13.0% of the average manufacturer price of branded and generic drugs, respectively;
- a methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs and biologics, including our product candidates, that are inhaled, infused, instilled, implanted, or injected;
- extension of a manufacturer's Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- a Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- establishment of a Center for Medicare and Medicaid Innovation at the Centers for Medicare & Medicaid Services ("CMS"), to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending;
- expansion of the entities eligible for discounts under the Public Health Service program; and
- a licensure framework for follow on biologic product candidates.

Since its enactment, there have been judicial, executive and congressional challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. In addition, other legislative changes have been proposed and adopted since the ACA was enacted. For example, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, beginning January 1, 2024.

Moreover, heightened governmental scrutiny is likely to continue over the manner in which manufacturers set prices for their marketed products, which has resulted in several recent U.S. Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. On August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was into law. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023), and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the Department of Health and Human Services to implement many of these provisions through guidance, as opposed to regulation, for the initial years. For that and other reasons, it is currently unclear how the IRA will be effectuated. We expect that additional U.S. federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U.S. federal government will pay for healthcare product candidates and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Legally-mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, results of operations, financial condition, and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical product candidates and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our product candidates or put pressure on our product pricing.

In the EU, similar political, economic and regulatory developments may affect our ability to profitably commercialize, or co-commercialize, our product candidates, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the EU, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of product candidates in that context. In general, however, the healthcare budgetary constraints in most EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever- increasing EU and national regulatory burdens on those wishing to develop and market product candidates, this could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to commercialize, or co-commercialize, our product candidates, if approved.

On December 13, 2021, EU Regulation No 2021/2282 on Health Technology Assessment (“HTA”) amending Directive 2011/24/EU, was adopted. While the Regulation entered into force in January 2022, it will only begin to apply from January 2025 onwards, with preparatory and implementation-related steps to take place in the interim. Once the Regulation becomes applicable, it will have a phased implementation depending on the concerned products: oncology and advanced therapy medicinal products (“ATMPs”) as of 2025, orphan medicinal products as of 2028 and 2030 for all other medicinal products. This Regulation intends to boost cooperation among EU member states in assessing health technologies, including new medicinal products, and providing the basis for cooperation at the EU level for joint clinical assessments in these areas, using methodologies adapted to the specificities of the type of product in question. The Regulation will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the most potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU 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.

In markets outside of the United States, the EU and the U.K., reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific product candidates and therapies.

We cannot predict the likelihood, nature, or extent of government regulation that may arise from future legislation or administrative action in the United States, the EU, the U.K., or any other jurisdiction. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, our product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.

There have been, and likely will continue to be, additional legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. Such reforms could have an adverse effect on anticipated revenues from product candidates that we may successfully develop and for which we may obtain marketing approval and may affect our overall financial condition and ability to develop product candidates.

Our business operations and current and future relationships with investigators, healthcare professionals, consultants, third-party payors, patient organizations, and customers will be subject to applicable healthcare regulatory laws, which could expose us to penalties.

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations, and customers, may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell, and distribute our product candidates, if approved. Such laws include:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving, or providing any remuneration (including any kickback, bribe, or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order, or recommendation of, any good, facility, item, or service, for which payment may be made, in whole or in part, under U.S. federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. The U.S. federal Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers, and formulary managers on the other hand;
- the U.S. federal false claims laws, including the civil False Claims Act (“FCA”) which, among other things, impose criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the U.S. federal government, claims for payment or approval that are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the FCA. As a result of a modification made by the Fraud Enforcement and Recovery Act of 2009, a claim includes “any request or demand” for money or property presented to the federal government. In addition, manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to “cause” the submission of false or fraudulent claims;
- the U.S. federal Health Insurance Portability and Accountability Act of 1996 (“HIPAA”), which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services; similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- the U.S. federal legislation commonly referred to as the "Physician Payments Sunshine Act," enacted as part of the ACA, and its implementing regulations, which requires certain manufacturers of drugs, devices, biologics, and medical supplies that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program to report annually to the government information related to certain payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain other non-physician practitioners (physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists, anesthesiology assistants and certified nurse midwives), and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members;
- analogous U.S. state laws and regulations, including: state anti-kickback and false claims laws, which may apply to our business practices, including but not limited to, research, distribution, sales, and marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities; and
- similar healthcare laws and regulations in the EU, the U.K. and other jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available under such laws, it is possible that some of our business activities could be subject to challenge under one or more of such laws. The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Ensuring that our current and future internal operations and business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations.

If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to the imposition of civil, criminal and administrative penalties, damages, disgorgement, monetary fines, possible exclusion from participation in government funded healthcare programs (including Medicare, Medicaid and other federal healthcare programs in the United States), individual imprisonment, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements and/or oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, and curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. If any of the physicians or other providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and imprisonment, which could affect our ability to operate our business. Further, defending against any such actions can be costly, time-consuming and may require significant personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired.

We are subject to governmental regulation and other legal obligations related to privacy, data protection and data security. Our actual or perceived failure to comply with such obligations could harm our business.

The global data protection landscape is rapidly evolving, and we are or may become subject to numerous state, federal and foreign laws, requirements and regulations governing the collection, use, disclosure, retention, and security of personal information, such as information that we may collect in connection with clinical trials in the U.S. and abroad. Implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, and we cannot yet determine the impact future laws, regulations, standards, or perception of their requirements may have on our business. This evolution may create uncertainty in our business, affect our ability to operate in certain jurisdictions or to collect, store, transfer use and share personal information, necessitate the acceptance of more onerous obligations in our contracts, result in liability or impose additional costs on us. The cost of compliance with these laws, regulations and standards is high and is likely to increase in the future. Any failure or perceived failure by us to comply with federal, state or foreign laws or regulations, our internal policies and procedures or our contracts governing our processing of personal information could result in negative publicity, government investigations and enforcement actions, claims by third parties and damage to our reputation, any of which could have a material adverse effect on our business, results of operation, and financial condition.

Our operations abroad may also be subject to increased scrutiny or attention from data protection authorities. For example, we are subject to diverse laws and regulations relating to data privacy and security in the EU, and the U.K. including the GDPR and the GDPR, as implemented into U.K. law (the "UK GDPR"). New global privacy rules are being enacted and existing ones are being updated and strengthened. We are likely to be required to expend capital and other resources to ensure ongoing compliance with these laws and regulations.

The GDPR and UK GDPR implement stringent operational requirements for controllers and processors of personal data, including comprehensive data privacy compliance obligations in relation to our collection, processing, sharing, disclosure, transfer and other use of personal data, including a principal of accountability and the obligation to demonstrate compliance through policies, procedures, training and audit. In addition, some of the personal data we process in respect of clinical trial participants is considered special category or sensitive personal data under the GDPR and UK GDPR, and subject to additional compliance obligations. We may be subject to diverging requirements under EU member state laws and UK law, such as whether consent can be used as the legal basis for processing of clinical trial data and the roles, responsibilities and liabilities as between CROs and sponsors. As these laws develop, we may need to make operational changes to adapt to these diverging rules, which could increase our costs and adversely affect our business. There is also potential exposure under the UK's emerging civil tort for misuse of private information, which is distinct from breach of confidence. Complying with these numerous, complex and often changing regulations is expensive and difficult. Failure by us, or our partners or service providers, to comply with the GDPR or UK GDPR could result in regulatory investigations, enforcement notices and/or fines of up to the higher of €20 million or £17.5 million or up to 4% of our total worldwide annual turnover. In addition to the foregoing, any breach of privacy laws or data security laws, particularly those resulting in any security incident or breach involving the misappropriation, loss or other unauthorized use or disclosure of sensitive or confidential patient or consumer information, could have a material adverse effect on our business, reputation and financial condition. We may also face civil claims seeking compensation for both material and immaterial harms arising from a GDPR or UK GDPR violation.

The GDPR and UK GDPR also regulate cross-border transfers of personal data out of the EEA and the U.K. Recent legal developments in Europe have created complexity and uncertainty regarding such transfers, in particular in relation to transfers to the United States. On July 16, 2020, the Court of Justice of the European Union ("CJEU") invalidated the EU-US Privacy Shield Framework, or Privacy Shield, under which personal information could be transferred from the EEA (and the U.K.) to relevant self-certified U.S. entities. The CJEU further noted that reliance on the standard contractual clauses (a standard form of contract approved by the European Commission as an adequate personal data transfer mechanism and potential alternative to the Privacy Shield) alone may not necessarily be sufficient in all circumstances and that transfers must be assessed on a case-by-case basis. European court and regulatory decisions subsequent to the CJEU decision of July 16, 2020 have taken a restrictive approach to international data transfers. As the enforcement landscape further develops, and supervisory authorities issue further guidance on international data transfers, we could incur additional costs, complaints and/or regulatory investigations or fines; we may have to stop using certain tools and vendors and make other operational changes.

As a data controller, we are accountable for any third-party data service providers we engage to process personal data on our behalf. We attempt to address the associated risks by performing security assessments, detailed due diligence and regularly performing privacy and security reviews of our vendors and requiring all such third-party providers with data access to sign agreements, including business associate agreements, and where required under EU or U.K. law, obligating them to only process data according to our instructions and to take sufficient security measures to protect such data. There is no assurance that these contractual measures and our own privacy and security-related safeguards will protect us from the risks associated with the third-party processing, storage and transmission of such information. Any violation of data or security laws by our third-party processors could have a material adverse effect on our business and result in the fines and penalties outlined above.

We are also subject to European privacy laws regulating electronic marketing and cookies (and related technologies), which are strictly enforced by regulators and can engender fines, claims and reputation damage in cases where those laws are infringed.

Further, in the United States, numerous state and federal laws, regulations, standards and other legal obligations, including consumer protection laws and regulations, which govern the collection, dissemination, use, access to, confidentiality, security and processing of personal information, including health-related information, could apply to our operations or the operations of our partners. In addition, we may obtain health information from third parties (including research institutions from which we obtain clinical trial data) that are subject to privacy and security requirements under HIPAA. Depending on the facts and circumstances, we could be subject to significant penalties if we violate HIPAA.

Certain states have also adopted data privacy and security laws and regulations that govern the privacy, processing and protection of health-related and other personal information. Such laws and regulations will be subject to interpretation by various courts and other governmental authorities, thus creating potentially complex compliance issues for us and our future customers and strategic partners. For example, the California Consumer Privacy Act of 2018 (CCPA) went into effect on January 1, 2020. The CCPA creates individual privacy rights for California consumers and increases the privacy and security obligations of entities handling certain personal information. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that has increased the likelihood of, and risks associated with data breach litigation. Further, the California Privacy Rights Act (CPRA) generally went into effect on January 1, 2023, and significantly amends the CCPA. It imposes additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It also creates a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. Additional compliance investment and potential business process changes may also be required. Similar laws have passed in Virginia, Colorado, Connecticut and Utah, and have been proposed in other states and at the federal level, reflecting a trend toward more stringent privacy legislation in the United States. The enactment of such laws could have potentially conflicting requirements that would make compliance challenging. In the event that we are subject to or affected by HIPAA, the CCPA, the CPRA or other domestic privacy and data protection laws, any liability from failure to comply with the requirements of these laws could adversely affect our financial condition.

Due to our international operations, we are subject to anti-corruption laws, as well as export control laws, customs laws, sanctions laws and other laws governing our operations. If we fail to comply with these laws, we could be subject to civil or criminal penalties, other remedial measures and legal expenses.

Our operations are subject to anti-corruption laws, including the U.K. Bribery Act 2010 (the “Bribery Act”); the U.S. Foreign Corrupt Practices Act (the “FCPA”); and other anti-corruption laws that apply in countries where we do business and may do business in the future. The Bribery Act, the FCPA, and these other laws generally prohibit us, our officers and our employees and intermediaries from bribing, being bribed by, or providing prohibited payments or anything else of value to government officials or other persons to obtain or retain business or gain some other business advantage. We may in the future operate in jurisdictions that pose a high risk of potential Bribery Act or FCPA violations, and we may participate in collaborations and relationships with third parties whose actions could potentially subject us to liability under the Bribery Act, the FCPA, or local anti- corruption laws. In addition, we cannot predict the nature, scope, or effect of future regulatory requirements to which any of our international operations might be subject or the manner in which existing laws might be administered or interpreted.

We are also subject to other laws and regulations governing any international operations, such as applicable export controls, embargoes, economic, financial and trade sanctions laws and regulations, including those administered and enforced by the United Kingdom, the United States and the European Union (and its Member States), (collectively, the “Trade Controls”). These Trade Controls prohibit or restrict dealings relating to certain countries, regions or persons.

Compliance with Trade Controls, which are subject to frequent changes, may delay or hinder our business operations (particularly in respect of cross-border business), and, in some cases, prevent certain of our business operations altogether. It is difficult for us to predict how Trade Controls will change in the future and the impact they may have on our business. For example, as stated above, a result of Russia’s invasion of Ukraine, Trade Controls relating to Russia have been significantly expanded.

There is no assurance that we will be completely effective in ensuring our compliance with all applicable anti-corruption laws, including the Bribery Act, the FCPA, or other legal requirements, including Trade Control Laws. If we are not in compliance with the Bribery Act, the FCPA, and other anti-corruption laws or Trade Control Laws, we may be subject to criminal and civil penalties, disgorgement, and other sanctions and remedial measures and legal expenses. Any investigation of any potential violations of the Bribery Act, the FCPA, other anti-corruption laws, or Trade Control Laws by U.K., U.S., or other authorities, even if it is ultimately determined that we did not violate such laws, could be costly and time-consuming, require significant personnel resources, and harm our reputation.

We will seek to build and continuously improve our systems of internal controls and to remedy any weaknesses identified. There can be no assurance, however, that the policies and procedures will be followed at all times or effectively detect and prevent violations of the applicable laws by one or more of our employees, consultants, agents, collaborators or other person who performs services on our behalf and, as a result, we could be subject to fines, penalties, or prosecution.

Risks Related to Commercialization

We operate in a highly competitive and rapidly changing industry, which may result in others acquiring, developing, or commercializing competing product candidates before or more successfully than we or our partners do.

The biopharmaceutical and pharmaceutical industries are highly competitive and subject to significant and rapid technological change. Our success is highly dependent on our ability to acquire, develop, and obtain marketing approval for new product candidates on a cost-effective basis and to market them successfully. If etigilimab, alvelestat, setrusumab, acumapimod or leflutrozole is approved, we will face intense competition from a variety of businesses, including large, fully integrated pharmaceutical and biopharmaceutical companies in the United States, Europe, and other jurisdictions. These organizations may have significantly greater resources than we have and conduct similar research; seek patent protection; and establish collaborative arrangements for research, development, manufacturing, and marketing of product candidates that may compete with our product candidates.

We expect to face competition for each of our current product candidates, including specifically:

- We consider setrusumab's current closest potential competitors in development for the treatment of OI to be Amgen and UCB's anti-sclerostin antibody, romosozumab (Evenity), which was approved for osteoporosis in the United States in April 2019 and in December 2019 in Europe for osteoporosis. In December 2019, the European Commission approved the MAA for romosozumab can delete sentence as consolidated above (Evenity) for osteoporosis. Romosozumab is also in a Phase 1 trial in OI in Europe, investigating at the pharmacokinetics and pharmacodynamics of romosozumab in OI. In addition, Jiangsu Hengrui has commenced Phase 1 development of an anti-sclerostin antibody for osteoporosis in China, and Transcenta Holding has licensed the Chinese rights to the anti-sclerostin antibody blosozumab from Eli Lilly and Company ("Lilly") and plans to develop it for osteoporosis. Baylor College of Medicine has conducted a Phase 1 open label trial of fresolimumab, a TGF-B inhibitor, in adult OI patients, and Sanofi is conducting a Phase 1 trial of SAR439459, a related TGF-B inhibitor, in adult OI patients. Amgen has also conducted two studies of denosumab (Prolia) an anti-resorptive agent in pediatric patients with OI, however, both studies were terminated.
- We consider alvelestat's current closest potential competitors for the treatment of severe AATD to be alpha1-proteinase inhibitors that are administered intravenously in AAT augmentation therapy. Currently, there are four inhibitors on the market in the United States and the EU: Prolastin-C from Grifols, S.A. ("Grifols"), Aralast from Shire plc, now a subsidiary of Takeda Pharmaceutical Company Ltd ("Shire"), Zemaira from CSL Limited ("CSL"), and Glassia from Kamada Ltd. ("Kamada"). Kamada is also developing an inhaled version of augmentation therapy which is in Phase 3, and has a recombinant alpha-1 antitrypsin in early development. InhibRx, Inc. ("InhibRx") has completed a Phase 1 trial of INBRX-101, a recombinant human alpha-1 antitrypsin Fc fusion protein (rhAAT-Fc) for replacement therapy, and plans to initiate a potential registration study for potential accelerated approval in the second half of 2023. Apic Bio, Inc. ("Apic Bio") is in the early stages of developing a dual function vector (df-AAV) gene-therapy approach for AATD silencing the mutant Z-AAT protein and augmenting wildtype M-AAT production. Wave Life Sciences is in early stages of development of RNA base-editing oligonucleotide (WVE-0006) to restore wild-type protein in lung and liver disease, a program that has been recently partnered with GSK. Intellia Therapeutics, Inc. is in early stages of developing CRISPR/Cas9 -based insertion of normal SERPINA1 gene, targeting lung disease (NTLA-3001). Peak Bio acquired an oral NE inhibitor, PHP-303 from Ph Pharma in March 2022. Peak Bio plans to conduct a Phase 2 proof-of-concept clinical trial in patients with severe AATD with trial initiation, potentially, in 2023 once they have received the necessary funding. Vertex Pharmaceuticals Inc. ("Vertex") has a small molecule corrector program for AATD in a Phase 1 trial focused on the liver disease, following Phase 2 trials with two other molecules with the same mechanism of action that were discontinued due to toxicity and efficacy. Centessa (previously Z-factor) was previously in a Phase 1trial with ZF874 protein folding corrector for Z-AATD but this has been terminated. Biomarin Pharmaceutical, Inc. is in early stages of development of a small molecule corrector (BMN 349).

- There are no therapies with regulatory approval for Bronchiolitis Obliterans Syndrome (“BOS”) following SCT or lung transplant. We consider alvelestat’s closest potential competitors to be the Janus Kinase (JAK1) inhibitor, itacitinib, and JAK2 inhibitor, ruxolitinib, (Incyte Corporation) in Phase 1/Phase2 studies in lung transplant-associated and SCT-associated BOS, respectively; AI Therapeutics inhaled formulation of sirolimus (LAM-001) in Phase 1 for BOS in lung transplant; Isopogen allogeneic bone marrow derived Mesenchymal Stem Cells for Chronic Lung Allograft Dysfuntion (CLAD) in Phase 1 (NCT02709343); and liposomal inhaled cyclosporin-A (Zambon) in Phase 2 in BOS following SCT and in Phase 3 global pivotal trials in BOS associated with lung transplant. In other disease indications, we consider alvelestat’s closest potential competitors to be Santhera Pharmaceuticals (“Santhera”) which has in-licensed the inhaled NE inhibitor POL6014 and has completed a multiple ascending dose study, in the initial indication of CF; and CHF-6333 is an inhaled human NE inhibitor that has completed a Phase 1 trial by Chiesi Farmaceutici S.p.A. (“Chiesi”) for the treatment of non-cystic fibrosis bronchiectasis and CF.
- We consider etigilimab’s current closest potential competitors to include other anti-TIGIT agents being developed by companies including Roche, Merck, iTeos and GSK, Beigene/Novartis, Seattle Genetics, Inc., Arcus/Gilead and Compugen amongst others. In addition, there are other combinations of existing cancer therapies available commercially for example, Yervoy and Opdivo and Opidivo or Keytruda in combination with chemotherapy agents. There are a number of bispecific antibodies with an anti-TIGIT arm in development including a Phase 3 program in NSCLC being developed by AstraZeneca. There are also a number of other agents in development to other immuno-oncology targets that could compete with an anti-TIGIT approach, for example anti-LAG3.
- For acumapimod, although we are not aware of any approved therapies for the treatment of AECOPD, there are a wide range of established therapies available for COPD as well as a number of product candidates in development, with Verona Pharma plc (“Verona Pharma”), GlaxoSmithKline plc. (“GlaxoSmithKline” or “GSK”), and AstraZeneca each conducting Phase 2 trials on drugs for the treatment of COPD. In addition, Pulmatrix, Inc. (“Pulmatrix”) has PUR1800, a narrow-spectrum kinase inhibitor (NSKI) that completed a Phase 1b trial in COPD. We consider acumapimod’s current closest potential competitor in development for the treatment of AECOPD to be Verona Pharma’s nebulized and inhaled ensifentrine (RPL554), a PDE3 / PDE4 dual inhibitor that is currently being developed as a bronchodilator and anti-inflammatory agent for COPD, Asthma and Cystic Fibrosis patients. In August 2022, Verona announced positive results (FEV1 and AECOPD exacerbation frequency) from two Phase 3 trials (ENHANCE-1 and ENHANCE-2) in COPD.
- We consider leflutrozole’s current closest potential competitors for the treatment of male infertility due to HH are Follicle Stimulating Hormone (FSH), injectable recombinant follitropin alpha (Gonal-F, Serono) which is FDA approved for male infertility. Injectable Human Chorionic Gonadotropin (HCG) is not approved for male infertility, but is used ‘off-label.’ AZD-5904 (myeloperoxidase inhibitor) from the AstraZeneca and St George Street Capital collaboration is in a Phase 1b trial for idiopathic male infertility.

We also anticipate that new companies will enter these markets in the future. If we, or our partners, successfully develop and commercialize any of setrusumab, alvelestat, etigilimab, acumapimod or leflutrozole, they will compete with existing therapies and new therapies that may become available in the future. The highly competitive nature of and rapid technological changes in the biopharmaceutical and pharmaceutical industries could render our product candidates obsolete, less competitive, or uneconomical. Our competitors may, among other things:

- have significantly greater name recognition, financial, manufacturing, marketing, drug development, technical, and human resources than we do, and future mergers and acquisitions in the biopharmaceutical and pharmaceutical industries may result in even more resources being concentrated in our competitors;
- develop and commercialize product candidates that are safer, more effective, less expensive, more convenient, or easier to administer, or have fewer or less severe effects, or in certain cases could be curative for the condition;
- obtain quicker regulatory approval;
- establish superior proprietary positions covering our product candidates and technologies;
- implement more effective approaches to sales and marketing; or
- form more advantageous strategic alliances.

Smaller and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel; establishing clinical trial sites and patient registration; and in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize product candidates that are more effective, have fewer or less severe side effects, are more convenient or are less expensive than our product candidates. Our competitors may also obtain FDA, EMA, or other regulatory approval for their product candidates more rapidly than we may obtain approval for our own product candidates, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, existing products approved for other indications could be used off-label and may compete with our products. For example, the only treatments available to OI patients are drugs such as bisphosphonates, which are not approved for this indication but are commonly used off-label in children.

We have obtained orphan drug designation for setrusumab for the treatment of OI in the United States and EU and for alvelestat for the treatment of AATD in the United States, but we may be unable to obtain orphan drug designation for alvelestat for AATD in the EU or for the treatment of BOS in the United States or EU, or any future product candidates. We may also be unable to obtain or maintain the benefits associated with orphan drug designation, including the potential for orphan drug exclusivity, for setrusumab or any other product for which we obtain orphan drug designation.

Regulatory authorities in some jurisdictions, including the U.S., may designate biologics or drugs designed to address relatively small patient populations as “orphan drugs.”

Under the Orphan Drug Act of 1983 (the “Orphan Drug Act”), the FDA may designate a product as an orphan drug if it is intended to treat a rare disease or condition, defined as one occurring in a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the EU, the European Commission grants orphan designation after receiving the opinion of the EMA’s Committee for Orphan Medicinal Products (“COMP”). In the EU, orphan designation is intended to promote the development of medicinal products that (1) are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (a) such condition affects no more than five in 10,000 persons in the EU, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the EU to justify investment; and (3) there exists no satisfactory method of diagnosis, prevention, or treatment has been authorized (or the product would be a significant benefit to those affected).

Post-Brexit, the U.K. has retained the EU Regulation which governs the designation of medicinal products as orphan drugs and which establishes incentives thereto (Regulation (EC) No. 141/2000) as part of U.K. law by virtue of the EU (Withdrawal) Act 2018. However, under the Retained EU Law (Revocation and Reform) Bill, which is currently before the U.K. Parliament, unless this legislation is expressly preserved and “assimilated” into domestic law or extended by ministerial regulations (to no later than June 23, 2026) it will automatically expire and be revoked by December 31, 2023. There is therefore uncertainty about the future regulations relating to orphan designation in Great Britain, and any future changes to the legal requirements could lead to greater regulatory complexity and increased costs to our business.

There is no pre-MA orphan designation in Great Britain. Instead, the MHRA will review applications for orphan designation in parallel to the corresponding MAA. The criteria are essentially the same, but have been tailored for the market, i.e., the prevalence of the condition in Great Britain, rather than the EU, must not be more than five in 10,000. Should an orphan designation be granted, the period or market exclusivity will be set from the date of first approval of the product in Great Britain. If a medicinal product has been designated orphan in the EU under Regulation (EC) 141/2000, a Great Britain orphan MAA can be made under regulation 50G of the Human Medicines Regulation 2012 (as amended). A U.K.-wide orphan MAA can only be considered in the absence of an active EU orphan designation.

If a U.K.-wide orphan MA is granted and the medicinal product subsequently receives EU orphan designation, the MA holder would need to submit a variation to change this to a Great Britain orphan MA. In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax credits for qualified clinical testing, and user-fee waivers. In addition, if a product receives the first FDA approval of that drug for the indication for which it has orphan designation, the product is entitled to

orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same disease or condition for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity or where the manufacturer is unable to assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the rare disease or condition. In the EU, orphan designation entitles a party to financial incentives such as reduction of fees or fee waivers, protocol assistance, and access to the centralized MA procedure. Upon grant of MA, orphan medical products are entitled to a ten year period of market exclusivity. This period can be extended by two years if studies in children are performed in accordance with a Pediatric Investigation Plan ("PIP"). This period may be reduced to six years if , at the end of the fifth year the orphan designation criteria are no longer met, including where it is shown that the drug is sufficiently profitable not to justify maintenance of market exclusivity. Additionally, a MA may be granted to a similar product for the same indication at any time if (i) the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior; (ii) the applicant consents to a second orphan medicinal product application; or (iii) the applicant cannot supply enough orphan medicinal product.

We have obtained orphan drug designation from the FDA and the European Commission for setrusumab for the treatment of OI (designated by the FDA as "human monoclonal antibody targeting human sclerostin" and designated by the European Commission as "recombinant humanised monoclonal IgG2 lambda antibody against human sclerostin"). Additionally, we have obtained orphan drug designation for alvelestat for the treatment of AATD from the FDA. We may also plan to seek orphan drug designation from the FDA and the European Commission for alvelestat for the treatment of AATD or BOS and/or future rare disease product candidates. Even with orphan drug designation, we may not be the first to obtain marketing approval for any particular orphan indication due to the uncertainties associated with developing pharmaceutical product candidates, which could prevent us from marketing our product candidates if another company is able to obtain orphan drug exclusivity before we do. In addition, exclusive marketing rights in the United States may be unavailable if we seek approval for disease or condition broader than the orphan-designated disease or condition or may be lost in the United States if the FDA later determines that the request for designation was materially defective or if we are unable to assure sufficient quantities of the drug to meet the needs of patients with the rare disease or condition following approval. Further, even if we obtain orphan drug exclusivity, that exclusivity may not effectively protect our product candidates from competition because different drugs can be approved for the same condition. In addition, the FDA and foreign regulatory authorities can subsequently approve product candidates with the same active ingredients for the same condition if the FDA or the foreign regulatory authority concludes that the later drug is safer, more effective, or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process. In addition, while we intend to seek orphan drug designation for other existing and future product candidates, including alvelestat, we may never receive such designations.

Although we have obtained a rare pediatric disease designation for setrusumab, there is no guarantee that FDA approval of will result in issuance of a priority review voucher.

In 2012, Congress authorized the FDA to award priority review vouchers to sponsors of certain rare pediatric disease product applications. This program is designed to encourage development of new drug and biological products for prevention and treatment of certain rare pediatric diseases. Specifically, under this program, a sponsor who receives an approval for a drug or biologic for a "rare pediatric disease" that meets certain criteria may qualify for a voucher that can be redeemed to receive a priority review of a subsequent marketing application for a different product. The sponsor of a rare pediatric disease drug product receiving a priority review voucher may transfer (including by sale) the voucher to another sponsor. The voucher may be further transferred any number of times before the voucher is used, as long as the sponsor making the transfer has not yet submitted the application. The FDA may also revoke any priority review voucher if the rare pediatric disease drug for which the voucher was awarded is not marketed in the U.S. within one year following the date of approval.

We have obtained a rare pediatric disease designation for setrusumab for osteogenesis imperfecta, however, there is no guarantee that we will be able to obtain a priority review voucher, even if setrusumab is approved by the FDA. For example, the FDA may determine that an a BLA or NDA, even if ultimately approved, does not meet the eligibility criteria for a priority review voucher, including for the following reasons:

- the product no longer meets the definition of a rare pediatric disease;
- the product contains an active ingredient (including any ester or salt of the active ingredient) that has been previously approved in another marketing application;

- the application does not rely on clinical data derived from studies examining a pediatric population and dosages of the drug intended for that population;
- the application is approved for a different adult indication than the rare pediatric disease for which the product is designated

Moreover, Congress included a sunset provision in the statute authorizing the rare pediatric disease priority review voucher program. Under the current statutory sunset provisions, after September 30, 2024, FDA may only award a voucher for an approved rare pediatric disease product application if the sponsor has rare pediatric disease designation for the product candidate, and that designation was granted by September 30, 2024. After September 30, 2026, FDA may not award any rare pediatric disease priority review vouchers.

A Fast Track Designation from the FDA, even if granted for any of our product candidates, may not lead to a faster development or regulatory review or approval process, and does not increase the likelihood that our product candidates will receive marketing approval.

The FDA has granted Fast Track designation for the investigation of alvelestat for the treatment of alpha-1-antitrypsin deficiency-associated lung disease. We intend to seek such designation for some or all of our other product candidates. The Fast Track program is intended to expedite or facilitate the process for reviewing new product candidates that meet certain criteria. Specifically, new drugs and biologic are eligible for Fast Track designation if they are intended, alone or in combination with one or more drugs or biologics, to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast Track designation applies to the combination of the product candidate and the specific indication for which it is being studied. The sponsor of a Fast Track product candidate has opportunities for more frequent interactions with the applicable FDA review team during product development and, once a BLA or NDA is submitted, the application may be eligible for priority review. An NDA or BLA submitted for a Fast Track product candidate may also be eligible for rolling review, where the FDA may consider for review sections of the NDA or BLA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA or BLA, the FDA agrees to accept sections of the NDA or BLA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the application.

The FDA has broad discretion whether or not to grant this designation. Even if we believe a particular product candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Even if we do receive Fast Track Designation for any of our product candidates, such product candidates may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may also withdraw Fast Track Designation if it believes that the designation is no longer supported by data from our clinical development program. Furthermore, such a designation does not increase the likelihood that alvelestat or any other product candidate that may be granted Fast Track designation will receive regulatory approval in the U.S. Many product candidates that have received Fast Track Designation have ultimately failed to obtain approval.

We or our partners may seek and fail to obtain Breakthrough Therapy designation by the FDA for setrusumab, alvelestat or etigilimab or any future product candidates or access to the PRIME scheme by the EMA for alvelestat, etigilimab or any future product candidates. Even if we obtain such designation or access, the designation or access may not lead to faster development or regulatory review or approval, and it does not increase the likelihood that our product candidates will receive marketing approval.

In 2012, the FDA established a Breakthrough Therapy designation which is intended to expedite the development and review of product candidates that treat serious or life-threatening diseases where preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically-significant endpoints, such as substantial treatment effects observed early in clinical development. The designation of a product as a Breakthrough Therapy provides potential benefits that include but are not limited to more frequent meetings with the FDA to discuss the development plan for the product and ensure collection of appropriate data needed to support approval; more frequent written correspondence from the FDA about such things as the design of the proposed clinical trials and use of biomarkers; intensive guidance on an efficient drug development program, beginning as early as Phase 1; organizational commitment involving senior managers; and eligibility for rolling review and priority review, if the relevant criteria are met.

Designation as a Breakthrough Therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a Breakthrough Therapy, the FDA may disagree and instead determine not to make such designation. We cannot be sure that our evaluation of our product candidates as qualifying for Breakthrough Therapy designation will meet the FDA's expectations. In any event, the receipt of a Breakthrough Therapy designation for a product may not result in a faster development process, review, or approval compared to product candidates considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as Breakthrough Therapies, the FDA may later decide that such product candidates no longer meet the conditions for qualification and rescind the designation or decide that the time period for FDA review or approval will not be shortened. Similarly, access to the PRIME scheme is at the discretion of the EMA, and we cannot be sure that alvelestat or any future product candidates will be granted access to the scheme; that participation in the scheme will result in expedited regulatory review or approval of our product candidates; or that access to the scheme, once granted, will not be revoked.

In November 2017, setrusumab was admitted to the PRIME (Priority Medicines) scheme of the EMA. We may seek EMA PRIME designation or other designations, schemes or tools for other product candidates. In the EU, innovative products that target an unmet medical need and are expected to be of major public health interest may be eligible for a number of expedited development and review programs, such as the PRIME scheme, which provides incentives similar to the Breakthrough Therapy designation in the United States. PRIME is a voluntary scheme aimed at enhancing the EMA's support for the development of medicines that target unmet medical needs. It is based on increased interaction and early dialogue with companies developing promising medicines, to optimize their product development plans and speed up their evaluation to help them reach patients earlier. The benefits of a PRIME designation include the appointment of a rapporteur before submission of a MAA, early dialogue and scientific advice at key development milestones, and the potential to qualify products for accelerated review earlier in the application process.

Even if we believe one of our product candidates is eligible for PRIME, the EMA may disagree and instead determine not to make such designation. The EMA PRIME scheme or other schemes, designations, or tools, even if obtained or used for any of our product candidates may not lead to a faster development, regulatory review or approval process compared to therapies considered for approval under conventional procedures and do not assure ultimate approval. In addition, even if one or more of our product candidates is eligible to the PRIME scheme, the EMA may later decide that such product candidates no longer meet the conditions for qualification or decide that the time period for review or approval will not be shortened.

Product developers that benefit from PRIME designation may be eligible for accelerated assessment (in 150 days instead of 210 days), which may be granted for medicinal products of major interest from a public health perspective or that target an unmet medical need, but this is not guaranteed.

The competent regulatory authorities in the EU have broad discretion whether to grant such an accelerated assessment, conditional MA or MA under exceptional circumstances, and, even if such assessment or authorization is granted, we may not experience a faster development process, review or authorization compared to conventional procedures. Moreover, the removal or threat of removal of such MAs may create uncertainty or delay in the clinical development of our product candidates and threaten the commercialization prospects of our products and product candidates, if approved. Such an occurrence could materially impact our business, financial condition and results of operations.

We intend to directly commercialize or co-commercialize our product candidates for rare diseases and to out-license or sell our other product candidates for further development and/or commercialization. If we are unable to develop our own sales, marketing, and distribution capabilities or enter into business arrangements, we may not be successful in commercializing our product candidates.

We have no marketing, sales, or distribution capabilities and we currently have no experience with marketing, selling or distributing pharmaceutical product candidates. We have partnered setrusumab in a global licensing transaction with Ultragenyx, under which we retained EU and U.K. commercial rights. We have entered into a global out-licensing agreement with OncXerna for development and commercialization of navicixizumab. We currently intend to commercialize setrusumab for children and adults with OI in the EU and U.K. We may seek to partner or commercialize our other product candidates based on the outcome of clinical trials, cost of the registrational trials and other strategic considerations.

We currently intend to enter into out-licensing or sales arrangements with pharmaceutical, biopharmaceutical or other partners for the continued development and commercialization of our non-core disease product candidates, acumapimod and leflutrozole, and we may take the same approach for our other product candidates.

As a result of the entering into any such planned partnerships or arrangements, our revenue from product sales may be lower than if we directly marketed or sold these product candidates on our own. In addition, any revenue we receive will depend upon the terms of such partnership or arrangement, which may not be as favorable to us as possible, and the efforts of the other party, which may not be adequate or successful and are likely to be beyond our control. We may not be successful in identifying a suitable partner or partners, and we may not be able to reach agreement with them at all. If we are unable to enter into these partnerships or arrangements on acceptable terms or at all, we may not be able to successfully commercialize these product candidates.

These commercialization approaches are expensive and time consuming, and some or all of the costs associated with such efforts may be incurred in advance of any approval of our product candidates. If we are not successful in commercializing our product candidates, either on our own or through arrangements with third parties, our future product revenue will suffer and we may incur significant losses.

The successful commercialization of our product candidates will depend in part on the extent to which governmental authorities and health insurers establish adequate coverage, reimbursement levels, and pricing policies. Failure to obtain or maintain coverage and adequate reimbursement for our product candidates, if approved, could limit our ability to market those product candidates and decrease our ability to generate revenue.

The availability and adequacy of coverage and reimbursement by governmental healthcare programs such as Medicare and Medicaid, private health insurers, and other third-party payors are essential for most patients to be able to afford prescription medications such as our product candidates, assuming approval. Our ability to achieve acceptable levels of coverage and reimbursement for product candidates by governmental authorities, private health insurers, and other organizations will have an effect on our ability to successfully commercialize our product candidates. Assuming we obtain coverage for our product candidates by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. Third-party payors may also elect to restrict coverage to a subset of patients that could potentially be treated with our products, if approved. We cannot be sure that coverage and reimbursement in the United States, the EU, or elsewhere will be available for our product candidates or any product that we may develop, and any reimbursement that may become available may be decreased or eliminated in the future.

Third-party payors increasingly are challenging prices charged for pharmaceutical product candidates and services, and many third-party payors may refuse to provide coverage and reimbursement for particular drugs or biologics when an equivalent generic drug, biosimilar, or a less expensive therapy is available. It is possible that a third-party payor may consider our product candidates as substitutable and only offer to reimburse patients for the less expensive product. Even if we show improved efficacy or improved convenience of administration with our product candidates, pricing of existing drugs may limit the amount we will be able to charge for our product candidates. These payors may deny or revoke the reimbursement status of a given product or establish prices for new or existing marketed product candidates at levels that are too low to enable us to realize an appropriate return on our investment in our product candidates. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our product candidates, and may not be able to obtain a satisfactory financial return on our product candidates.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved product candidates. In the United States, third-party payors, including private and governmental payors, such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs and biologics will be covered. The Medicare and Medicaid programs increasingly are used as models in the United States for how private payors and other governmental payors develop coverage and reimbursement policies for drugs and biologics. Some third-party payors may require pre-approval of coverage for new or innovative devices or drug therapies before they will reimburse healthcare providers who use such therapies. It is difficult to predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our product candidates.

No uniform policy for coverage and reimbursement for product candidates exists among third-party payors in the United States. Therefore, coverage and reimbursement for product candidates can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our product candidates to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases at short notice, and we believe that changes in these rules and regulations are likely.

Our operations are also subject to extensive governmental price controls and other market regulations in the United Kingdom and other countries outside of the United States, and we believe the increasing emphasis on cost-containment initiatives in European and other countries will put pressure on the pricing and usage of our product candidates. In many countries, the prices of medical product candidates are subject to varying price control mechanisms as part of national health systems. To obtain reimbursement or pricing approval, some of these countries might compare the new product to an existing standard of care, including other treatments aimed at the same disease, if they exist. Health technology assessments, including cost- effectiveness evaluations, may be conducted in order to assess the medical value or added clinical benefit of a therapy. Countries may also conduct budget-impact assessments for a new therapy. In some cases, tendering is used to decide which therapy will be reimbursed and made available for a group of patients where more than one treatment exists. Countries might also require further studies or in-use evidence to be developed, or create coverage with evidence generation under some form of so-called managed access agreements. Some countries allow for a company to set the price, which is then agreed in negotiation with the country authorities, who might then monitor sales for that product and re-assess or re-evaluate when a certain statutory health insurance expenditure threshold is reached. Other countries might set their price based on prices in a selected country or group of countries under international or external reference pricing systems. If an agreement cannot be reached, confidential discounts might be negotiated between the manufacturer and the healthcare system authorities. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our product candidates may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits.

Moreover, increasing efforts by governmental and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved product candidates and, as a result, they may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of our product candidates due to the trend toward managed health care, the increasing influence of health maintenance organizations, and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and biologics and surgical procedures and other treatments, has become intense. As a result, increasingly high barriers are being erected to the entry of new product candidates.

Our existing and future product candidates may not gain market acceptance, in which case our ability to generate revenues from product sales will be compromised.

Even if the FDA, or any other regulatory authority approves the marketing of our product candidates, whether developed on our own or with a collaborator, physicians, healthcare providers, patients, or the medical community may not accept or use our product candidates. If our product candidates do not achieve an adequate level of acceptance, we may not generate significant product revenue or any profits from operations. The degree of market acceptance of our product candidates will depend on a variety of factors, including:

- the timing of market introduction;
- the number and clinical profile of competing product candidates;
- the clinical indications for which our product candidates are approved;
- our ability to provide acceptable evidence of safety and efficacy;
- the prevalence and severity of any side effects;
- relative convenience and ease of administration;
- cost-effectiveness;
- marketing and distribution support;
- availability of adequate coverage, reimbursement, and adequate payment from health maintenance organizations and other insurers, both public and private; and
- other potential advantages over alternative treatment methods.

If our product candidates fail to gain market acceptance, our ability to generate revenues will be adversely affected. Even if our product candidates achieve market acceptance, the market may prove not to be large enough to allow us to generate significant revenues.

Any product candidates for which we intend to seek approval as biologic product candidates in the United States may face competition sooner than anticipated.

In the United States, the Biologics Price Competition and Innovation Act of 2009 (the "BPCIA") created an abbreviated approval pathway for biological product candidates that are biosimilar to or interchangeable with an FDA-licensed reference biological product. Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor's own pre-clinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity, and potency of its product.

We believe that if any product is approved as a biological product under a BLA, it should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider our product candidates to be reference product candidates for competing product candidates, potentially creating the opportunity for generic competition sooner than anticipated. Moreover, the extent to which a biosimilar, once approved, will be substituted for a reference product in a way that is similar to traditional generic substitution for non-biological product candidates is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

In the EU, MAAs for product candidates that are biosimilar to an already authorized biological product, the so-called reference product, can rely on the safety and efficacy data contained in the dossier of the reference product. To qualify as a biosimilar product the MA applicant must demonstrate, through comprehensive comparability studies with the reference product, that its product is: (i) highly similar to the reference product notwithstanding the natural variability inherent to all biological medicines, and (ii) that there are no clinically meaningful differences between the biosimilar and the reference product in terms of safety, quality, and efficacy. Biosimilars can only be authorized for use after the period of exclusivity of the reference biological medicine has expired. In general, this means that the biological reference product must have been authorized for at least 10 years before a biosimilar can be made available by another company.

Risks Related to Our Dependence on Third Parties

We rely, and expect to continue to rely, on our partners to develop and commercialize our licensed or partnered product candidates. If our partners do not secure adequate funding or satisfy their obligations under our agreements with them, or if they terminate our licenses, partnerships or collaborations with them, we may not be able to develop or commercialize our licensed or partnered product candidates as planned.

We have announced two out-licensing collaborations. On December 17, 2020, we announced a license and collaboration agreement with Ultragenyx, for setrusumab, a monoclonal antibody in clinical development for OI. Under the terms of the collaboration, Ultragenyx will lead future global development of setrusumab in both pediatric and adult patients. We granted Ultragenyx an exclusive license to develop and commercialize setrusumab in the U.S. and rest of the world, excluding Europe and the U.K. where we retain commercial rights. Under the terms of the agreement, Ultragenyx will pay up to $254 million in development, regulatory and commercial milestones and tiered double digit percentage royalties to us on net sales outside of Europe and we will pay a fixed double digit percentage royalty to Ultragenyx on net sales in Europe. On January 13, 2020, we announced a global out-licensing agreement with OncXerna for development and commercialization of navicixizumab. Under the terms of the agreement OncXerna will pay up to $300 million in future clinical, development and commercial milestones and royalties ranging from the mid-single digit to sub-teen percentages on global annual net sales of navicixizumab, as well as a negotiated percentage of sublicensing revenues from certain sublicensees. Our future plans may include entering into out-licensing or collaboration agreements on some or all of our other development programs.

We also have existing acquisition agreements with Novartis which we entered into in 2015 in respect of our purchase of setrusumab, leflutrozole and acumapimod, and an existing in-licensing agreement with AstraZeneca which we entered into in 2017 in respect of our exclusive license of alvelestat.

Our partners might not fulfill all of their obligations under these agreements, and, in certain circumstances, including our licensing agreement with AstraZeneca, they or we may terminate our partnerships with them. In either event, we may be unable to assume the development and commercialization responsibilities covered by these agreements or enter into alternative arrangements with a third-party to develop and commercialize product candidates. If a partner elected to promote alternative products and product candidates such as its own products and product candidates in preference to those licensed from us, is unable to secure adequate funding to develop our product candidates, does not devote an adequate amount of time and resources to our product candidates or is otherwise unsuccessful in its efforts with respect to our product candidates, the development and commercialization of product candidates covered by the agreements could be delayed or terminated and our business and financial condition could be materially and adversely affected. Accordingly, our ability to receive any revenue from the product candidates covered by these agreements is dependent on the efforts of our partners.

If a partner terminates or breaches its agreements with us, otherwise fails to complete its obligations in a timely manner or alleges that we have breached our contractual obligations under these agreements, the chances of successfully developing or commercializing product candidates under the collaboration could be materially and adversely affected. We could also become involved in disputes with a partner, which could lead to delays in or termination of our development and commercialization programs and time-consuming and expensive litigation or arbitration. Furthermore, termination of an agreement by a partner could have an adverse effect on the price of our ADSs.

We rely, and expect to continue to rely, on third parties, including independent investigators and CROs, to conduct our clinical trials. If these CROs do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates, or such approval or commercialization may be delayed, and our business could be substantially harmed.

We have relied upon and plan to continue to rely upon independent clinical investigators and CROs to conduct our clinical trials and to monitor and manage data for our planned and ongoing clinical programs. We rely on these parties for the execution of our clinical trials and control only certain aspects of these parties' activities. Nevertheless, we are responsible for ensuring that each of our studies and trials is conducted in accordance with the applicable protocol and legal, regulatory and scientific standards, and our reliance on these third parties does not relieve us of our regulatory responsibilities. We and our independent investigators and CROs are required to comply with GCP requirements, which are regulations and guidelines enforced by the FDA, the competent authorities of the EU member states, and comparable foreign regulatory authorities for all of our product candidates in clinical development. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, principal investigators and trial sites. If we fail to exercise adequate oversight over any of our independent investigators or CROs or if we or any of our independent investigators or CROs fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, the EMA, or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon a regulatory inspection of us or our independent investigators or CROs, such regulatory authority will determine that any of our clinical trials complies with GCP requirements. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

Further, these independent investigators and CROs are not our employees and we are not able to control, other than by contract, the amount of resources, including time, which they devote to our clinical trials. If our independent investigators or CROs fail to devote sufficient resources to the development of our product candidates, or if their performance is substandard, it may delay or compromise the prospects for approval and commercialization of our product candidates. In addition, the use of third-party service providers requires us to disclose our proprietary information to these parties, which could increase the risk that this information is misappropriated.

If any of our relationships with our independent investigators or CROs terminate, we may not be able to enter into arrangements with alternative independent investigators or CROs or to do so on commercially reasonable terms. Switching or adding additional investigators or CROs involves additional cost and potential delays and requires our management's time and focus. In addition, there is a natural transition period when a new independent investigator or CRO commences work. As a result, delays could occur, which could materially impact our ability to meet our desired clinical development timelines.

If our independent investigators or CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to a failure to adhere to our clinical protocols, regulatory requirements, or for other reasons, our clinical trials may be extended, delayed, or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenue could be delayed.

We currently rely on third-party CMOs for the production of clinical supply of our product candidates and intend to rely on CMOs for the production of commercial supply of our product candidates, if approved. Our dependence on CMOs may impair the development of our product candidates and may impair the commercialization of our product candidates, which would adversely impact our business and financial position.

We have limited personnel with experience in manufacturing and CMC development requirements and we do not own facilities for manufacturing and testing of our product candidates. Instead, we rely on and expect to continue to rely on CMOs for the supply, testing and release of cGMP grade clinical trial materials, performance of process and product development activities to facilitate supply of commercial quantities of our product candidates, if approved. Reliance on CMOs may expose us to more risk than if we were to manufacture our product candidates ourselves. While the COVID-19 vaccine supply constraints related to raw material supply and CMO manufacturing capacity have begun to ease, the shortage of, and diversion of, certain raw material supplies experienced as a result of the COVID-19 pandemic response have demonstrated that both internal and external manufacturing activities are subject to disruption and risk. Novartis previously provided clinical supplies for setrusumab, acumapimod, and leflutrozole and certain transitional services. We have transitioned the clinical supply manufacture for these product candidates to CMOs while demonstrating the manufactured product is equivalent to the Novartis form. We have also contracted with CMOs for the clinical supply of etigilimab and alvelestat.

The facilities used to manufacture and test our product candidates must be approved by the FDA, and comparable foreign authorities pursuant to inspections. While we provide oversight of manufacturing activities, we do not and will not control the execution of our manufacturing activities by, and are or will be essentially dependent on, our CMOs for compliance with cGMP or similar foreign requirements for the manufacture of our product candidates. We aim to minimize this risk by entering into quality agreements, by auditing of the CMOs and by ongoing review of all activities linked to product manufacture. Due to this dependence on CMOs, we are potentially subject to the risk that our product candidates may have manufacturing defects that we have limited ability to prevent. If a CMO cannot successfully manufacture material that conforms to our specifications and the regulatory requirements it may delay ongoing clinical studies as we will not be able to secure or maintain regulatory approval for the use of our investigational medicinal product candidates in clinical trials, or for commercial distribution of our product candidates, if approved. In addition, while we have limited direct control over the ability of our CMOs to maintain adequate quality control, quality assurance and qualified personnel, we aim to maintain control through the use of quality agreements and manufacturing supply agreements. If the FDA or the comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would delay our development program and significantly impact our ability to develop, obtain regulatory approval for or commercialize our product candidates, if approved. In addition, any failure to achieve and maintain compliance with these laws, regulations and standards could subject us to the risk that we may have to suspend the manufacturing of our product candidates, recall our product candidates or that obtained approvals could be revoked. Furthermore, CMOs may breach existing agreements they have with us because of factors beyond our control. They may also terminate or refuse to renew their agreement at a time that is costly or otherwise inconvenient for us. In addition, Novartis has a contractual right to approve or reject any additional CMO we wish to engage for the manufacture of setrusumab, other than those CMOs that we and Novartis have already agreed upon. Following the license of setrusumab to Ultragenyx, CMO capacity in relation to the manufacture of clinical trial and commercial supplies is a key focus and most likely means additional CMO capacity will be a future priority to secure sufficient supplies. If we or our partners were unable to find an acceptable CMO within a reasonable timeframe, our clinical trials could be delayed or our commercial activities could be negatively impacted.

We rely on and will continue to rely on CMOs to purchase from third-party suppliers the raw materials meeting for our specifications that are necessary to produce our product candidates. We do not and will not have control over the process or timing of the acquisition of these raw materials by our CMOs. Moreover, we currently do not have any agreements for the production of these raw materials. Supplies of raw material could be interrupted from time to time and we cannot be certain that alternative supplies could be obtained within a reasonable timeframe, at an acceptable cost, or at all. In addition, a disruption in the supply of raw materials could delay the commercial launch of our product candidates, if approved, or result in a shortage in supply, which would impair our ability to generate revenues from the sale of our product candidates. Growth in the costs and expenses of raw materials may also impair our ability to cost effectively manufacture our product candidates. There are a limited number of suppliers for the raw materials that we may use to manufacture our product candidates and we may need to assess alternate suppliers to prevent a possible disruption of the manufacture of our product candidates. The restrictions imposed by various governments, including the United States, United Kingdom and EU, among others, on use of certain raw materials required for the manufacture of therapeutics and vaccines in response to the COVID-19 pandemic has demonstrated this vulnerability.

We rely on our CMOs to conduct all product and process development activities necessary to support regulatory submissions. These activities are critical to the meeting the regulatory expectations and if these studies are not considered adequate by FDA, the EMA or comparable foreign regulatory authority then significant delays could be encountered as a result. This risk is mitigated by following all relevant guidance's and using staff knowledge and previous experience to guide the product and process development programs but is still a potential risk of regulatory non-compliance.

Finding new CMOs or third-party suppliers involves additional cost and requires our management's time and focus. In addition, there is typically a transition period when a new CMO commences work. Although we generally do not begin a clinical trial unless we believe we have on hand, or will be able to obtain, a sufficient supply of our product candidates to complete the clinical trial, any significant delay in the supply of our product candidates or the raw materials needed to produce our product candidates, could considerably delay conducting our clinical trials and potential regulatory approval of our product candidates.

As part of their manufacture of our product candidates, our CMOs and third-party suppliers are expected to comply with and respect the proprietary rights of others. If a CMO or third-party supplier fails to acquire the proper licenses or otherwise infringes the proprietary rights of others in the course of providing services to us, we may have to find alternative CMOs or third-party suppliers or defend against claims of infringement, either of which would significantly impact our ability to develop, obtain regulatory approval for or commercialize our product candidates, if approved.

We intend to enter into strategic relationships with third parties, based on a product-by-product assessment, for the development of some of our product candidates. If we fail to enter into these arrangements, our business, development and commercialization prospects could be adversely affected.

Our development program for our product candidates, particularly those entering late-stage development, will require substantial additional funds. We currently intend to enter into out-licensing or sales arrangements with pharmaceutical, biopharmaceutical or other partners for the continued development of our product candidates, acumapimod and leflutrozole, and we may take the same approach for other product candidates.

The types of development arrangements referred to above are complex and time-consuming to negotiate and document, and we may not be able to enter into these arrangements on favorable terms or at all. In addition, we face significant competition from other companies in seeking out these types of development arrangements. If we are successful in entering into such an arrangement, we will be subject to other risks, including our inability to control the amount of time and resources the third party will dedicate to our product candidates, financial or other difficulties experienced by such third party, relinquishing important rights to such third party, and the arrangement failing to be profitable to us.

If we are unable to enter into an appropriate arrangement for the development of our selected product candidates, we may have to reduce, delay, or terminate the development of such product candidates. If we, instead, decide to increase our expenditures to fund development activities on our own, we will need to obtain additional capital, which may not be available to us on acceptable terms or at all. As a result, our business may be substantially harmed.

Risks Related to Intellectual Property

We rely on patents and other intellectual property rights to protect our product candidates, the obtainment, enforcement, defense and maintenance of which may be challenging and costly. Failure to enforce or protect these rights adequately could harm our ability to compete and impair our business.

Our commercial success depends in part on obtaining and maintaining patents and other forms of intellectual property protection, for example, for compositions-of-matter of our product candidates, formulations of our product candidates, polymorphs, salts and analogs of our product candidates, methods used to manufacture our product candidates, methods for manufacturing of the final drug product candidates, and methods of using our product candidates for the treatment of the indications we are developing or plan to develop, or on in-licensing such rights. Our patent portfolio comprises patents and patent applications which cover navicixizumab (which was licensed to OncXerna in January 2020) and our etigilimab product candidate (solely owned by Mereo BioPharma 5 (formerly OncoMed)), patents and patent applications which cover our setrusumab, acumapimod, and leflutrozole product candidates acquired from Novartis and patents and patent applications which cover our alvelestat product candidate exclusively licensed (with the option to purchase) from AstraZeneca. The assignments of those patents and patent applications which we acquired from Novartis have been registered with the relevant authorities in key territories. The patent and patent applications for setrusumab are subject to a license agreement with

Ultragenyx from January 2021. There is no assurance that our pending patent applications will result in issued patents, or if issued as patents, will include claims with sufficient scope of coverage to protect our product candidates, or that any pending patent applications will be issued as patents in a timely manner. Failure to obtain, maintain or extend adequate patent and other intellectual property rights could adversely affect our ability to develop and market our product candidates, resulting in harm to our business.

The patent prosecution process is expensive and time-consuming. We or our licensors may not be able to prepare, file and prosecute all necessary or desirable patent applications for a commercially reasonable cost or in a timely manner or in all jurisdictions. It is also possible that we or our licensors may fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection for them. Moreover, depending on the terms of any future in-licenses to which we may become a party, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology in-licensed from third parties. Therefore, these patents and patent applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

Further, the issuance, scope, validity, enforceability, and commercial value of our and our current or future licensors' patent rights are highly uncertain. Our and our licensors' pending and future patent applications may not result in issued patents that protect our technology or product candidates, in whole or in part, or that effectively prevent others from commercializing competitive technologies and product candidates. The patent examination process may require us or our licensors to narrow the scope of the claims of our or our licensors' pending and future patent applications, which may limit the scope of patent protection that may be obtained. We cannot assure that all of the potentially relevant prior art relating to our patents and patent applications has been found. If such prior art exists, it can invalidate a patent or prevent a patent application from being issued as a patent. Even if patent applications do successfully issue as patents and even if such patents cover our product candidates, third parties may initiate an opposition, interference, reexamination, post grant review, inter partes review, nullification or derivation action in courts or before patent offices, or similar proceedings challenging the validity, enforceability, or scope of such patents, which may result in the patent claims being narrowed or invalidated. Our and our licensors' patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent is issued from such patent applications, and then only to the extent the issued claims cover the technology.

Because patent applications are confidential for a period of time after filing, and some remain so until issued, we cannot be certain that we or our licensors were the first to file any patent application related to our product candidates. Furthermore, in the United States, if third parties have filed such patent applications on or before March 15, 2013, the date on which the United States changed from a first to invent to a first to file patent system, an interference proceeding can be initiated by such third parties to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. If third parties have filed such applications after March 15, 2013, a derivation proceeding can be initiated by such third parties to determine whether our invention was derived from such third parties' product candidates. Even where we have a valid and enforceable patent, we may not be able to exclude others from practicing our invention where the other party can show that they used the invention in commerce before our filing date or the other party benefits from a compulsory license.

We enjoy only limited geographical protection with respect to certain patents and may not be able to protect our intellectual property rights throughout the world.

Filing and prosecuting patent applications and maintaining and defending patents covering our product candidates in all countries throughout the world would be prohibitively expensive. Competitors may use our and our licensors' technologies in jurisdictions where we have not obtained patent protection to develop their competitor's own product candidates and, further, may export otherwise infringing product candidates to territories where we and our licensors have patent protection, but enforcement rights are not as strong as that in the United States or Europe. These product candidates may compete with our product candidates, and our and our licensors' patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

In addition, we may decide to abandon national and regional patent applications before grant. The examination of each national or regional patent application is an independent proceeding. As a result, patent applications in the same family may issue as patents in some jurisdictions, such as in the United States, but may issue as patents with claims of different scope or may even be refused in other jurisdictions, such as in China, which has different requirements for patentability, including a stringent requirement for a detailed description of medical uses of a claimed drug. It is also quite common that depending on the country, the scope of patent protection may vary for the same product or technology.

The laws of some jurisdictions do not protect intellectual property rights to the same extent as the laws or rules and regulations in the United States, United Kingdom and Europe, and many companies have encountered significant difficulties in protecting and defending such rights in such jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, which could make it difficult for us to stop the infringement of our patents or marketing of competing product candidates in violation of our proprietary rights generally. Proceedings to enforce our patent rights in other jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing as patents, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. Furthermore, while we intend to protect our intellectual property rights in our expected significant markets, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our product candidates. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate, which may have an adverse effect on our ability to successfully commercialize our product candidates in all of our expected significant foreign markets. If we or our licensors encounter difficulties in protecting, or are otherwise precluded from effectively protecting, the intellectual property rights important for our business in such jurisdictions, the value of these rights may be diminished and we may face additional competition from others in those jurisdictions.

Some countries also have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, some countries limit the enforceability of patents against government agencies or government contractors. In those countries, the patent owner may have limited remedies, which could materially diminish the value of such patents. If we or any of our licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired.

Our patents and other proprietary rights may not adequately protect our technologies and product candidates, and may not necessarily address all potential threats to our competitive advantage.

The degree of protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business, or permit us to maintain our competitive advantage. The following examples are illustrative:

- others may be able to make compounds that are the same as or similar to our product candidates but that are not covered by the claims of the patents that we own or have exclusively licensed;
- the patents of third parties may impair our ability to develop or commercialize our product candidates;
- the patents of third parties may be extended beyond the expected patent term and thus may impair our ability to develop or commercialize our product candidates;
- we or our licensors or any future strategic collaborators might not have been the first to conceive or reduce to practice the inventions covered by the issued patents or pending patent applications that we own or have exclusively licensed;
- we or our licensors or any future strategic collaborators might not have been the first to file patent applications covering our inventions, our product candidates, or uses of the product candidates in the indications under our development or to be developed;
- it is possible that the pending patent applications that we own or have exclusively licensed may not lead to issued patents;
- issued patents that we own or have exclusively licensed may not provide us with any competitive advantage, or may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- issued patents that we own or have exclusively licensed may not provide coverage for all aspects of our product candidates in all countries, such as for uses of our product candidates in the indications under our development or to be developed;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;

- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive product candidates for sale in our major commercial markets;
- others performing manufacturing or testing for us using our product candidates or technologies could use the intellectual property of others without obtaining a proper license;
- our or our licensors' inventions or technologies may be found to be not patentable; and
- we may not develop additional technologies that are patentable.

We may become subject to third parties' claims alleging infringement of third-party patents and proprietary rights, or we may be involved in lawsuits to protect or enforce our patents and other proprietary rights, which could be costly and time consuming, delay or prevent the development and commercialization of our product candidates, or put our patents and other proprietary rights at risk.

Our commercial success depends, in part, upon our ability to develop, manufacture, market, and sell our product candidates without alleged or actual infringement, misappropriation, or other violation of the patents and proprietary rights of third parties. Litigation relating to patents and other intellectual property rights in the biopharmaceutical and pharmaceutical industries is common, including patent infringement lawsuits and interferences, oppositions, and reexamination proceedings before the U.S. Patent and Trademark Office (the "USPTO"), and foreign patent offices. The various markets in which we plan to operate are subject to frequent and extensive litigation regarding patents and other intellectual property rights. In addition, many companies in intellectual property-dependent industries, including in the biopharmaceutical and pharmaceutical industries, have employed intellectual property litigation as a means to gain an advantage over their competitors. Numerous U.S., European, and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing product candidates. Some claimants may have substantially greater resources than we have and may be able to sustain the costs of complex intellectual property litigation to a greater degree and for longer periods of time than we could. In addition, patent holding companies that focus solely on extracting royalties and settlements by enforcing patent rights may target us. As the biopharmaceutical and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the intellectual property rights of third parties.

We may be subject to third-party claims including infringement, interference or derivation proceedings, post-grant review and inter partes review before the USPTO, or similar adversarial proceedings or litigation in the U.S. and other jurisdictions. Even if we believe such claims are without merit, a court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, and the holders of any such patents may be able to block our ability to commercialize the applicable product unless we obtained a license under the applicable patents, or until such patents expire or are finally determined to be invalid or unenforceable. Similarly, if any third-party patents were held by a court of competent jurisdiction to cover aspects of our compositions, formulations, or methods of treatment, prevention, or use, the holders of any such patents may be able to block our ability to develop and commercialize the applicable product unless we obtained a license or until such patent expires or is finally determined to be invalid or unenforceable. In addition, defending such claims would cause us to incur substantial expenses and could cause us to pay substantial damages, if we are found to be infringing a third party's patent rights. These damages potentially include increased damages and attorneys' fees if we are found to have infringed such rights willfully. As an example of the foregoing risks, we are aware of a third-party patent family which currently includes a patent granted by the European Patent Office ("EPO"), containing claims that appear to cover the use of etigilimab in the treatment of cancer. The patent owner could assert such patent against us, which could present the foregoing risks and impose limitations in our ability to develop, manufacture or sell etigilimab for such use in the EU, unless we obtain a license under such patent, such patent is determined to be invalid or unenforceable by the EPO or a national court in one or more relevant territories, or such patent is revoked or otherwise limited by the EPO. This patent is currently the subject of ongoing opposition proceedings before the EPO, but there can be no assurance as to the outcome of such proceedings.

Any of our patents may be challenged, narrowed, circumvented, or invalidated by third parties. The issuance of a patent is not conclusive as to its inventorship, scope, validity, or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. We may be subject to a third party preissuance submission of prior art to the USPTO or become involved in opposition, derivation, revocation, reexamination, post-grant and inter partes review, or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. Moreover, we may have to participate in

interference proceedings declared by the USPTO to determine priority of invention or in post-grant challenge proceedings, such as oppositions in a foreign patent office, that challenge priority of invention or other features of patentability. Such challenges may result in loss of patent rights, loss of exclusivity, or in patent claims being narrowed, invalidated, or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and product candidates. Such proceedings also may result in substantial cost and require significant time from us, even if the eventual outcome is favorable to us.

Further, if a patent infringement suit is brought against us or our third-party service providers, our development, manufacturing or sales activities relating to the product or product that is the subject of the suit may be delayed or terminated. As a result of patent infringement claims, or in order to avoid potential infringement claims, we may choose to seek, or be required to seek, a license from the third party, which would be likely to include a requirement to pay license fees or royalties or both. These licenses may not be available on acceptable terms or at all. Even if a license can be obtained on acceptable terms, the rights may be nonexclusive, which would give our competitors access to the same intellectual property rights. If we are unable to enter into a license on acceptable terms, we could be prevented from commercializing one or more of our product candidates, or forced to modify such product candidates, or to cease some aspect of our business operations, which could harm our business significantly. We might, if possible, also be forced to redesign our product candidates so that we no longer infringe the third-party intellectual property rights, which may result in significant cost and delay to us, or which redesign could be technically infeasible. Any of these events, even if we were ultimately to prevail, could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business.

If we were to initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that our patent is invalid or unenforceable. In patent litigation in the United States and in Europe, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, for example, lack of novelty, obviousness, or non-enablement. Third parties might allege unenforceability of our patents because someone connected with prosecution of the patent withheld relevant information, or made a misleading statement, during prosecution. The outcome of proceedings involving assertions of invalidity and unenforceability during patent litigation is unpredictable. With respect to the validity of patents, for example, we cannot be certain that there is no invalidating prior art of which we and the patent examiner were unaware during prosecution. There is a risk that in connection with such proceedings, a court will decide that a patent of ours is invalid or unenforceable, in whole or in part, and that we do not have the right to stop the other party from using the invention at issue. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent’s claims narrowly or decide that we do not have the right to stop the other party from using the invention at issue on the grounds that our patent claims do not cover the invention. Even if we establish infringement, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy. An adverse outcome in a litigation or proceeding involving one or more of our patents could limit our ability to assert those patents against those parties or other competitors, and may curtail or preclude our ability to exclude third parties from making and selling similar or competing product candidates. In addition, if the breadth or strength of protection provided by our patents is threatened, it could dissuade companies from collaborating with us to license, develop, or commercialize our current or future product candidates.

Furthermore, our patents and other intellectual property rights also will not protect our technology if competitors and other third parties design around our protected technology without infringing our patents or other intellectual property rights. For example, a third party may develop a competitive product that provides benefits similar to our product candidates but that uses a technology that falls outside the scope of our patent protection. Our competitors may also seek approval to market generic versions of any approved products and in connection with seeking such approval may claim that our patents are invalid, unenforceable or not infringed. In these circumstances, we may need to defend or assert our patents, or both, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or other agency with jurisdiction may find our patents invalid or unenforceable, or that our competitors are competing in a non-infringing manner. Thus, even if we have valid and enforceable patents, these patents still may not provide protection against competing products or processes sufficient to achieve our business objectives. If the patent protection provided by the patents and patent applications we hold or pursue with respect to our product candidates is not sufficiently broad to impede such competition, our ability to successfully commercialize our product candidates could be negatively affected.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. Such litigation or proceedings could substantially increase our operating losses and reduce our resources available for development activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have an adverse effect on our ability to compete in the marketplace. There could also be public announcements of the results of hearings, motions, or other interim proceedings or developments. If securities analysts or investors view these announcements in a negative light, the price of our ADSs could be adversely affected.

We may not identify relevant third-party patents or may incorrectly interpret the relevance, scope or expiration of a third-party patent which might adversely affect our ability to develop, manufacture and market our product candidates.

We cannot guarantee that any of our, our licensors', or the previous owners' patent searches or analyses, including but not limited to the identification of relevant patents, the scope of patent claims, or the expiration of relevant patent applications or patents, are complete or thorough, nor can we be certain that we have identified each and every third-party patent and patent application in the United States, Europe and elsewhere that is relevant to or necessary for the commercialization of our product candidates in any jurisdiction. For example, in the United States, patent applications filed before November 29, 2000 and, upon request, certain patent applications filed after that date that will not be filed outside the United States, remain confidential until those patent applications issue as patents. Patent applications in the United States, EU, and elsewhere are published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Therefore, patent applications covering our product candidates could have been filed by others without our knowledge, including any such patent applications that may claim priority from patent applications for patents that we have determined will expire before we commercialize our product candidates. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our product candidates or the use of our product candidates. Moreover, as we study our product candidates during development, we may learn new information regarding their structure, composition, properties, or functions that may render third-party patent applications or patents that we had not identified as being, or that we had not believed to be, relevant to our product candidates instead to be relevant to or necessary for the commercialization of our product candidates in a jurisdiction. The scope of a patent claim is determined by an interpretation of the law, the written disclosure in the patent, and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending patent application may be incorrect. We may incorrectly determine that our product candidates are not covered by a third-party patent or may incorrectly predict whether a third party's pending patent application will issue with claims of relevant scope. Our determination of the expiration date or the possibility of an extension of patent term of any patent in the United States, Europe, or elsewhere that we consider relevant also may be incorrect. Any of the foregoing circumstances, failures, or errors may negatively impact our ability to develop and market our product candidates.

If we fail to comply with our obligations under our existing and any future intellectual property licenses with third parties, we could lose license rights that are important to our business, and our business may be substantially harmed as a result.

We are party to agreements with licensors, including Novartis, AstraZeneca, and Ultragenyx under which we in-license certain intellectual property and were assigned, in the case of Novartis, or granted an option to acquire, in the case of AstraZeneca, certain patents and patent applications related to our business. In addition, we are party to agreements with OncXerna and Ultragenyx pursuant to which we have out-licensed certain intellectual property. We may enter into additional license agreements in the future. Our existing license agreements impose and any future license agreements are likely to impose various diligence, milestone payment, royalty, insurance and other obligations on us. Any uncured, material breach under these license agreements could result in the loss of our rights to practice such in-licensed intellectual property, and could compromise our development and commercialization efforts for any current or future product candidates.

We may not be successful in maintaining necessary rights to our product candidates or obtaining patent or other intellectual property rights important to our business through acquisitions and in-licenses.

We currently own and have in-licensed rights to intellectual property, including patents, patent applications and know-how, relating to our product candidates, and our success will likely depend on maintaining these rights. Because our programs may require the use of proprietary rights held by third parties, the growth of our business will likely depend in part on our ability to continue to acquire, in-license, maintain, or use these proprietary rights. In addition, our product candidates may require specific formulations to work effectively and the rights to those formulations or methods of making those formulations may be held by others. We may be unable to acquire or in-license any compositions, methods of use, processes, or other third-party intellectual property rights that we identify as necessary for the development and commercialization of our product candidates. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies also are pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources, and greater clinical development and commercialization capabilities.

In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We may also be unable to license or acquire third-party intellectual property rights on a timely basis, on terms that would allow us to make an appropriate return on our investment, or at all. Even if we are able to obtain a license to intellectual property of interest, we may not be able to secure exclusive rights, in which case others could use the same rights and compete with us. If we are unable to successfully obtain a license to third-party intellectual property rights necessary for the development of our product candidates or a development program on acceptable terms, we may have to abandon development of our product candidates or that development program.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment, and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance and annuity fees on any issued patent are due to be paid to the USPTO and foreign patent agencies over the lifetime of a patent. In addition, the USPTO and other foreign patent agencies require compliance with a number of procedural, documentary, fee payment, and other similar provisions during the patent application process. While an inadvertent failure to make payment of such fees or to comply with such provisions can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which such non-compliance will result in the abandonment or lapse of the patent or patent application, and the partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include failure to respond to official actions within prescribed time limits, and non-payment of fees and failure to properly legalize and submit formal documents within prescribed time limits. If we or our licensors fail to maintain the patents and patent applications covering our product candidates or if we or our licensors otherwise allow our patents or patent applications to be abandoned or lapse, our competitors might be able to enter the market, which would hurt our competitive position and could impair our ability to successfully commercialize our product candidates in any indication for which they are approved.

We may be subject to claims challenging the inventorship of our patents and other intellectual property.

We may be subject to claims challenging the inventorship of our patents and patent applications or ownership of our intellectual property. In particular, we may be subject to claims that former employees or other third parties have an interest in our patents or other intellectual property as an inventor or co-inventor. While it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. For example, the assignment of intellectual property rights may not be self-executing or the assignment agreements may be breached, or we may have inventorship disputes arise from conflicting obligations of consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

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

As is the case with other biopharmaceutical and pharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical and pharmaceutical industries involve both technological complexity and legal complexity. Therefore, obtaining and enforcing biopharmaceutical and pharmaceutical patents is costly, time-consuming and inherently uncertain. In addition, the America Invents Act (the

"AIA"), which was passed in September 2011, resulted in significant changes to the U.S. patent system. An important change introduced by the AIA is that, as of March 16, 2013, the United States transitioned to a "first-to-file" system for deciding which party should be granted a patent when two or more patent applications are filed by different parties claiming the same invention. A third party that files a patent application in the USPTO after that date but before us could therefore be awarded a patent covering an invention of ours even if we made the invention before it was made by the third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application, but circumstances could prevent us from promptly filing patent applications on our inventions.

Among some of the other changes introduced by the AIA are changes to the limitation where a patent may be challenged, thus providing opportunities for third parties to challenge any issued patent in the USPTO. This applies to all of our U.S. patents, even those issued before March 16, 2013. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action.

Accordingly, a third party may attempt to use the USPTO proceedings to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. It is not clear what, if any, impact the AIA will have on the operation of our business. However, the AIA and its implementation could increase the uncertainties and costs surrounding the prosecution of our or our licensors' patent applications and the enforcement or defense of our or our licensors' issued patents.

Additionally, the U.S. Supreme Court has ruled on several patent cases in recent years either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. Similarly, the complexity and uncertainty of European patent laws have also increased in recent years. In addition, the European patent system is relatively stringent in the type of amendments that are allowed during prosecution. Complying with these laws and regulations could limit our ability to obtain new patents in the future that may be important for our business.

If we do not obtain protection under the Hatch-Waxman Amendments and similar non-U.S. legislation for extending the term of patents covering our product candidates, our ability to compete effectively could be impaired.

Depending upon the timing, duration and conditions of FDA marketing approval of our product candidates, one or more of our U.S. patents may be eligible for 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 term extension of up to five years for a patent covering an approved product or method of use as compensation for patent term lost during product development and the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval. Similar patent term extensions may be available in other jurisdictions. For example, a supplementary protection certificate in Europe may be applied for approval to recover some of the time lost between the patent application filing date and the date of first marketing authorization. However, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents, or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is less than we request, the period during which we can enforce our patent rights for that product will be shortened and our competitors may obtain approval to market competing product candidates sooner. As a result, our revenue from applicable product candidates could be reduced, possibly materially.

If our trademarks and trade names are not adequately protected, we may not be able to build name recognition in our markets of interest and our competitive position may be adversely affected.

We currently own registered trademarks. We may not be able to obtain trademark protection in territories that we consider of significant importance to us. In addition, any of our trademarks or trade names, whether registered or unregistered, may be challenged, opposed, infringed, cancelled, circumvented or declared generic, or determined to be infringing on other marks, as applicable. We may not be able to maintain and protect our rights to these trademarks and trade names, which we will need to build name recognition by potential collaborators or customers in our markets of interest. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected.

If we are unable to protect the confidentiality of our trade secrets and know-how, our business and competitive position would be harmed.

We consider proprietary trade secrets and confidential know-how and unpatented know-how to be important to our business. In addition to seeking patents for some of our technology and product candidates, we also may rely on trade secrets or confidential know-how to protect our technology, especially where patent protection is believed to be of limited value. However, trade secrets and confidential know-how are difficult to maintain as confidential.

To protect this type of information against disclosure or appropriation by competitors, our policy is to require our employees, consultants, contractors and advisors to enter into confidentiality agreements with us. We also seek to preserve the integrity and confidentiality of our data, trade secrets, and know-how by maintaining physical security of our premises and physical and electronic security of our information technology systems. Monitoring unauthorized uses and disclosures is difficult, and we cannot know whether the steps we have taken to protect our proprietary technologies will be effective. In addition, current or former employees, consultants, contractors, and advisers may unintentionally or willfully disclose our confidential information to competitors, and confidentiality agreements may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. We therefore cannot guarantee that our trade secrets and other proprietary and confidential information will not be disclosed or that competitors will not otherwise gain access to our trade secrets. Enforcing a claim that a third party obtained illegally and is using trade secrets or confidential know-how is expensive, time consuming, and unpredictable. The enforceability of confidentiality agreements may vary from jurisdiction to jurisdiction. Furthermore, if a competitor lawfully obtained or independently developed any of our trade secrets, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret.

Failure to protect or maintain trade secrets and confidential know-how could adversely affect our business and our competitive position. Moreover, our competitors may independently develop substantially equivalent proprietary information and may even apply for patent protection in respect of the same. If successful in obtaining such patent protection, our competitors could limit our use of our own trade secrets or confidential know-how.

We may be subject to claims by third parties asserting that we or our employees have misappropriated third-party intellectual property, or claiming ownership of what we regard as our own intellectual property. These claims may be costly to defend and if we do not successfully do so, we may be required to pay monetary damages and lose valuable intellectual property rights or personnel.

Some of our employees, including our senior management, were previously employed at other biopharmaceutical or pharmaceutical companies, including our competitors or potential competitors. Some of these employees executed proprietary rights, non-disclosure and non-competition agreements in connection with such previous employment. Although we try to ensure that our employees do not use the know-how, trade secrets, or other proprietary information of others in their work for us, we may be subject to claims that we or these employees have used or disclosed confidential information or intellectual property, including know-how, trade secrets, or other proprietary information, of any such employee's former employer. Litigation may be necessary to defend against these claims.

If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. A loss of key research personnel or their work product could hamper or undermine our ability to develop and commercialize our product candidates, which would severely harm our business. In addition, if such intellectual property rights were to be awarded to a third party, we could be required to obtain a license from such third party to commercialize our technology or product candidates. Such a license may not be available on commercially reasonable terms or at all, which could hamper or undermine our ability to develop and commercialize our product candidates, which would severely harm our business. Even if we successfully prosecute or defend against such claims, litigation could result in substantial costs and distract management from the development and commercialization of our product candidates.

Our business and operations may suffer, and proprietary information may be lost, in the event of information technology system failures, cyberattacks or deficiencies in our cybersecurity.

In the ordinary course of our business, we collect and store sensitive data, including intellectual property, clinical trial data, proprietary business information, personal data and personally identifiable information of our clinical trial subjects and employees, in our data centers and on our networks. The secure processing, maintenance and transmission of this information is critical to our operations. Despite our security measures, our information technology and infrastructure and those of our CROs or other contractors or consultants may be vulnerable to attack and damage from computer viruses and malware (e.g., ransomware), cybersecurity threats, unauthorized access, natural disasters, terrorism, war and telecommunications and electrical failures or breached due to employee error, malfeasance, or other disruptions. Attacks upon information technology systems are increasing in their frequency, levels of persistence, sophistication and intensity, and are being conducted by sophisticated and organized groups and individuals with a wide range of motives and expertise. Furthermore, because the techniques used to obtain unauthorized access to, or to sabotage, systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We may also experience security breaches that may remain undetected for an extended period. Even if identified, we may be unable to adequately investigate or remediate incidents or breaches due to attackers increasingly using tools and techniques that are designed to circumvent controls, to avoid detection, and to remove or obfuscate forensic evidence.

We and certain of our service providers are from time to time subject to cyber security incidents. Although, to our knowledge, we have not experienced any significant system failure, accident or security breach to date, any such event could compromise our networks and the information stored there could be accessed, publicly disclosed, lost, or stolen. Any such access, disclosure, or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information, and significant regulatory penalties; disrupt our operations; damage our reputation; and cause a loss of confidence in us and our ability to conduct clinical trials, which could adversely affect our reputation and delay our clinical development of our product candidates.

The loss of clinical trial data from completed, ongoing, or planned trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. We could also incur liability and the further development and commercialization of our product candidates could be delayed. In addition, we also rely on third parties to manufacture our product candidates, so similar events relating to their computer systems could also have a material adverse effect on our business. Further, our insurance coverage may not be sufficient to cover the financial, legal, business or reputational losses that may result from an interruption or breach of our systems.

In addition, in response to the COVID-19 pandemic, and continued hybrid working environment, varying parts of our workforce may work remotely on a part or full-time basis. This could increase our cyber security risk, create data accessibility concerns, and make us more susceptible to communication disruptions. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations or prospects.

Risks Related to our ADSs

The trading price of our ADSs may be volatile, and you could lose all or part of your investment.

The trading price of our ADSs is likely to be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. The stock market in general and the market for biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, investors may not be able to sell their ADSs at or above the price paid for the ADSs. In addition to the factors discussed in this “Risk Factors” section and elsewhere in this report, factors that are expected to affect the market price of our ADSs include:

- positive or negative results from, or delays in, testing or clinical trials conducted by our or our competitors;
- delays in entering into strategic relationships with respect to development or commercialization of our product candidates or entry into strategic relationships on terms that are not deemed to be favorable to us;
- technological innovations or commercial product introductions by us or competitors;
- changes in government regulations;
- developments concerning proprietary rights, including patents and litigation matters;
- the impact of public health epidemics, such as the COVID-19 pandemic, and government efforts to slow their spread;

- economic, public health, financial or geopolitical events that affect us or the financial markets generally, including the duration and severity of the impact of the COVID-19 pandemic, the conflict between Ukraine and the Russian Federation, and unexpected rises in inflation and interest rates;
- public concern relating to the commercial value or safety of our product candidates;
- financing or other corporate transactions;
- publication of research reports or comments by securities or industry analysts, and variances in our periodic results of operations from securities analysts' estimates;
- general market conditions in the biopharmaceutical and pharmaceutical industries or in the economy as a whole;
- the loss of any of our key scientific or senior management personnel;
- sales of our ADSs by us, our senior management and board members, holders of ADSs or our other security holders in the future;
- actions by institutional shareholders;
- speculation in the press or the investment community; or
- other events and factors, many of which are beyond our control.

In the past in the United States, when the market price of a security has been volatile, holders of that security have often instituted securities class action litigation against the issuer of such securities. If any of the holders of ADSs were to bring such a lawsuit against us, we could incur substantial costs defending the lawsuit and the attention of our senior management would be diverted from the operation of our business. Any adverse determination in litigation could also subject us to significant liabilities.

We may not satisfy Nasdaq's requirements for continued listing. If we cannot satisfy these requirements, Nasdaq could delist our ADSs, which could have an adverse impact on the liquidity and market price of our ADSs.

On November 1, 2022, we received a letter (the "Notification Letter") from the Listings Qualifications Department of Nasdaq notifying us that our ADSs failed to maintain a minimum bid price of $1.00 over the previous 30 consecutive business days as required by the Listing Rules of Nasdaq. We have a compliance period of 180 calendar days, or until May 1, 2023, to regain compliance with Nasdaq's minimum bid price requirement by maintaining a closing bid price of $1.00 per ADS for a minimum of ten consecutive business days. If at any time during this period the bid price of our ADSs closes at $1.00 per ADS or more for a minimum of ten consecutive business days, Nasdaq will provide us with written confirmation of compliance. We may also transfer to the Nasdaq Capital Market following which we may have an additional 180 calendar days to comply with the minimum bid requirement. We have not yet regained compliance with the Nasdaq's minimum bid price rule, and our failure to do so could lead to the delisting of our ADSs from Nasdaq.

There can be no assurance that we will be able to comply in the future with Nasdaq's minimum bid price rule. If we continue to be in non-compliance with the minimum bid price rule and the applicable six-month grace period ends, Nasdaq may commence delisting procedures against us during which we may have additional time of up to six months to correct our non-compliance. If our ADSs were ultimately delisted by Nasdaq, trading of the ADSs could be limited to "over-the-counter" trades and the market liquidity and market price of our ADSs could be adversely affected.

You may be subject to limitations on the transfer of ADSs and the withdrawal of the underlying ordinary shares.

ADSs are transferable on the books of the depositary. However, the depositary may close its books at any time or from time to time when the depositary, in good faith, determines such action is necessary or advisable pursuant to the deposit agreement. 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 thinks it is necessary or advisable to do so because of any requirement of law, government or governmental body, or under any provision of the deposit agreement, or for any other reason, subject to your right to cancel your ADSs and withdraw the underlying ordinary shares. Temporary delays in the cancellation of your ADSs and withdrawal of the underlying ordinary shares may arise because the depositary has closed its transfer books or we have closed our transfer books, the transfer of ordinary shares is blocked to permit voting at a shareholders' meeting or because we are paying a dividend on our ordinary shares.

In addition, you may not be able to cancel your ADSs and withdraw the underlying ordinary shares when you owe money for fees, taxes and similar charges to the depositary and when it is necessary to prohibit withdrawals in order to comply with any laws or governmental regulations that apply to our ADSs or to the withdrawal of our ordinary shares or other deposited securities.

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 U.K. Companies Act 2006, or 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.

The principal differences include the following:

- under English law, holders of ordinary shares generally have preemptive rights (in proportion to their existing holdings) in relation to ordinary shares or rights to subscribe for, or to convert securities into, ordinary shares proposed to be allotted for cash, 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. Under U.S. law, shareholders generally do not have preemptive rights unless specifically granted in the certificate of incorporation or otherwise;
- under English law and our articles of association, certain matters require the approval of 75% of the shareholders who vote (in person or by proxy) on the relevant resolution (or, on a poll, the approval of shareholders representing 75% of the ordinary shares voting (in person or by proxy)), including changes to our name, permitting us to issue new ordinary shares for cash without the shareholders' pre-emptive rights and amendments to the articles of association. Under U.S. law, generally only majority shareholder approval is required to amend the certificate of incorporation or to approve other significant transactions;
- in the United Kingdom, takeovers may be structured as takeover offers or as schemes of arrangement. Under English law, a bidder seeking to acquire us by means of a takeover offer who has acquired or unconditionally contracted to acquire not less than 90% of the shares (not held by the bidder) to which the offer relates may complete a "squeeze out" on the same terms as the takeover offer to obtain 100% control of us. Accordingly, acceptances of 90% of our outstanding ordinary shares/ADSs will likely be a condition in any takeover offer to acquire us (albeit a condition that the bidder will typically reserve the right to waive down to anything above 50%), not 50% as is more common in tender offers for corporations organized under Delaware law. By contrast, a scheme of arrangement, the successful completion of which would result in a bidder obtaining 100% control of us, requires the approval of a majority of shareholders voting at the meeting and representing at least 75% of the ordinary shares voting for approval;
- under English law and our articles of association, shareholders and other persons whom we know or have reasonable cause to believe are, or have been, interested in our shares may be required to disclose information regarding their interests in our shares upon our request, and if a person defaults in providing the required information our directors may certain directions, including that the relevant shareholder will not be entitled to vote at general meetings, that dividends in respect of the default shares will be retained and that no transfers of the default shares may be registered. Comparable provisions generally do not exist under U.S. law; and
- the quorum requirement for a shareholders' meeting is a minimum of two shareholders entitled to vote at the meeting and present in person or by proxy or, in the case of a shareholder which is a corporation, represented by a duly authorized representative. Under U.S. law, a majority of the shares eligible to vote must generally be present (in person or by proxy) at a shareholders' meeting in order to constitute a quorum. The minimum number of shares required for a quorum can be reduced pursuant to a provision in a company's certificate of incorporation or bylaws, but typically not below one-third of the shares entitled to vote at the meeting.

If securities or industry analysts do not publish research or publish inaccurate research or unfavorable research about our business, the price and trading volume of ADSs could decline.

The trading market for our ADSs depends in part on the research and reports that securities or industry analysts publish about us or our business. If one or more of the analysts who covers us downgrades our ADSs or publishes incorrect or unfavorable research about our business, the price of our ADSs would likely decline. If one or more of these analysts ceases coverage of us or fails to publish reports on us regularly, or downgrades our ADSs, demand for ADSs could decrease, which could cause the price of ADSs and/or ordinary shares and/or trading volume to decline.

Our ADS holders may not be entitled to a jury trial with respect to claims arising under the deposit agreement, which could result in less favorable results to the plaintiff(s) in any such action.

The deposit agreement governing our ADSs provides that holders and beneficial owners of ADSs irrevocably waive the right to a trial by jury in any legal proceeding arising out of or relating to the deposit agreement or our ADSs, including claims under U.S. federal securities laws, against us or the depositary to the fullest extent permitted by applicable law. If this jury trial waiver provision is prohibited by applicable law, an action could nevertheless proceed under the terms of the deposit agreement with a jury trial. Although we are not aware of a specific federal decision that addresses the enforceability of a jury trial waiver in the context of U.S. federal securities laws, it is our understanding that jury trial waivers are generally enforceable. Moreover, insofar as the deposit agreement is governed by the laws of the State of New York, New York laws similarly recognize the validity of jury trial waivers in appropriate circumstances. In determining whether to enforce a jury trial waiver provision, New York courts and federal courts will consider whether the visibility of the jury trial waiver provision within the agreement is sufficiently prominent such that a party has knowingly waived any right to trial by jury. We believe that this is the case with respect to the deposit agreement and our ADSs.

In addition, New York courts will not enforce a jury trial waiver provision in order to bar a viable setoff or counterclaim sounding in fraud or one which is based upon a creditor's negligence in failing to liquidate collateral upon a guarantor's demand, or in the case of an intentional tort claim (as opposed to a contract dispute). No condition, stipulation or provision of the deposit agreement or ADSs serves as a waiver by any holder or beneficial owner of ADSs or by us or the depositary of compliance with any provision of U.S. federal securities laws and the rules and regulations promulgated thereunder.

If any holder or beneficial owner of ADSs brings a claim against us or the depositary in connection with matters arising under the deposit agreement or our ADSs, including claims under U.S. federal securities laws, such holder or beneficial owner may not be entitled to a jury trial with respect to such claims, which may have the effect of limiting and discouraging lawsuits against us or the depositary. If a lawsuit is brought against us or the depositary under the deposit agreement, it may be heard only by a judge or justice of the applicable trial court, which would be conducted according to different civil procedures and may result in different results than a trial by jury would have had, including results that could be less favorable to the plaintiff(s) in any such action, depending on, among other things, the nature of the claims, the judge or justice hearing such claims and the venue of the hearing.

You may not receive distributions on ordinary shares represented by ADSs or any value for them if it is unlawful or impractical to make them available to holders of ADSs.

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

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

Holders of ADSs are not able to exercise voting rights attaching to ordinary shares underlying our ADSs on an individual basis. Each holder of ADSs has appointed the depositary or its nominee as the holder's representative to exercise, pursuant to the instructions of the holder, the voting rights attaching to our ordinary shares underlying our ADSs. Holders of ADSs may not receive voting materials in time to instruct the depositary to vote, and it is possible that they, or persons who hold their ADSs through brokers, dealers or other third parties, will not have the opportunity to exercise a right to vote.

We are entitled to amend the deposit agreement and to change the rights of ADS holders under the terms of such agreement, or to terminate the deposit agreement, without the prior consent of the ADS holders.

We are entitled to amend the deposit agreement and to change the rights of the ADS holders under the terms of such agreement, without the prior consent of the ADS holders. We and the depositary may agree to amend the deposit agreement in any way we decide is necessary or advantageous to us or to the depositary. Amendments may reflect, among other things, operational changes in the ADS program, legal developments affecting ADSs or changes in the terms of our business relationship with the depositary. In the event that the terms of an amendment are materially disadvantageous to ADS holders, ADS holders will only receive 30 days' advance notice of the amendment, and no prior consent of the ADS holders is required under the deposit agreement. Furthermore, we may decide to direct the depositary to terminate the ADS facility at any time for any reason. For example, terminations may occur when we decide to list our ordinary shares on a non-U.S. securities exchange and determine not to continue to sponsor an ADS facility or when we become the subject of a takeover or a going-private transaction. If the ADS facility will terminate, ADS holders will receive at least 30 days' prior notice, but no prior consent is required from them. Under the circumstances that we decide to make an amendment to the deposit agreement that is disadvantageous to ADS holders or terminate the deposit agreement, the ADS holders may choose to sell their ADSs or surrender their ADSs and become direct holders of the underlying ordinary shares, but will have no right to any compensation whatsoever.

It may be difficult for you to bring any action or enforce any judgment obtained in the United States against us or members of our Board, which may limit the remedies otherwise available to us.

We are incorporated as a public limited company in England and Wales, and the majority of our assets are located outside the United States. In addition, several members of our board of directors (our "Board") are nationals and residents of countries, including the United Kingdom, outside of the United States. Most or all of the assets of these individuals are located outside the United States. As a result, it may be difficult or impossible for you to bring an action against us or against these individuals in the United States if you believe your rights have been infringed under the securities laws or otherwise. In addition, a United Kingdom court may prevent you from enforcing a judgment of a U.S. court against us or these individuals based on the securities laws of the United States or any state thereof. A United Kingdom court may not allow you to bring an action against us or our directors based on the securities laws of the United States or any state thereof.

Shareholders in countries other than the United Kingdom will suffer dilution if they are unable to participate in future pre-emptive equity offerings.

Under English law, shareholders (being those shareholders that are included in a company's register of members as holders of the legal title to that company's shares) usually have pre-emptive rights to subscribe on a pro rata basis in the issuance of new shares for cash. The exercise of those pre-emptive rights by certain shareholders not resident in the United Kingdom may be restricted by applicable law or practice in the United Kingdom and overseas jurisdictions. In particular, the exercise of pre-emptive rights by United States shareholders would be prohibited unless an offering is registered under the Securities Act or an exemption from the registration requirements of the Securities Act applies. Furthermore, under the deposit agreement for our ADSs, the depositary generally will not make available those pre-emptive rights to holders of ADSs unless certain conditions are met, including that the provision of such pre-emptive rights to the ADS holders is reasonably practicable. If no exemption applies and we determine not to register such offering, shareholders in the United States may not be able or permitted to exercise their pre-emptive rights. We are also permitted under English law to disapply pre-emptive rights (subject to the approval of our shareholders by special resolution or the inclusion in the articles of a power to disapply such rights) either generally or in relation to a specific allotment and thereby exclude certain shareholders, such as overseas shareholders, from participating in a rights offering (usually to avoid a breach of local securities laws).

We are currently a "foreign private issuer" under the rules and regulations of the SEC and, as a result, are exempt from a number of rules under the Exchange Act and are permitted to file less information with the SEC than a company incorporated in the United States.

We are incorporated as a public limited company in England and Wales and are deemed to be a "foreign private issuer" under the rules and regulations of the SEC. As a foreign private issuer, we are exempt from certain rules under the Exchange Act that would otherwise apply if we were a company incorporated in the United States, including:

- the requirement to file periodic reports and financial statements with the SEC as frequently or as promptly as United States companies with securities registered under the Exchange Act;
- the requirement to file financial statements prepared in accordance with U.S. GAAP;
- the proxy rules, which impose certain disclosure and procedural requirements for proxy solicitations; and
- the requirement to comply with Regulation Fair Disclosure ("Regulation FD"), which imposes certain restrictions on the selective disclosure of material information.

In addition, our officers, directors and principal shareholders are exempt from the reporting and "short-swing" profit recovery provisions of Section 16 of the Exchange Act and the related rules with respect to their purchases and sales of our ADSs.

As a foreign private issuer, we are not required to comply with some of the corporate governance standards of Nasdaq applicable to companies incorporated in the United States.

Our Board is required to meet certain corporate governance standards under Nasdaq Listing Rules, including the requirement to maintain an audit committee comprised of three or more directors satisfying the independence standards of Nasdaq applicable to audit committee members. While foreign private issuers are not required to comply with most of the other corporate governance rules of Nasdaq, we believe we currently comply with, and intend to continue to comply with, the majority of such requirements, including the requirements to maintain a majority of independent directors and the nominating and compensation committees of our Board to comprise solely of independent directors. We follow U.K. requirements with respect to shareholder meetings including shareholder meetings required to disapply preemption rights and issue ordinary shares to investors in connection with private placements or public offering of our securities. As a result, holders of our ADSs may not be afforded the benefits of the corporate governance standards of Nasdaq to the same extent applicable to companies incorporated in the United States. See "Item 16G. Corporate Governance—Foreign Private Issuer Exemption" elsewhere in this annual report.

We expect to lose our foreign private issuer status in the future which could result in significant additional costs and expenses.

We expect to lose our foreign private issuer status in the future, which could result in significant additional costs and expenses. In the future, we would lose our foreign private issuer status if a majority of our shareholders, directors or management are U.S. citizens or residents and if we fail to meet additional requirements necessary to avoid loss of foreign private issuer status. The regulatory and compliance costs to us under U.S. securities laws as a U.S. domestic issuer may be significantly higher than our current reporting and compliance costs. If we are not a foreign private issuer, we will be required to file periodic reports and registration statements on U.S. domestic issuer forms with the SEC, which are more detailed and extensive than the forms available to a foreign private issuer. We would have to mandatorily comply with U.S. federal proxy requirements, and our officers, directors, and principal shareholders will 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 Nasdaq corporate governance requirements that are available to foreign private issuers.

Although our reporting obligations as a foreign private issuer are fewer than those of a public company incorporated in the United States, our costs of complying with our SEC reporting requirements are significant, and our management is required to devote substantial time to complying with SEC regulations.

As a company with securities listed in the United States, and particularly after we no longer qualify as an emerging growth company, we will incur significant legal, accounting and other expenses that we did not incur previously. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of Nasdaq and other applicable securities rules and regulations impose various requirements on non-U.S. reporting public companies, including the establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our senior management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time- consuming and costly. For example, we expect that these rules and regulations may make it more expensive for us to obtain director and officer liability insurance, which in turn could make it more difficult for us to attract and retain qualified senior management personnel or members for our Board. In addition, these rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

We are an "emerging growth company," and the reduced disclosure requirements applicable to emerging growth companies may make the ADSs less attractive to investors.

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. As such, we are eligible to, and intend to, take advantage, for up to five years (until 2024), of certain exemptions from various reporting requirements applicable to other public companies that are not emerging growth companies, such as not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002. These exemptions include:

- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

We expect to continue to take advantage of some or all of the available exemptions. We cannot predict whether investors will find the ADSs less attractive if we rely on these exemptions. If some investors find the ADSs less attractive as a result, there may be a less active trading market for the ADSs and the market price of the ADSs may be more volatile.

Failure to establish and maintain effective internal controls could have a material adverse effect on our business and stock price.

Pursuant to Section 404, we are required to furnish a report by our senior management on our internal control over financial reporting. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404, we have been engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially continue to engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

We may be a passive foreign investment company ("PFIC") for any taxable year, which could result in material adverse U.S. federal income tax consequences if you are a U.S. investor.

In general, a non-U.S. corporation will be a PFIC for any taxable year in which (i) 75% or more of its gross income consists of passive income (the "income test") or (ii) 50% or more of the value of its assets consists of assets (generally determined on a quarterly average basis) that produce, or are held for the production of, passive income (the "asset test"). For purposes of the above calculations, a non-U.S. corporation that directly or indirectly owns at least 25% by value of the shares of another corporation is treated as if it held its proportionate share of the assets of the other corporation and received directly its proportionate share of the income of the other corporation. Passive income generally includes interest, dividends, gains from certain property transactions, rents and royalties (other than certain rents or royalties derived in the active conduct of a trade or business). Cash is a passive asset for PFIC purposes. Goodwill (the value of which may be determined by reference to the company's market capitalization) is treated as an active asset to the extent attributable to activities intended to produce active income.

Based on our gross income, the average value of our assets, including goodwill, and the nature of the current state of our business, we believe we were a PFIC for the year ended December 31, 2022. There can be no assurance regarding our PFIC status for any particular year in the future because PFIC status is factual in nature, depends upon factors not wholly within our control, generally cannot be determined until the close of the taxable year in question and is determined annually. Whether we will be a PFIC in the current or any future taxable year is uncertain because, among other things, we currently own a substantial amount of passive assets, including cash, and because the valuation of our assets that generate non-passive income for PFIC purposes, including our goodwill and other intangible assets, is uncertain and may vary substantially over time. In addition, the composition of our assets and income may vary substantially over time. The average quarterly value of our assets for purposes of determining our PFIC status for any taxable year (to the extent applicable) will generally be determined in part by reference to our market capitalization, which has fluctuated and may continue to fluctuate significantly over time. Accordingly, there can be no assurance that we will not be a PFIC in the current or for any future taxable year. In addition, we may, directly or indirectly, hold equity interests in other entities, including certain of our subsidiaries that are PFICs. Accordingly, U.S. investors should invest in our ADSs only if they are willing to bear the U.S. federal income tax consequences associated with investments in PFICs.

If we are a PFIC for any taxable year during which a U.S. investor owns ADSs, certain adverse U.S. federal income tax consequences could apply to such U.S. investor. We will provide the information necessary for a U.S. investor to make a qualified electing fund election with respect to us. See “Item 10. Additional Information—E. Taxation” for further information. U.S. investors should consult their tax advisers regarding our PFIC status for any taxable year and the potential application of the PFIC rules to an investment in our ADSs.

Item 4. Information On The Company

4.A. History and Development of the Company

Our legal and commercial name is Mereo BioPharma Group plc. Our company was incorporated on March 10, 2015 and was registered as a private limited company under the laws of England and Wales with the company number 09481161. On June 3, 2016, we were re-registered as a public limited company under the laws of England and Wales. Our principal executive offices are located at 4th Floor, 1 Cavendish Place, London, W1G 0QF, United Kingdom, and our telephone number is +44 333 023 7300. Our website is www.mereobiopharma.com. Information on Mereo’s website is not incorporated by reference into or otherwise part of this annual report. We have included our website address in this annual report solely for informational purposes. The SEC also maintains a website that contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC. The address of this website is http://www.sec.gov.

Mereo’s portfolio consists of six clinical-stage product candidates, four of which were acquired from large pharmaceutical companies and two oncology anti-cancer product candidates which we acquired in the Merger. Mereo does not have any approved products and, as a result, has not generated any revenue from product sales. Pursuant to the terms of a global out-licensing agreement for navicixizumab to OncXerna in January 2020, the Company received an upfront payment of $4 million and an additional payment of $2 million in February 2022. In December 2020, the Company entered into a license and collaboration agreement with Ultragenyx for setrusumab, under which the Company subsequently received an upfront payment of $50 million in 2021.

On April 23, 2019, we completed the Merger, with OncoMed, now called Mereo BioPharma 5, Inc., surviving as a wholly owned subsidiary of Mereo US Holdings, Inc. and as an indirect subsidiary of Mereo BioPharma Group plc.

Since April 24, 2019, our ADSs commenced trading on Nasdaq under the symbol “MREO.”

On December 18, 2020, admission of our ordinary shares to trading on the AIM market of London Stock Exchange plc was cancelled upon our delisting.

We are an Emerging Growth Company. As such, we are eligible to, and intend to, take advantage, for up to five years, of certain exemptions from various reporting requirements applicable to other public companies that are not Emerging Growth Companies, such as not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002.

We will remain an Emerging Growth Company until the earliest of: (i) the last day of our fiscal year during which we have total annual gross revenues of at least $1.235 billion; (ii) the last day of our fiscal year following the fifth anniversary of the closing of our initial public offering; (iii) the date on which we have, during the previous three-year period, issued more than $1.0 billion in non-convertible debt; (iv) the date on which we are deemed to be a Large Accelerated Filer under the Exchange Act, with at least $700 million of equity securities held by non-affiliates.

For information regarding our capital expenditures, see “Item 5. Operating and Financial Review and Prospects—B. Liquidity and Capital Resources.”

4.B. Business Overview

We are a biopharmaceutical company focused on the development of innovative therapeutics for rare diseases. We have developed a robust portfolio of clinical stage product candidates. Our two rare disease product candidates are setrusumab for the treatment of osteogenesis imperfecta (OI) and alvelestat for the treatment of severe alpha-1-anti-trypsin deficiency-associated lung disease (AATD-LD) and Bronchiolitis Obliterans Syndrome (BOS) following allogenic stem cell transplant.

Following the announcement of the results for setrusumab in a Phase 2b study in adults with OI which demonstrated a dose dependent statistically significant increase in bone mineral density and bone strength, we announced a strategic partnership with Ultragenyx in December 2020 for the development of setrusumab in children and adults with OI. Ultragenyx initiated a pivotal, Phase 2/3 pediatric and young adult study (5-25 years old) in the first half of 2022, with the Phase 3 transition expected in mid-2023. Ultragenyx also intends to initiate a study of pediatric patients under age five with OI in the first half of 2023.

We announced successful completion of a Phase 2, dose-finding study for alvelestat in AATD-LD in May 2022 which demonstrated statistically significant changes in Neutrophil Elastase (NE) activity and biomarkers of disease severity at different time points up to 12 weeks. Further, in October 2022 we announced that Fast Track designation was granted by the U.S. Food and Drug Administration (FDA) for alvelestat in AATD-LD, along with additional program updates. In March 2023, we announced the outcome of the end-of-Phase 2 discussions with the FDA and the EMA (Scientific Advice) and based on clear recommendations from both Agencies, we are designing a single, global, Phase 3 study evaluating the 240 mg dose of alvelestat versus placebo in patients with AATD-LD to support applications for full marketing approvals in both the U.S. and EU. Alvelestat is also in an ongoing Phase 2 investigator-led study in AATD, including in patients who may be on augmentation therapy. This study has enrolled 60 patients with data expected in the third quarter of 2023. Following successful completion of a Phase 1b investigator-sponsored study in patients with BOS following allogenic stem cell transplant, a Phase 2 study was initiated in the second half of 2022.

Our oncology product candidate, etigilimab (an anti-TIGIT antibody), has completed a Phase 1a dose escalation clinical trial in patients with advanced solid tumors and has been evaluated in a Phase 1b study in combination with nivolumab in select tumor types. We have completed Simon Stage 1 of the open label Phase1b/2 basket study (the ACTIVATE study) evaluating etigilimab in combination with nivolumab in three rare tumors, two specific subtypes of soft-tissue sarcomas, uveal melanoma and testicular germ cell cancer, three gynecological carcinomas, cervical, ovarian and endometrial carcinomas, and any solid tumor with high mutation burden, all in the recurrent/metastatic setting. Etigilimab, in combination with nivolumab, is also in an ongoing investigator-led Phase 1b/2 study in clear cell ovarian cancer at The University of Texas MD Anderson Cancer Center (MD Anderson), financed by the Cancer Focus Fund.

We plan to develop our product candidates through the next key clinical milestone and then partner where it makes sense strategically to do so, but also in select cases for our rare disease product candidates, to develop them through regulatory approval and potentially commercialization.

Our second oncology product, navicixizumab for the treatment of late line ovarian cancer, has completed a Phase 1b study and was partnered in January 2020 for further development with OncXerna on a global basis.

We plan to partner or sell our other two product candidates acumapimod for the treatment of AECOPD and leflutrozole for the treatment of male infertility, recognizing the need for greater resources to take these product candidates to market.

Our strategy is selectively to acquire and develop product candidates for rare diseases that have already received significant investment from large pharmaceutical and biotechnology companies and that have substantial pre-clinical, clinical and manufacturing data packages. Since our formation in March 2015, we have successfully executed on this strategy by acquiring six clinical-stage product candidates of which four were in oncology and rare diseases. Four of our six clinical-stage product candidates were acquired from large pharmaceutical companies and two were acquired in the Merger. We aim to efficiently develop our product candidates through the clinic and have successfully commenced or completed large, randomized Phase 2 clinical trials for five of our product candidates.

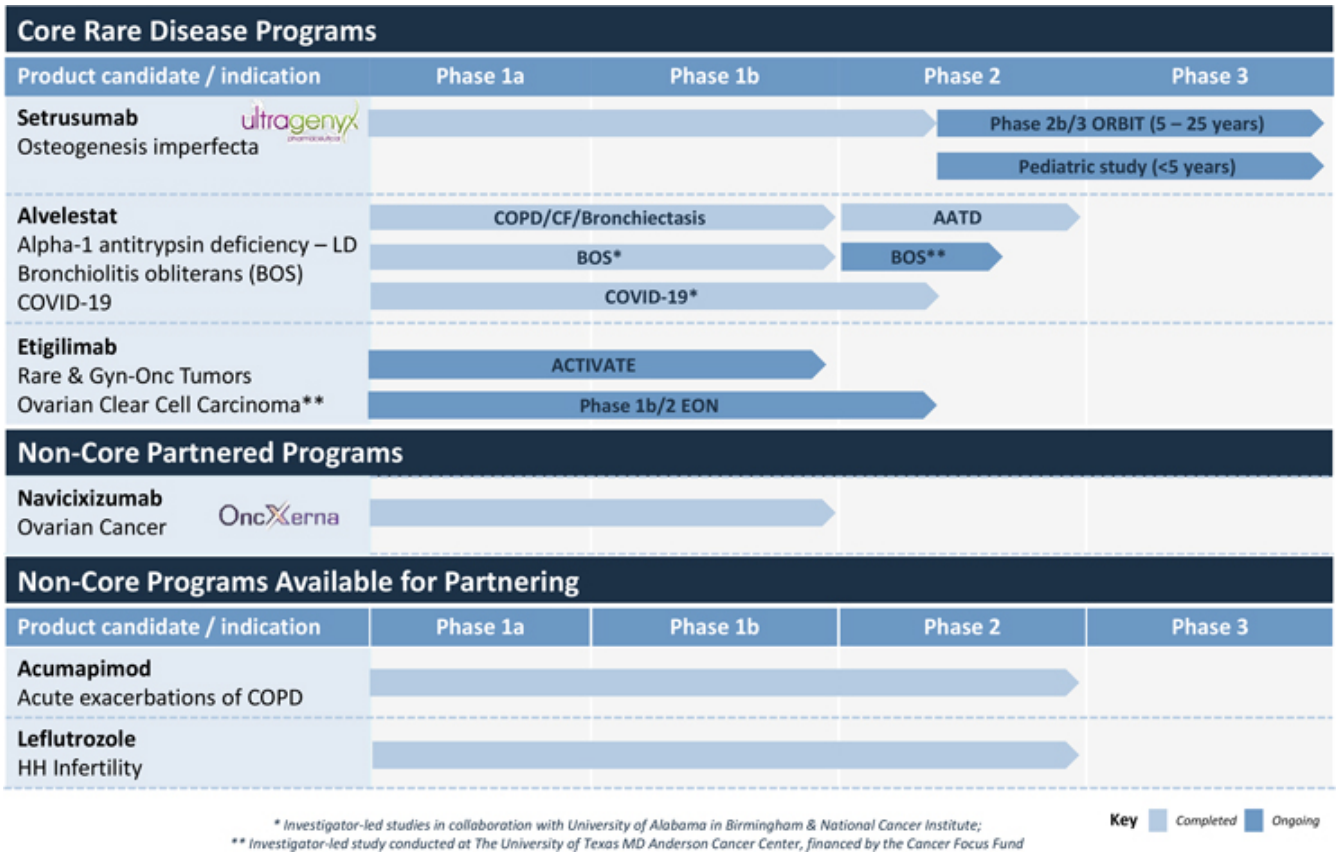
Rare diseases represent an attractive development and, in some cases, commercialization opportunity for us since they typically have high unmet medical need and can utilize regulatory pathways that facilitate acceleration to approval and to the potential market. Development of products for oncology and rare diseases both involve close collaboration with key opinion leaders and investigators. Development of rare disease products generally involves close coordination with the patient organizations and patients are treated at a limited number of specialized sites which helps identification of the patient population and enables a small targeted sales infrastructure to commercialize the products in key markets.

Our team has extensive experience in the pharmaceutical and biotechnology sector in the identification, acquisition, development, manufacturing and commercialization of product candidates in multiple therapeutic areas including oncology

and rare diseases. Our senior management has long- standing relationships with senior executives of large pharmaceutical and biotechnology companies which we believe enhances our ability to form strategic partnerships on our product candidates and to identify and acquire additional product candidates.

Our Pipeline

The following tables summarize our pipeline for our product candidates. We have global commercial rights to alvelestat, etigilimab, acumapimod and leflutrozole and commercial rights to setrusumab in Europe and the U.K. We granted Ultragenyx an exclusive license to develop and commercialize setrusumab in the U.S. and rest of the world, and we have licensed global rights for navicixizumab to OncXerna.



Core Rare Disease Product Candidates

- **Setrusumab (BPS-804/UX143):** Setrusumab is a novel antibody designed to inhibit sclerostin, a protein that inhibits the activity of bone-forming cells. Inhibiting sclerostin has been shown to promote increases in bone mineral density through stimulation of bone-formation (through osteoblasts) and inhibition of bone-resorption (through osteoclasts). We are developing setrusumab as a treatment for OI, a rare genetic disease that results in bones that can break easily and is commonly known as brittle bone disease. OI is a debilitating orphan disease for which there are no treatments approved by the FDA or EMA. It is estimated that OI affects a minimum of 25,000 people in the United States and approximately an aggregate of 32,000 people in Germany, Spain, France, Italy and the United Kingdom. We believe setrusumab's mechanism of action is well suited for the treatment of OI and has the potential to become a novel treatment option for patients that could reduce fractures and improve patient quality of life.

  Prior to our acquisition of setrusumab, Novartis conducted four clinical trials in 106 patients and healthy volunteers. In 2016, we obtained orphan drug designation in OI for setrusumab in the United States and the EU and, in November 2017, it was accepted into the Priority Medicines scheme ("PRIME") of the EMA. In September 2020 we received rare pediatric disease designation for setrusumab in OI from the FDA. In November 2019 we reported top-line data on a Phase 2b clinical trial of setrusumab for adults with OI. The Phase 2b was a dose ranging study with three blinded arms at high, medium and low doses to establish the dose response curve and an open label arm at the top dose. Setrusumab demonstrated statistically significant improvements in bone formation biomarkers and bone mineral density (measured by Dual Energy X-ray Absorptiometry) and a trend to a reduction in fractures at the high dose, compared to the other doses, even though the study was not powered for fracture reduction. The results support the progression of setrusumab into a pediatric pivotal study in OI. The data was also presented, as a podium presentation, at the American Society of Bone and Mineral Research ("ASBMR") in October 2021.

  In December 2020 we announced a partnership with Ultragenyx for the development of setrusumab for OI. Under the terms of the partnership, Ultragenyx will lead future global development of setrusumab in both pediatric and adult patients. We granted Ultragenyx an exclusive license to develop and commercialize setrusumab in the US and rest of the world, excluding Europe and the U.K. where we retain commercial rights. Each party will be responsible for post-marketing commitments in their respective territories.

Ultragenyx made an upfront payment of $50 million to Mereo and will fund global development of the program until approval and has agreed to pay a total of up to $254 million upon achievement of certain clinical, regulatory and commercial milestones. Ultragenyx will pay tiered double digit percentage royalties to us on net sales outside of Europe and the U.K. and we will pay a fixed double digit percentage royalty to Ultragenyx on net sales in Europe and the U.K. Under the terms of our 2015 agreement with Novartis, we will pay Novartis a percentage of proceeds, subject to certain deductions, with Mereo receiving a substantial majority of the payments from Ultragenyx.

Ultragenyx initiated a pivotal Phase 2/3 study in pediatric and young adult patients (5-25 years old) in the first half of 2022 and plans to transition to the Phase 3 part of the study in mid-2023. The objective of the Phase 2/3 study will first focus on determining the optimal dose based on increases in collagen production using serum P1NP levels and an acceptable safety profile. Following determination of the dose, Ultragenyx currently intend to adapt the study into a pivotal Phase 3 stage, evaluating fracture reduction over an estimated 15 to 24 months as the primary endpoint, subject to regulatory review. In the first half of 2023, Ultragenyx initiated a randomized study in OI in children under five with serious bone disease, comparing bisphosphonates to BPS804/UX143. Younger pediatric patients with OI often have a much higher fracture rate than other age groups and a greater medical need, driving clinical urgency for better treatment options. Annualized rate of fractures is the primary end-point in the study.

- **Alvelestat (MPH-966):** Alvelestat is a novel, oral small molecule we are developing for the treatment of severe AATD-associated Lung Disease (AATD-LD) and BOS. AATD is a potentially life-threatening, rare, genetic condition caused by a lack of effective alpha-1 antitrypsin ("AAT"). The lungs are normally protected from enzymatic degradation by neutrophil elastase by the AAT protein, but in severe AATD the AAT is either misfolded and fails to be released into the circulation, inactive or completely missing. The degradation of tissue by unopposed neutrophil elastase leads to severe debilitating diseases, including early-onset pulmonary emphysema, a disease that irreversibly destroys the tissues that support lung function. There are an estimated 50,000 patients in North America and 60,000 patients in Europe with severe AATD, although due to underdiagnosis, there are estimated to be approximately 10,000 patients diagnosed in North America. BOS is a progressive, ultimately fatal fibrotic lung disease due to graft versus host disease following stem cell transplant, or lung transplant rejection. An estimated fifty percent of lung transplant recipients will develop BOS by five years post-transplant, with an average survival of less than five years. There are an estimated 10,000 people living with lung transplant and BOS in the US and Europe. Alvelestat is designed to inhibit NE, a neutrophil protease, which is a key enzyme involved in the destruction of lung tissue. We believe the inhibition of NE has the potential to protect patients with AATD-LD from further lung damage. BOS is characterized by anti-organ auto-immune responses, either graft versus host (in SCT) or host versus graft (in lung transplant), exacerbated by elevated neutrophils in the lung and excess NE activity, leading to lung damage through elastin breakdown in the tissue and progressive fibrosis, and ultimately respiratory failure. By inhibiting NE, alvelestat will reduce the accelerating effects of NE-driven inflammation on BOS.

Prior to our license of alvelestat, AstraZeneca conducted 12 clinical trials involving 1,776 subjects, including trials in bronchiectasis and CF. Although these trials were conducted in diseases other than AATD, we believe the data demonstrated potential clinical benefit and biomarker evidence of treatment effect for AATD patients. These trials created a safety database of 1,149 subjects treated with alvelestat.

We announced successful completion of a Phase 2, placebo-controlled, dose-ranging, proof-of-concept clinical trial in 99 patients with AATD-LD in the United States and the EU in May 2022 which demonstrated statistically significant changes in Neutrophil Elastase (NE) activity and biomarkers of disease severity at different time points up to 12 weeks. We subsequently announced additional Phase 2 data from this study in October 2022 demonstrating the association of biomarker responders in alvelestat-treated patients to improvement in the activity domain of the St George's Respiratory Questionnaire, but not in patients treated with placebo. No new safety signals were detected in patients with AATD-LD. The most frequent adverse event was of headache which was more frequently observed at the higher doses of alvelestat (120 mg and 240 mg) used in AATD-LD than was observed at lower doses used previous studies in COPD, bronchiectasis and cystic fibrosis, There was evidence of tolerance to headache being induced, and we intend to use a dose-escalation regime for initiation of treatment in future trials. A single treatment-emergent adverse event (TEAE) of liver function abnormality (raised hepatic transaminases, withour meeting Hy's Law) and one TEAE of prolonged QTc, in which study-drug stopping criteria were met were reported in the Phase 2. Both events fully resolved on study drug cessation. We obtained Fast Track designation for alvelestat for AATD-LD in the U.S. in October 2022. In March 2023, we announced the outcome of the end-of-Phase 2 discussions with the FDA and the EMA. Based on clear recommendations from both Agencies, we are designing a single, global, Phase 3 study evaluating the 240 mg dose of alvelestat versus placebo in patients with AATD-LD to support applications for full marketing approvals in both the U.S. and EU. The proposed Phase 3 study has two independent primary endpoints, i) a Patient-Reported Outcome (PRO), as guided by the FDA, and ii) lung density measured by CT scan, as guided by the EMA.

Alvelestat is also in an ongoing Phase 2 investigator-led study in AATD-LD, including in patients who may be on augmentation therapy, with data expected in the third quarter of 2023.

Emerging data on the potential of NE inhibition to reduce the inflammatory and thrombotic effects of Neutrophil Extracellular Traps (NETs) in COVID-19, led to the initiation of a study in this disease. The top-line results were reported in December 2021. The results demonstrated a safety profile consistent with previous studies, and in the alvelestat arm, a reduction (an improvement) of 2 points or more in the World Health Organization (WHO) Severity Score in 62.5% (5/9) of the patients versus 28.5% (2/7) in the placebo arm at day 5. At day 7 87.5% (7/8) patients in the alvelestat arm had improved by 2 points or more vs 57% (4/7) in the placebo arm. Inflammatory and pro-coagulopathy biomarkers were also supportive.

An open-label Phase 1b/2 investigator-sponsored study in BOS following allogeneic stem cell transplant is ongoing. Interim results of Phase 1b were reported in December 2021 showing stabilization or improvement in lung function measured by Forced Expiratory Volume in 1 second, (FEV1) in 6 of 7 patients, and supportive biomarker responses, with reduction in neutrophil elastase and the mature elastin breakdown product (desmosine) and reductions in markers of collagen synthesis associated with fibrosis. Evaluation of the clinical and safety data from 10 patients in Phase 1 supported the dose to be progressed and expansion into the Phase 2 portion of the study was initiated in the second half of 2022.

- **Etigilimab (MPH-313):** Etigilimab is an antibody against TIGIT (T-cell immunoreceptor with Ig and ITIM domains). TIGIT is a next generation checkpoint receptor shown to block T-cell activation and the body's natural anti-cancer immune response. Etigilimab is an IgG1 monoclonal antibody which binds to the human TIGIT receptor on immune cells with a goal of improving the activation and effectiveness of T-cell and NK cell anti-tumor activity. We completed a Phase 1a dose escalation clinical trial with etigilimab in patients with advanced solid tumors and enrolled patients in a Phase 1b study in combination with nivolumab in selected tumor types.

23 patients were treated in the Phase 1a dose escalation study with doses up to 20mg/kg Q2W. Tumor types included colorectal cancer, endometrial cancer, head and neck cancer, pancreatic cancer, ovarian cancer, and other tumor types. No dose limiting toxicities were observed. In the Phase 1b combination study, a total of ten patients, nine of whom had progressed on prior anti-PD1/PD-L1 therapies, were enrolled at doses of 3, 10 and 20 mg/kg. Tumor types included gastric cancer and six other tumor types. Eight patients were evaluable for tumor growth assessment, and all of these patients had progressed on PD1/PD-L1 therapies with best responses, including two patients with a partial response and stable disease. Patients remained on study for up to 224 days. No dose limiting toxicities (DLTs) were observed.

Treatment emergent adverse events (TEAEs) related to study drug were reported by 16 patients (69.6%) in the Phase 1a portion of the study and 7 patients (70.0%) in the Phase 1b portion of the study. The most commonly reported related TEAEs in the Phase 1a portion of the study were pruritus (4 patients, 17.4%) and fatigue, nausea, rash and maculopapular rash (each reported by 3 patients, 8.7%). In the Phase 1b portion of the study, the most commonly reported related TEAEs were fatigue (3 patients, 30.0%) and pruritus, rash and pruritic rash (each reported by 2 patients, 20.0%).

There were no treatment-related serious adverse events in the Phase 1a portion and there was only one treatment-related serious adverse event (autoimmune hepatitis) in the Phase 1b portion of the study. The Phase 1b study has now been completed.

The ACTIVATE open label Phase 1b/2 basket study of Etigilimab in combination with nivolumab in multiple tumor types enrolled 76 patients and has completed Simon Stage 1of the study. Parallel cohorts in the study have focused on three rare tumors, two subtypes of soft-tissue sarcomas, uveal melanoma and testicular germ cell cancer, three gynecological carcinomas, cervical, ovarian and endometrial carcinomas and any solid tumor with high mutation burden, all in the recurrent/metastatic setting.

We enrolled a total of 76 patients in the Phase 1b part of the study. The trial is evaluating objective response rate as a primary endpoint and will also evaluate safety, duration of response, pharmacokinetics, anti-drug antibodies, progression-free survival and additional secondary and exploratory endpoints. The study was designed to expand select cohorts of patients, based on outcomes, to further evaluate responses to etigilimab and anti-PD1. Biomarker analyses will be conducted on tumor tissues and blood samples from treated patients, including quantification of levels of tumor- associated TIGIT, PVR and related biomarkers to evaluate their potential utility for selecting patients most likely to respond to the combination of etigilimab and anti-PD1.

We reported an interim clinical and biomarker data update on this study in September 2022. At the time of the data cut-off, there were 63 efficacy-evaluable checkpoint inhibitor-naïve (CPI-naive) subjects with a minimum of 1 staging scan at 8 (+/-1) weeks and RECIST 1.1 response assessment or documented clinical progression.

We have completed enrollment in an open label Phase1b/2 basket study (the ACTIVATE study) evaluating etigilimab in combination with nivolumab on three rare tumors, two specific subtypes of soft-tissue sarcomas, uveal melanoma and testicular germ cell cancer, three gynecological carcinomas, cervical, endometrial and ovarian carcinomas and any solid tumor with high mutation burden, all in the recurrent/metastatic setting. These indications were selected based on observations of clinical activity in our prior Phase 1a/1b study and/or based on a comprehensive biomarker analysis of solid tumors which revealed tumor types with a high prevalence of expression of TIGIT and its principal ligand poliovirus receptor (PVR) and concordant expression of TIGIT and PD1. The selected tumor types have shown responsiveness to anti-PD1 therapies with response rates generally ranging from 5-20%. The combination of etigilimab and anti-PD1 may lead to improved responses in these patients.

In April 2021, the Company entered into partnership with Cancer Focus Fund for a Phase 1b/2 study of etigilimab in Clear Cell Ovarian Cancer to be conducted at The University of Texas MD Anderson Cancer Center. The Phase 1b/2 study is being financed by Cancer Focus Fund in exchange for upfront consideration of $1.5 million of the Company’s shares and additional payments based on the achievement of certain milestones. Clear cell ovarian cancer is a rare cancer that accounts for approximately 5 to 10% of all ovarian carcinomas in North America. MD Anderson are planning to follow the per protocol procedure to expand the Phase 1b/2 study from an initial 10 patients to 20 patients in the Phase 2 portion of the study.

Our Non-Core Partnered Programs

Following completion of successful Phase 1b or Phase 2 studies the products below are programs which we have successfully partnered.

- Navicixizumab (OMP-305B83): Navi is a bispecific antibody that inhibits delta-like ligand 4 (DLL4) and vascular endothelial growth factor (VEGF). We acquired this therapeutic product in the merger with Mereo BioPharma 5 (formerly OncoMed). In a Phase 1a clinical trial, Navi demonstrated single agent activity. Following this we conducted a Phase 1b clinical trial in ovarian cancer, in combination with paclitaxel, in platinum-resistant ovarian cancer. A successful FDA Type B meeting was held in July 2019 the potential for accelerated approval was discussed. Navicixizumab has also been granted Fast Track designation by the FDA. In January 2020, Navi was licensed by the Company to OncXerna pursuant to the terms of a global licensing agreement. Under the terms of the contingent value rights agreement between us and Computershare from April 2019 (the "Mereo CVR Agreement"), the holders of contingent value rights are entitled to receive the benefit of certain cash milestone payments made to Mereo under the license agreement. Pursuant to the terms of the Mereo CVR Agreement, if a milestone occurs prior to the fifth anniversary of the closing of the Merger, April 23, 2024, then holders of CVRs will be entitled to receive an amount in cash equal to 70% of the aggregate principal amount received by Mereo after deduction of costs, charges and expenditures set out in detail in the Mereo CVR Agreement. Such milestone payments are also subject to a cash consideration cap, pursuant to which the aggregate principal amount of all cash payments made to holders of CVRs under the Mereo CVR Agreement shall in no case exceed $79.7 million. See "—Material Agreements—CVR Agreement Between Us and Computershare—The NAVI Milestones."

Our Non-Core Programs Available for Partnering

Following completion of successful Phase 1 or Phase 2 studies the products below are programs which we intend to out-license or sell.

- **Acumapimod (BCT-197):** Acumapimod is a p38 MAP kinase inhibitor therapy for treatment during severe acute exacerbations of COPD (AECOPD). In a Phase 2 trial, acumapimod given over 5 days in patients hospitalized with AECOPD demonstrated a statistically significant reduction in re-hospitalization for treatment failure and recurrent exacerbations. Acumapimod was reported to be safe and well tolerated. Following meetings with FDA and EMA a global Phase 3 registrational program has been designed and we intend to explore out-licensing or sale opportunities with third parties for the further development of acumapimod.

- **Leflutrozole (BGS-649):** Leflutrozole is an oral inhibitor of aromatase for the treatment of male infertility associated with HH. Excess aromatase in fat tissue reduces testosterone, LH and FSH, leading to HH. In Phase 2 trials, leflutrozole normalized testosterone, increased LH and FSH and was reported to be well- tolerated. Effects on sperm counts supported that future development of leflutrozole should focus on male infertility associated with HH. We intend to explore out-licensing or sale opportunities with third parties for the further development of leflutrozole.

Our Strategy

We intend to become a leading biopharmaceutical company developing innovative therapeutics that aim to improve outcomes for patients with rare diseases. The key elements of our strategy to achieve this goal include:

- ***Rapidly develop our product candidates and potentially commercialize our rare disease product candidates.*** We have completed and announced top-line data on a Phase 2b clinical trial of setrusumab for the treatment of OI in adults in the United States, Europe and Canada. We reported top-line data on the three blinded dose ranging arms in November 2019 with the results supporting progression of setrusumab into a pediatric pivotal study in OI. Following the completion of the dosing part of the study, patients were followed for a further twelve months to examine the off-effects of setrusumab. In September 2020, the FDA granted Rare Pediatric Disease designation to setrusumab for the treatment of OI. Following our completion of the Phase 2b ASTEROID study, we met with both the FDA (end-of-Phase 2 (EOP2) meeting in February 2020) and the EMA (PRIME meeting in May 2020) to discuss the principles of a design of a single Phase 2/3 registrational pediatric study in OI. In December 2020, we signed a license and collaboration agreement for setrusumab in OI with Ultragenyx Pharmaceutical Inc. Ultragenyx initiated a pivotal Phase 2/3 study in young adults and pediatric patients (5-25 years old) in the first half of 2022 and expects to provide an update on the Phase 2 dose ranging part of this study in mid-2023, when the trial will transition into Phase 3. Following selection of the dose for the Phase 3 study, Ultragenyx intend to initiate an additional registrational trial in young pediatric patients (<5 years old) in the first half of 2023.

  We reported successful top-line data from a Phase 2 proof-of-concept clinical trial of alvelestat for the treatment of severe AATD-LD in May 2022 and provided an additional data update in October 2022. We received regulatory feedback on the design of a single, global, pivotal registrational trial for alvelestat in AATD-LD for full approval in Q1 2023 and will now determine the optimum path forward for development of alvelestat towards approval and commercialization, including potential partnering. We also announced the completion and top-line data of a Phase 1b/2 placebo-controlled clinical trial to evaluate the safety and efficacy of alvelestat in hospitalized adult patients with moderate to severe COVID-19 respiratory disease. The investigator-led Phase 1b/2 study in BOS following SCT has completed the Phase 1b stage (10 patients) and commenced the Phase 2 portion of the study in the second half of 2022 to evaluate clinical efficacy on lung function (FEV1) in a 6-month study in up to an additional 24 patients, with expansion for responders to 12 months.

  Etigilimab, our lead oncology program, has completed a Phase 1a dose escalating monotherapy study and has been evaluated in a Phase 1b combination study with nivolumab in a range of tumor types. We have also completed enrollment in an open label Phase 1b/2 basket study evaluating our anti- TIGIT in combination with nivolumab in a range of tumor types including three rare tumors, sarcoma, uveal melanoma and germ cell cancer, three gynecological carcinomas, cervical, endometrial and ovarian carcinomas and tumors with high mutation burden. We enrolled a total of 76 patients in the Phase 1b part of the study and we reported an interim clinical and biomarker data update on this study in September 2022.

- ***Efficiently advance our other product candidates and explore out-licensing or sale opportunities with third parties for further clinical development and/or commercialization.*** Our second oncology product, navicixizumab, for the treatment of late line ovarian cancer, has completed a Phase 1 study and has been partnered on a global basis with OncXerna. Based on the results from our Phase 2 clinical trial of acumapimod, we plan to enter into one or more strategic relationships with third parties for acumapimod to undertake the next phase of clinical development and, if approved, commercialization. In March 2018, we reported top-line Phase 2b data for leflutrozole for the treatment of HH and in December 2018, we reported positive results from the safety extension study for leflutrozole. We intend to explore out-licensing or sale opportunities with third parties for the further development and commercialization of leflutrozole.
- ***Continue to be a partner of choice for pharmaceutical and biotechnology companies.*** We believe that we are a preferred partner for pharmaceutical and biotechnology companies as they seek to unlock the potential in their development pipelines and deliver therapeutics to patients in areas of high unmet medical need. We have strong relationships with these companies, as evidenced by our agreements with Novartis and AstraZeneca, as well as by the Merger, and a track record of structuring transactions that enable us to leverage our core capabilities while creating value for all stakeholders. We intend to continue to enter into strategic relationships that align our interests with those of pharmaceutical and biotechnology companies and that we believe to be mutually beneficial.
- ***Leverage our expertise in business development.*** Our senior management team has extensive relationships with large pharmaceutical and biotechnology companies. These relationships are important to us as we seek to form strategic partnerships on our product candidates and as appropriate, to grow our pipeline of product candidates in rare diseases.

Therapeutic Candidates

Core Rare Disease Candidates

Setrusumab (BPS-804/UX143) for the Treatment of Osteogenesis Imperfecta

Overview

We are developing setrusumab for the treatment of OI in collaboration with Ultragenyx. Setrusumab is a novel, intravenously administered antibody that is designed to inhibit sclerostin, a protein that inhibits the activity of bone-forming cells, known as osteoblasts. We believe that by blocking sclerostin, setrusumab has the potential to induce or increase osteoblast function and maturation of these cells, increasing overall bone mass and thereby reducing fractures in OI patients.

Background of Osteogenesis Imperfecta

OI is a genetic disorder characterized by fragile bones and reduced bone mass, resulting in bones that break easily, loose joints and weakened teeth. In severe cases, patients may experience hundreds of fractures in a lifetime. In addition, people with OI often suffer from muscle weakness, early hearing loss, fatigue, curved bones, scoliosis (curved spine), brittle teeth, respiratory problems and short stature. The disease can be extremely debilitating and even fatal in newborn infants with a severe form of the disease. OI is a rare condition that affects a minimum of 25,000 people, an incidence rate of 6.2 out of 100,000, in the United States, according to estimates by the Osteogenesis Imperfecta Foundation, and approximately 32,000 people, an incidence rate of 10 out of 100,000, in Germany, Spain, France, Italy and the United Kingdom, according to estimates by Orphanet. OI occurs across the globe without any currently described discernable higher prevalence in one population specifically.

There are eight recognized forms of OI, designated type I through type VIII. Type I is the least severe form, although it still has a significant impact on patients' lives, including fractures and other physical manifestations, while type II is the most severe and frequently causes death at or shortly after birth. The most prevalent form of OI is type I, which is estimated to occur in approximately 50% to 60% of OI patients. The less severe forms of OI, such as type I and type IV, are still serious conditions and are characterized by broken bones, often as a result of minor trauma. Patients typically have a blue or gray tint to the sclera, the part of the eye that is usually white, and there is a risk of early hearing loss in adults.

The most severe forms of OI, particularly type II, may be characterized by an extremely small, fragile rib cage and underdeveloped lungs. Infants with these abnormalities have life-threatening problems related to breathing and often die shortly after birth.

Current Treatment Landscape for Osteogenesis Imperfecta

There are no therapies approved by the FDA or European Commission for the treatment of OI. The only treatments available to OI patients are the acute management of fractures as they occur and drugs such as bisphosphonates, which are not approved for this indication but are commonly used off-label in children.

Current treatment of OI is directed towards management of fractures with casting or surgical fixation. Following either of these, physical therapy will often be required. Preventative surgeries, such as intramedullary, or in-bone, radding fixation are also undertaken. Supportive care for the disease involves surgery to correct deformities, internal splinting of bones with metal rods, bracing to support weak limbs and decrease pain, physical therapy and muscle strengthening and aerobic conditioning to improve bone mass and strength.

Some OI patients are treated off-label with drugs indicated for osteoporosis. Bisphosphonate drugs slow down the rate at which osteoclasts, which are cells which resorb or take away bone, reduce the bones' mass. These include Aredia (pamidronate), Fosamax (alendronate) and Reclast (zoledronic acid). However, bisphosphonate drugs are not approved by the FDA or the EMA for use in OI. We are not aware of any long-term clinical studies demonstrating an improvement in fractures in adults and the effect of long-term therapy with these drugs remains unclear. Therefore, we believe the effect of bisphosphonate drugs on fractures, growth, bone deformity, mobility and pain remains unclear in both adults and children.

Our Approach

Our product for treating OI is setrusumab, a fully human monoclonal antibody that is designed to inhibit sclerostin. Sclerostin is produced in osteocytes, which are mature bone cells that are thought to be the mechanoreceptor cells that regulate the activity of bone-building osteoblasts and bone- resorbing osteoclasts. Sclerostin inhibits the activity of osteoblasts. We believe that by blocking sclerostin, setrusumab has the potential to induce or increase osteoblast activity and maturation of these cells, increasing overall bone mass and, thereby reducing fractures in OI patients.

In 2016, we obtained orphan drug designation in OI for setrusumab in the United States and the EU and, in November 2017, it was accepted into PRIME by the EMA. In Europe, the EMA has an adaptive pathways program which allows for early and progressive patient access to medicine. In July 2016, the EMA launched the PRIME scheme, a voluntary scheme aimed at enhancing the EMA's support for the development of medicines that target unmet medical needs. In February 2017 setrusumab was accepted into the adaptive pathways program and in November 2017, the EMA granted PRIME designation for setrusumab for the treatment of OI. In September 2020 we received rare pediatric disease designation for setrusumab in OI from the FDA. See "—Government Regulation—Foreign Government Regulation."

Clinical Development of Setrusumab

In April 2017, we commenced a Phase 2b clinical trial of setrusumab in adults in the United States, Europe and Canada. The Phase 2b clinical trial is a multi-center, randomized trial with three blinded arms at a high, medium and low doses to establish the dose response curve and an open label arm at the top dose. The trial completed enrollment of 112 patients and we reported 12-month top-line data from the trial in November 2019. Following the 12-month dosing part of the trial, patients were followed for a further twelve months to examine the off-effects of setrusumab. Similar to the Phase 2 clinical trial conducted by Novartis, we enrolled patients with type I, III and IV OI.

12 month Top-line Data From Setrusumab Phase 2b Dose-ranging Study in Adult Patients

On November 11, 2019, we reported 12-month top-line data from our Phase 2b dose-ranging clinical trial for setrusumab in adults with Type I, III or IV OI. The study enrolled 112 adults (69 with type I, 28 with type IV and 15 with type III OI) at 27 clinical sites across the United States and Europe and randomized patients originally to one of four different blinded monthly dosing regimens of setrusumab: high, medium, low and placebo. The study was subsequently revised to convert the placebo arm into an open-label arm where patients received the high dose regimen of setrusumab. The top-line 12-month results reported on November 11, 2019, and on January 14, 2020, are from the three-arm blinded portion of the study.

The primary endpoint of the trial was change in trabecular volumetric bone mineral density ("Tr vBMD") of the radius (wrist) over baseline after 12 months of treatment as measured by high resolution peripheral quantitative computerized tomography ("HRpQCT"). As a result of the unexpected high heterogeneity of the trial patients' trabecular bone baseline values at the wrist (including both very low and very high trabecular bone at baseline as compared to the literature available), the primary endpoint was not met at any of the three setrusumab dose levels. HRpQCT is a relatively new imaging technique that has not been used widely in clinical studies and was chosen in order to improve the understanding of the effect of setrusumab on the bone biology in OI patients, given it can measure both trabecular and cortical volumetric BMD separately.

Importantly, when the percentage change in trabecular and cortical volumetric bone mineral density ("BMD") at the wrist were combined (the total volumetric BMD as measured by HRpQCT, a secondary endpoint of the study), an increase in total volumetric BMD was observed and reached statistical significance in the medium and high dose cohorts. Mean increases in total volumetric BMD were 4.11% (p=0.004), 4.5% (p=0.028), and 0.58% (p=0.97) in the high, medium and low dose cohorts (post hoc analysis), respectively. This suggests total volumetric BMD increases were driven by the ability of setrusumab to increase cortical volumetric BMD.

The study achieved its important secondary endpoint of increase in areal BMD at the lumbar spine at six and 12 months over baseline using dual energy x-ray absorptiometry ("DXA"), a well-established measurement tool of BMD (cortical and trabecular bone), reaching statistical significance in the high and medium doses cohorts at both six and 12 months, with a clear dose-dependent response. Mean increases in areal BMD at the lumbar spine were 8.8% (p<0.001), 6.8 % (p<0.001), and 2.6% (p=0.057) in the high, medium, and low dose cohorts at 12 months, respectively. Moreover, increases in areal BMD were consistent across all OI subtypes (I, III and IV) represented in the study and improved with duration of treatment. Statistically significant changes in areal BMD were also observed by DXA at the femoral neck and total hip with mean increases of 3.1% (p=0.022) and 2.2% (P=0.011), respectively, at 12 months in the high dose cohort.

On January 14, 2020, we reported additional data to the above from our Phase 2b dose-ranging clinical trial for setrusumab. This additional data demonstrated a dose dependent increase in bone strength (stiffness and failure load) as measured by Finite Element Analysis ("FEA"). This was a second pre-specified primary end point and reached statistical significance in the high dose cohort. FEA is a technique that, based on the HRpQCT, allows for the estimation of physical properties of bone.

We also reported on the end point of Trabecular Bone Score (TBS) at the lumbar spine. Setrusumab demonstrated a statistically significant increase in TBS at both the high (p<0.001) and medium dose cohorts (p<0.001). TBS is a gray-level texture index determined from patient lumbar spine DXA scans that correlates with 3D parameters of trabecular bone architecture thought to help predict fracture.

Although the Phase 2b trial was not powered to show a difference in fracture rates, a trend of reduction in fractures was observed in the high-dose cohort. Setrusumab was safe and well-tolerated in the study. There were no cardiac-related safety concerns observed in the study.

Patients who completed 12 months of treatment in the ASTEROID study continued into a 12-month extension "off therapy" portion to examine the off effect of setrusumab. Patients had the option to receive 12 months of treatment with the bisphosphonate zoledronic acid (given at months six and/or 12) and received both DXA and HRpQCT scans at six and 12 months after entering the extension portion.

Summary of Top-line Safety Results

Top-line 12-month safety results suggest setrusumab was safe and well tolerated in the study. The adverse event profile was balanced across the arms. There were five, eight and four serious treatment emergent adverse events in the high, medium and low dose groups, three of which were initially recorded as treatment related. Two events occurred in one patient. These were headache and hydrocephalus. The patient had a history of basilar invagination, subdural hematoma and subdural hemorrhage; the neurologist and Data Monitoring Committee ("DMC") concluded that the events were unlikely related to the study drug. There was a temporary interruption to the study drug but the patient restarted treatment and continued the study with no complications. The other serious adverse event that was initially recorded as related was of anaphylactic reaction, which occurred two days following setrusumab infusion. This was the patient's sixth infusion. As the reaction was two days following the infusion and the patient previously had five doses, it was determined that it was unlikely to be a drug reaction and the patient continued therapy, without symptoms or signs with repeat infusions. All of the nine adverse events that were reported as potentially cardiac related were discussed at the DMC (including cardiology review), and none were concluded to represent a cardiovascular safety concern.

Partnership with Ultragenyx

In December 2020, we announced a partnership with Ultragenyx for the development of setrusumab for OI. Under the terms of the partnership, Ultragenyx will lead future global development of setrusumab in both pediatric and adult patients. We granted Ultragenyx an exclusive license to develop and commercialize setrusumab in the US and rest of the world, excluding Europe and the U.K. where we retain commercial rights. Each party will be responsible for post-marketing commitments in their respective territories.

In October 2021, at the ASBMR annual meeting, we, along with our partner, Ultragenyx, presented additional secondary endpoint data from the Phase 2b ASTEROID study demonstrating that treatment with setrusumab resulted in dose-dependent increase in P1NP serum levels, a marker of bone formation, and a decrease in CTx serum levels, a marker of bone resorption, confirming the mechanism of action of sclerostin inhibition over the 12-month treatment period. Observed improvements in bone mineral density were continuous over the 12 months of the study, with comparable gains achieved in the first and second six months of treatment in the high dose group despite temporal changes in biomarkers.

Ultragenyx initiated a pivotal Phase 2/3 study in young adults and pediatric patients (5-25 years old) in the first half of 2022 and plans to provide an update on the Phase 2 dose ranging part of this study in mid-2023. The objective of the Phase 2/3 study will first focus on determining the optimized dose based on increases in collagen production using serum P1NP levels and an acceptable safety profile. Following determination of the dose, Ultragenyx currently intend to adapt the study into a pivotal Phase 3 stage, evaluating fracture reduction over an estimated 15 to 24 months as the primary endpoint, subject to regulatory review. In addition, in the first half of 2023, Ultragenyx intends to initiate a randomized study in OI in children under age five with serious bone disease, comparing bisphosphonates to UX143. Younger pediatric patients with OI often have a much higher fracture rate than other age groups and a greater medical need, driving clinical urgency for better treatment options. The annualized rate of fractures is the primary endpoint in the study.

Alvelestat (MPH-966) for the Treatment of Severe Alpha-1-Antitrypsin Deficiency (“AATD”)-Associated Lung Disease and Brochiolitis Obliterans Syndrome (“BOS”)

Overview

We are developing alvelestat for the treatment of severe AATD-LD and BOS. AATD-LD is a potentially life-threatening rare, genetic condition that results in severe debilitating diseases, including early-onset pulmonary emphysema. Alvelestat is a novel, oral small molecule designed to inhibit NE. Scientific data indicate that the increased risk of lung tissue injury in patient with AATD may be due to inadequately controlled NE caused by insufficient AAT. We believe that by inhibiting NE, alvelestat has the potential to reduce the destruction of lung tissue and stabilize clinical deterioration in patients with severe AATD-LD patients. BOS is characterized by anti-organ auto-immune responses, either graft versus host (in SCT) or host versus graft (in lung transplant), exacerbated by elevated neutrophils in the lung and excess NE activity, leading to lung damage through elastin breakdown in the tissue and progressive fibrosis, and ultimately respiratory failure. By inhibiting NE, alvelestat will reduce the accelerating effects of NE-driven inflammation on BOS.

Background of Alpha-1-Antitrypsin Deficiency and Bronchiolitis Obliterans Syndrome

AATD is a genetic disease. There are estimated to be 50,000 people in North America and 60,000 in Europe with severe AATD, which we define as AATD in patients with either a PiZZ genotype or Null/Null genotype although there are approximately only 10,000 people diagnosed in North America. The major function of AAT in the lungs is to protect the connective tissue from NE released from triggered neutrophils. In the majority of people, the lungs are defended from NE attack by AAT, which is a highly effective inhibitor of NE. Severe AATD patients produce ineffective or no AAT and are, therefore, unable to defend against NE attack. As a result, severe AATD patients commonly experience degeneration of lung function, such as early-onset pulmonary emphysema, which significantly affects quality of life and life expectancy. They may require oxygen therapy in order to continue their daily lives and the most severe patients may require lung transplantation.

AATD is the result of a mutation of the SERPINA1 gene. Most people with severe AATD inherit two copies of the defective PiZ allele, or gene variant, of the SERPINA1 gene, resulting in a PiZZ genotype. Patients with a PiZZ genotype have approximately 15% of normal AAT levels. Individuals who inherit two copies of the Null allele, resulting in a Null/Null genotype, do not produce any AAT. These two groups are at very high risk of developing lung disease. AATD patients with the PiZZ genotype experience loss of lung tissue as measured by lung density on computed tomographic (CT) scanning, a decline in FEV1, a standard measure of exhalation and poor quality of life. Respiratory disease can progress to need for chronic oxygen therapy, lung transplant and death. The annual mortality rate in this genotype estimated to be 4%. Given that individuals with the Null/Null genotype do not produce any AAT, we believe that they are likely to experience an even greater annual decline in FEV1.

BOS is a rare progressive fibrosing disease of the lungs affecting approximately 6% of the estimated 12,000 stem cell transplants a year in the United States, often as part of graft versus host disease. For lung transplants, approximately 5% of the patients develop BOS by 5 years, which is the leading cause of retransplant and mortality. BOS is characterized by neutrophil infiltration in the lung, excess neutrophil elastase and inflammation. The pathology of BOS in stem cell transplant and lung transplant is overlapping.

Current Treatment Landscape for Alpha-1-Antitrypsin Deficiency and Bronchiolitis Obliterans Syndrome

AATD patients are monitored by pulmonary functions tests, including spirometry. Treatment involves bronchodilators and inhaled corticosteroid medications and pulmonary rehabilitation, with increased intensity of therapy guided by disease severity. Surgical options include lung volume reduction surgery and lung transplantation. Both are highly invasive, and transplantation is only an option for a portion of patients with end-stage disease despite optimal therapy.

Augmentation therapy is available for AATD, using a partially purified plasma preparation highly enriched for AAT that is administered weekly by intravenous infusion. This therapy was first approved by the FDA in the 1980s based on its biochemical efficacy, meaning its ability to raise blood levels of AAT, but not based on clinical outcome data. Several observational studies have suggested that AAT augmentation therapy may slow the rate of decline in lung function in a subgroup of AATD patients with moderate-to-severe airflow obstruction. In a randomized, controlled trial of augmentation therapy, patients had some reduction in the progression of emphysema, as assessed by measuring lung density using computed tomography. The study did not show significant slowing in the decline in FEV1.

We believe that current therapies for AATD are inadequate. Surgical options are limited to a few patients, are highly invasive, have variable results, and do not address the underlying pathology of AATD. AAT augmentation therapy, while FDA approved, was not approved on the basis of clinical outcome data. In Europe Regulatory approval was on efficacy based on slowing of CT density decline, without effects on other measures such as FEV1 or patient-reported outcome. Further, AAT augmentation therapy is generally not reimbursed and thus is not currently available to patients in several jurisdictions, including some key European markets. In addition, AAT augmentation therapy requires potentially inconvenient weekly intravenous infusions.

There are very limited options for patients with BOS associated with graft versus host disease following stem cell transplant (“SCT”) or those with host versus graft disease and chronic organ rejection following lung transplant. Current therapies are immunosuppressive regimes, with risk of infection along with azithromycin which has both anti-inflammatory and antimicrobial activity. However, there are no approved treatments and the outcome for patients with BOS has not improved in the last 20 years. In development are the Janus Kinase (JAK1) inhibitor, itacitinib and JAK2 inhibitor ruxolitinib (Incyte Corporation) in Phase 1/Phase2 studies in lung transplant-associated and SCT-associated BOS respectively, AI Therapeutics is investigating an inhaled formulation of sirolimus (LAM-001) in Phase 1 and Isopogen allogeneic bone marrow derived mesenchymal stem cells for chronic lung allograft dysfunction, also in Phase 1, and Liposomal inhaled cyclosporin-A (Zambon) in Phase 2 in BOS following SCT and in Phase 3 global pivotal trials in BOS associated with lung transplant.

Our Approach

Our product candidate for treating severe AATD is alvelestat, a potent, specific oral small molecule that is designed to inhibit NE. We believe that by inhibiting NE, alvelestat has the potential to reduce the enzymatic destruction of lung tissue. Furthermore, we believe that convenient oral dosing of alvelestat could provide a significant advantage compared to the current treatments for AATD of surgery or weekly intravenous AAT augmentation therapy. In our clinical development programs, we intend to generate data to allow healthcare authorities to take evidence-based decisions. We do not expect alvelestat to be effective in hepatic disease which is due to the damaging effect of accumulated abnormal ZZ protein in the liver, rather than the protein deficiency. Liver disease occurs in approximately 10% cases of severe AATD, predominantly in children.

As BOS is driven by elevated neutrophils in the lung and excess NE activity, leading to lung damage through elastin breakdown in the tissue and progressive fibrosis, and ultimately respiratory failure we believe our approach using alvelestat to inhibit NE has significant advantages. By inhibiting NE, we believe alvelestat will reduce the accelerating effects of NE-driven inflammation on BOS leading to increased success rate of SCT and lung transplant. The investigator-led clinical program is designed to generate data on clinical endpoints that would potentially support registration and reimbursement in SCT.

Clinical Development of Alvelestat

Phase 2 Clinical Trials

Although prior clinical trials of alvelestat were in respiratory indications other than AATD, we believe that the clinical benefit observed in these trials and the biomarker evidence of treatment effect make alvelestat a promising potential product candidate for treating severe AATD. In particular, we believe the results from the Phase 2 clinical trials in bronchiectasis and CF are most relevant in assessing alvelestat’s potential to treat severe AATD.

Phase 2 Clinical Trials in AATD

We successfully completed a Phase 2 proof-of-concept clinical trial of alvelestat in patients with severe AATD with emphysema in the United States and Europe. Due to the effects of the COVID-19 pandemic on this vulnerable population and the impact on enrollment timelines, we closed the study to enrollment at 99 patients at the end of 2021. This is lower than the protocol defined number of patients in the original study design. This was a 12-week, double-blind, placebo-controlled clinical trial examining two doses of alvelestat compared to placebo with three primary endpoints along the pathogenic pathway of lung disease in AATD patients. These primary endpoints were plasma desmosine (a biomarker of protease-driven elastin breakdown), Aα-Val360, a specific biomarker of NE proteolytic activity, and neutrophil elastase activity in blood. Secondary endpoints were safety, exacerbation frequency, and pharmacokinetics. Exploratory endpoints were St. Georges Respiratory Questionnaire (SGRQ) which is a patient-reported outcome of Respiratory Health Status and lung function tests, including FEV1.

We enrolled only adult patients with PiZZ or Null/Null genotypes or rare genotypes with severe deficiency of alpha-1 antitrypsin (<11 microMolar) with confirmed emphysema, who have not received AAT augmentation therapy or have undergone a wash-out period following AAT augmentation therapy.

Following successful completion of the Phase 2 study, we received regulatory feedback from end-of-Phase 2 meetings with FDA and the EMA related to our alvelestat program for the treatment of severe AATD-LD. Based on clear recommendations from the FDA and the EMA, the Company is designing a single, global, Phase 3 study evaluating the 240 mg dose of alvelestat versus placebo in patients with severe AATD-LD to support applications for full marketing approvals in both the U.S. and EU. The Company's proposed Phase 3 study has two independent primary endpoints, i) a Patient- Reported Outcome (PRO), as guided by the FDA, and ii) lung density measured by CT scan, as guided by the EMA.

The proposed primary endpoints are based on changes in the St. George's Respiratory Questionnaire (SGRQ) Activity domain and in lung density measured by CT scan. Additional supportive secondary endpoints are being proposed, including biomarker-based endpoints that may provide sufficient data to validate the biomarkers for future studies.

If successful, this proposed Phase 3 study, with an expected duration of 12-18 months and an enrollment target of approximately 200 patients, is expected to support full regulatory approvals in both the U.S. and EU without an additional confirmatory trial. This could provide the Company with a path to full approval of alvelestat based on a Phase 3 trial similar in size and length to what would be required for an accelerated or conditional approval based on biomarkers. Mereo also believes that this proposed study, if successful, will support more productive initial reimbursement discussions with payors following potential regulatory approvals.

An investigator-led, placebo-controlled-Phase 2 study in AATD is ongoing in the US. This has enrolled 60 patients with SZ as well as ZZ or Null/Null and rare severe mutations, and includes dosing alvelestat on top of stable augmentation. This study will provide additional supportive data for use of alvelestat. No safety signals of concern have been detected through the regular Independent Data Monitoring Committee review.

We received an investment from, and are collaborating with, the venture philanthropy arm of the Alpha-1 Foundation, The Alpha-1 Project Inc ("TAP"), with respect to our alvelestat development program. TAP is investing in the program subject to our meeting agreed-upon development milestones. We also agreed to issue warrants to TAP to subscribe for shares in us, at certain future dates and subject to TAP making agreed-upon investments in the alvelestat development program. On October 8, 2018, we entered into a funding agreement with TAP, which provided for funding of up to $0.4 million. On November 1, 2018, the first tranche of $0.1 million was received and as a result we issued 41,286 warrants to subscribe for our ordinary shares at an exercise price of £0.003 per share. On April 21, 2022, the second tranche of $0.2m was received, and 1,101,683 warrants to subscribe for our ordinary shares were issued at an exercise price of £0.003 per share.

Phase 1b/2 Clinical Trial in Bronchiolitis Obliterans Syndrome (BOS)

An investigator-sponsored open-label Phase1b/2 study in Bronchiolitis Obliterans Syndrome (BOS) following allogeneic stem cell transplant is being conducted to inform a potential future indication expansion strategy. The study uses within patient dose escalation from 60 mg BID up to 240 mg BID, over the initial 8 weeks of study, with treatment continued for up to 6 months. Interim results from 7 patients enrolled in the Phase 1b study were reported in December 2021 showing stabilization or improvement in lung function measured by Forced Expiratory Volume in 1 second, (FEV1) in 6 of 7 patients, and supportive biomarker responses, with reduction in neutrophil elastase and the mature elastin breakdown product (desmosine) and reductions in markers of collagen synthesis associated with fibrosis. The Phase 1b component (10 patients) has completed enrollment. Review of the safety and efficacy data from Phase 1 enabled the decision on the optimal dose and the study will progress to enroll up to an additional 24 patients to assess primary lung function endpoint in the Phase 2 component, with initiation in the second half of 2022. No safety signals have been detected in this study.

Phase 1b/2 Clinical Trial in Hospitalized Patients with COVID-19 Respiratory Disease

The top-line results of an investigator-initiated Phase 1b/2 double-blind, randomized, placebo-controlled study in hospitalized adult patients with COVID-19 Respiratory Disease were reported in December 2021. The results demonstrated a safety profile consistent with previous studies, and in the alvelestat arm, a reduction (an improvement) of 2 points or more in

the World Health Organization (WHO) Severity Score in 62.5% (5/9) of the patients compared to 28.5% (2/7) of patients in the placebo arm at day 5. At day 7, 87.5% (7/8) of patients in the alvelstat arm had improved by 2 points or more compared to 57% (4/7) of patients in the placebo arm. Inflammatory and pro-coagulopathy biomarkers were also supportive.

Etigilimab (MPH-313) for the Treatment of Advanced Solid Tumors

Overview

We acquired etigilimab in the Merger with Mereo BioPharma 5 (formerly OncoMed Pharmaceuticals, Inc.) in 2019. TIGIT (T-cell immunoreceptor with Ig and ITIM domains) is an inhibitory receptor and via interactions with its ligands may block T-cells from attacking tumor cells. The anti-TIGIT therapeutic candidate, etigilimab, is an IgG1 human-specific

antibody. It is intended to activate the immune system, through multiple mechanisms and enable anti- tumor activity. In preclinical studies with anti-TIGIT antibodies, immune activation and robust anti-tumor activity have been observed—both as a single agent and in combination with other cancer immunotherapeutics including anti-PD1. At the 2017 American Association of Cancer Research ("AACR") meeting, preclinical data demonstrating the capacity of an anti-TIGIT antibody to induce long-term immune memory and durable anti-tumor response was presented. Also, at the 2018 AACR meeting data that showed that anti-TIGIT antibody treatment reduced the abundance of regulatory T-cells (Tregs) within tumors in animal models, and mechanistic studies that demonstrated an important contribution of effector function for anti-tumor efficacy in animal models was presented.

Our Approach

A Phase 1a/b clinical trial of etigilimab enrolled patients with advanced solid tumors into either a Phase 1a single-agent portion (dose escalation in all patients and expansion in selected tumor types) or Phase 1b combination portion in with nivolumab (dose escalation). 23 patients were treated in the Phase 1a dose escalation portion of the study with doses up to 20mg/kg every two weeks and 10 patients were treated in the Phase 1b combination portion of the study at doses up to 20 mg/kg every two weeks in combination with nivolumab. Tumor types in the Phase 1a portion of the study were colorectal cancer (6 patients), endometrial cancer (4 patients), head & neck cancer (4 patients), pancreatic cancer (2 patients), triple negative breast cancer (2 patients) and five other tumor types and those included in the Phase 1b portion of the study included gastric cancer (3 patients) and six other tumor types. No dose limiting toxicities were observed in the Phase 1a or 1b portions of the study. The most common reported related TEAEs in the Phase 1a portion of the study were pruritus (4 patients, 17.4%) and fatigue, nausea, rash and maculopapular rash (each reported by 3 patients, 8.7%). In the Phase 1b portion of the study, the most common reported related TEAEs were fatigue (3 patients, 30.0%) and pruritus, rash, and pruritic rash (each reported by 2 patients, 20.0%). There was only one treatment-related serious adverse event in the Phase 1a portion (autoimmune hepatitis) and there were no treatment-related serious adverse events in the Phase 1b portion of the study.

None of the patients in the Phase 1a portion had an objective response and 30% had stable disease. One of the ten patients in the Phase 1b portion had an objective response and one additional patient had stable disease. The study has now completed enrollment. A biomarker analysis of patients enrolled in the Phase 1a portion (single agent etigilimab) revealed a dose-dependent reduction of peripheral Tregulatory cells (Treg) with no change evident in circulating CD8 cells, resulting in an increased CD8/Treg ratio. The study also revealed increased proliferation and activation of effector Tcells and NK cells in response to etigilimab.

We have completed enrollment in an open label Phase1b/2 basket study (the ACTIVATE study) evaluating etigilimab in combination with nivolumab on three rare tumors, two specific subtypes of soft-tissue sarcomas, uveal melanoma and testicular germ cell cancer, three gynecological carcinomas, cervical, endometrial and ovarian carcinomas and any solid tumor with high mutation burden, all in the recurrent/metastatic setting. These indications were selected based on observations of clinical activity in our prior Phase 1a/1b study and/or based on a comprehensive biomarker analysis of solid tumors which revealed tumor types with a high prevalence of expression of TIGIT and its principal ligand poliovirus receptor (PVR) and concordant expression of TIGIT and PD1. The selected tumor types have shown responsiveness to anti-PD1 therapies with response rates generally ranging from 5-20%. The combination of etigilimab and anti-PD1 may lead to improved responses in these patients.

We enrolled a total of 76 patients in the Phase 1b part of the study. The trial is evaluating objective response rate as a primary endpoint and is also evaluating safety, duration of response, pharmacokinetics, anti-drug antibodies, progression-free survival and additional secondary and exploratory endpoints. The study was designed to expand select cohorts of patients, based on outcomes, to further evaluate responses to etigilimab and anti-PD1. Biomarker analyses have been conducted on tumor tissues and blood samples from treated patients, including quantification of levels of tumor- associated TIGIT, PVR and related biomarkers to evaluate their potential utility for selecting patients most likely to respond to the combination of etigilimab and anti-PD1.

We reported an interim clinical and biomarker data update on this study in September 2022. At the time of the data cut-off, there were 63 efficacy-evaluable checkpoint inhibitor-naïve (CPI-naive) subjects with a minimum of 1 staging scan at 8 (+/-1) weeks and RECIST 1.1 response assessment or documented clinical progression.

As at the cut-off date, there 3/7 CPI-naïve cervical cancer subjects who had confirmed complete responses (cCRs), with duration on study of >143 days, 162 days and > 284 days. Two additional patients had stable disease (SD). Overall, the cervical cancer cohort had an objective response rate of 43% and a disease control rate of 71%.

Additionally, as of the cut-off date, 1/6 CPI-naïve metastatic uveal melanoma subjects had confirmed partial response (cPR) at >347 days and 2 subjects had SD for 175 and 294 days for an ORR of 17% and DCR of 50%.

Biomarker data presented at ESMO 2022 evaluated tumors for baseline expression of PVR, TIGIT, PD-L1 and CD 226 by multiple modalities including immunohistochemistry (IHC) assays. High PVR expression was observed in subjects with decreases in target lesions (TL) from baseline and RECIST 1.1 responses. Additional noteworthy responses observed in subjects with cancer types not typically responsive to CPI monotherapy, with tumors that had high PVR expression and were either PD-L1 negative (CPS <1%), or PD-L1 low (CPS≤3%) include, (i) an ovarian PR (-80% target lesion (TL) decrease, ongoing >255 days, PD-L1 negative), (ii) an endometrial PR (-69% TL decrease, ongoing >150 days, MMR proficient, PD-L1 CPS=3%), (iii) a dedifferentiated liposarcoma PR (-80% TL decrease, ongoing cPR >267 days, high TIGIT, PD-L1 CPS=1%), and (iv) a recurrent/metastatic testicular GCT patient with stable, near normalization of elevated tumor marker alpha feto protein (doing well clinically on study >127 days), PD-L1 negative. The presentation at ESMO 2022 demonstrated robust target engagement in patients as evidenced by significant decreases in peripheral T regulatory cells while maintaining circulation levels of CD8 cells. Increases in proliferating T-cells subsets (CD8, CD4), proliferating NK cells, and intracellular cytokines (IFNg, IL2, and TNFa) were observed and sustained longitudinally. Additionally, etigilimab plus nivolumab reduced TPEX cells (CD8+CCR7+PD1+TIGIT+), progenitor cells believed to be committed to an exhausted-like fate. Further data was reported showing reductions in circulating tumor DNA (ctDNA) measured at ~5-6 weeks post-treatment correlated with clinical benefit.

In April 2021, the Company entered into a partnership with Cancer Focus Fund for a Phase 1b/2 study of etigilimab in clear cell ovarian cancer to be conducted at The University of Texas MD Anderson Cancer Center. The Phase 1b/2 study of etigilimab in combination with nivolumab, in clear cell ovarian cancer, is being financed by Cancer Focus Fund in exchange for upfront consideration of $1.5 million of the Company's shares and additional payments based on the achievement of certain milestones. Clear cell ovarian cancer is a rare cancer that accounts for approximately 5 to 10% of all ovarian carcimomas in North America. MD Anderson are planning to follow the per protocol procedure to expand the Phase 1b/2 study from an initial 10 patients to 20 patients in the Phase 2 portion of the study.

We have worldwide rights to etigilimab.

Partnered Programs and Programs Available for Partnering

Navicixizumab (OMP-305B83) for Treatment of Ovarian Cancer

We acquired Navicixizumab ("Navi") in the Merger. In January 2020, we out-licensed Navi to OncXerna. See "—Material Agreements—Licensing Agreement for Navicixizumab." In addition, Navi is the subject of the CVR Agreement which sets forth certain rights and obligations of us with respect to Navi. See "—Material Agreements—CVR Agreement Between Us and Computershare—The NAVI Milestones."

In September 2022, OncXerna announced the initiation of dosing in a Phase 2 basket trial evaluating the anti-DLL4/VEGF bispecific antibody navicixizumab, alone or in combination with chemotherapy, in patients with select advanced solid tumors. The trial is a multicenter, open-label, signal finding study with cohorts in colorectal and triple negative breast cancer currently open for enrollment. The colorectal cancer cohort is evaluating navicixizumab alone and in combination with irinotecan, while the triple negative breast cancer cohort is evaluating navicixizumab alone and in combination with paclitaxel. Per the trial protocol, two additional cohorts designed to enroll patients with ovarian cancer and gastric or gastroesophageal cancer may be opened in the future.

Acumapimod (BCT-197) for the Treatment of AECOPD

Overview

Acumapimod is a novel, orally active p38 MAP kinase inhibitor in development for first-line acute therapy in patients with a severe hospitalized AECOPD.

Background of COPD and AECOPD

Of all COPD-related hospital admissions in the United States, approximately 63% are for AECOPD patients, representing more than 1.5 million emergency room visits in the United States accounting for approximately 45% to 50% of the total direct costs of COPD.

Current Treatment Landscape of AECOPD

The current recommended management for AECOPD includes bronchodilators, systemic corticosteroids and antibiotics, and with supportive oxygen therapy. We believe that there is a significant medical need for a drug which to improve the

outcome of severe hospitalized AECOPDs.

Clinical Development of Acumapimod

Phase 2 Dose-Ranging Clinical Trial in Severe AECOPD

Two dosing regimens of acumapimod were compared to placebo, in patients hospitalized for AECOPD. Both showed a statistically significant change in FEV1 from baseline to Day 7. The high-dose acumapimod group showed a greater than 50% reduction in the number of rehospitalization for recurrent AECOPD compared to the placebo group, at Days 90 through 150. Acumapimod was observed to be generally safe and well tolerated. In 2019, end of Phase 2 and Scientific Advice meetings were held with the FDA and EMA enabling design of a global Phase 3 program.

We intend to explore out-licensing or sale opportunities with third parties for further funding and development of acumapimod.

Leflutrozole (BGS-649) for the Treatment of Hypogonadotropic Hypogonadism (HH)

Overview

Leflutrozole is in development for the treatment of infertility associated with HH in obese and overweight men. Leflutrozole is a once-weekly oral aromatase inhibitor designed to normalize testosterone levels. In Phase 2 trials leflutrozole was also shown to increase fertility parameters.

Background of Infertility Associated with Hypogonadotropic Hypogonadism in Obese and Overweight Men

Symptoms that are most commonly associated with testosterone deficiency include reduced libido, erectile dysfunction, along with a decrease sperm counts. Overweight and obesity is associated with increased levels of aromatase. Aromatase converts testosterone to estradiol, which directly suppresses gonadotropins, Follicle Stimulating Hormone (FSH) and Luteinizing Hormone (LH), leading to testicular dysfunction, with impaired production of testosterone and sperm, resulting in infertility. Inhibition of excess aromatase may increase the levels of FSH and LH, resulting in normalization of testosterone production and improving sperm counts and potentially fertility.

Current Treatment Landscape of Infertility Associated with Hypogonadotropic Hypogonadism in Obese and Overweight men

The current treatment is with injectable FSH, either alone, or in combination with injectable Human Chorionic Gonadotropin which has LH-like activity. If unsuccessful, Assisted Reproductive Technology (ART) using intrauterine insemination, in vitro fertilization and intracytoplasmic sperm injection, and including testicular sperm extraction for those with very low sperm count may be required.

Clinical Development of Leflutrozole

Phase 2b Clinical Trial in Hypogonadotropic Hypogonadism

We conducted a randomized double-blind, dose-ranging, trial of three doses of leflutrozole or placebo in obese males with HH. The primary endpoint of the trial was percentage of patients whose testosterone levels normalized at week 24. Other endpoints were, changes in gonadotropins LH and FSH, sexual function and semen analysis, and evaluation of safety and tolerability.

All doses of leflutrozole normalized total testosterone levels in over 75% of subjects after 24 weeks of treatment, with a dose-dependent increase in both LH and FSH. The trial also showed an improvement in sperm counts. There was no effect on exploratory measures of erectile dysfunction and low libido.

Leflutrozole was observed to be well tolerated. An increased incidence of elevated haematocrit levels was observed in each of the treatment arms of the trial, consistent with increasing testosterone levels, with a small increase in blood pressure at the two highest doses. A subset of patients entered into a six-month extension study to examine if leflutrozole resulted in reduction in bone mineral density (BMD) at 48 weeks of treatment. None of the doses met the lower bound of the pre-specified safety criterion of reduction in BMD.

We concluded that the future development of leflutrozole should focus on male infertility associated with HH. We intend to develop a clinical and regulatory path accordingly. We intend to explore out-licensing or sale opportunities with third parties for the further development of leflutrozole.

Material Agreements

Licensing Agreement with Ultragenyx for setrusumab

On December 17, 2020, we announced that we entered into a license and collaboration agreement with Ultragenyx, for setrusumab for OI. Under the terms of the agreement, Ultragenyx will lead future global development of setrusumab in both pediatric and adult patients. We granted Ultragenyx an exclusive license to develop and commercialize setrusumab in the U.S. and rest of the world, excluding Europe, where we retain commercial rights. Each party will be responsible for post-marketing commitments in their respective territories. Under the terms of the agreement, Ultragenyx made an upfront payment of $50 million to Mereo and will pay up to $254 million in development, regulatory and commercial milestones and tiered double digit percentage royalties to us on net sales outside of Europe and we will pay a fixed double digit percentage royalty to Ultragenyx on net sales in Europe. Under the terms of our 2015 agreement with Novartis, we will pay Novartis a percentage of proceeds, subject to certain deductions, and we will receive a substantial majority of the payments from Ultragenyx.

Licensing Agreement with AstraZeneca

In October 2017, we announced that we entered into an exclusive license and option agreement (the "License Agreement"), to obtain from AstraZeneca an exclusive worldwide, sub-licensable license under AstraZeneca's intellectual property rights relating to certain product candidates containing a NE inhibitor, including product candidates that contain alvelestat, with an option to acquire such intellectual property rights following commencement of a pivotal trial and payment of related milestone payments (the "Option"), together with the acquisition of certain related assets.

Upon entering into the License Agreement, we made a payment of $3.0 million and issued 490,798 ordinary shares to AstraZeneca, for an aggregate upfront payment equal to $5.0 million. In connection with certain development and regulatory milestones, we have agreed to make payments of up to $115.5 million in the aggregate and issue additional ordinary shares (or ADS equivalent) to AstraZeneca for licensed product candidates containing alvelestat. In addition, we have agreed to make payments to AstraZeneca based on specified commercial milestones of the product candidate. In the event that we sub-license alvelestat, we have also agreed to pay a specified percentage of sublicensing revenue to AstraZeneca. Otherwise, we have agreed to make royalty payments to AstraZeneca equal to ascending specified percentages of tiered annual worldwide net sales by us or our affiliates of licensed product candidates (subject to certain reductions), ranging from the high single digits to low double digits. Royalties will be payable on a licensed product-by-licensed product and country-by-country basis until the later of ten years after the first commercial sale of such licensed product in such country and expiration of the last patent covering such licensed product in such country that would be sufficient to prevent generic entry. Under the License Agreement, we may freely grant sub-licenses to affiliates upon notice to AstraZeneca and we must obtain AstraZeneca's consent, not be unreasonably withheld, to grant sub-licenses to a third party. We have agreed to use commercially reasonable efforts to develop and commercialize at least one licensed product. In addition, we are generally responsible for costs related to the development and commercialization of the licensed products under the License Agreement.

The License Agreement will expire on the expiry of the last-to-expire royalty term with respect to all licensed product candidates. Upon the expiration of the royalty term for a licensed product in a particular country, the licenses to us for such product in such country will become fully-paid and irrevocable. Prior to exercise of the Option, if at all, we may terminate the License Agreement upon prior written notice. Either party may terminate the agreement upon prior written notice for the other party's material breach that remains uncured for a specified period of time or insolvency. AstraZeneca agreed not to assert any AstraZeneca intellectual property rights that were included in the scope of the License Agreement against us.

Licensing Agreement for Navicixizumab

On January 13, 2020, we entered into a global license agreement with OncXerna for the development and commercialization of navicixizumab, an anti-DLL4/VEGF bispecific antibody currently being evaluated in an ongoing Phase 1b study in combination with paclitaxel in patients with advanced heavily pretreated ovarian cancer. Navi previously completed a Phase 1a monotherapy study in patients with various types of refractory solid tumors and is one of two product candidates we acquired through the Merger.

Under the terms of the license agreement, OncXerna received an exclusive worldwide license to develop and commercialize Navi. We received an upfront payment of $4.0 million and in February 2022 we received an additional payment of $2.0 million, following satisfaction of a milestone. OncXerna will be responsible for all future research, development and commercialization of Navi. Additionally, we will be eligible to receive up to $300 million in future clinical, regulatory and commercial milestones, tiered royalties ranging from the mid-single-digit to sub-teen percentages on global annual net sales of Navi, as well as a negotiated percentage of sublicensing revenues from certain sublicensees.

As a consequence of the license agreement with OncXerna, and in accordance with the terms and conditions of the CVR Agreement, holders of CVRs pursuant to the CVR Agreement will be entitled to receive certain eligible cash milestone payments made to us under the license agreement relating to the development and commercialization of Navi. See "—CVR Agreement Between Us and Computershare."

In February 2022, we received a milestone payment of $2.0 million (£1.5 million) under the Navi License Agreement with OncXerna. An associated payment was made to the former shareholders of Mereo BioPharma 5, Inc. under the CVR Agreement of a total of $0.9 million (£0.7 million), after deductions of costs, charges and expenditures.

CVR Agreement Between Us and Computershare

Following the closing of the Merger, OncoMed's stockholders received, in exchange for each outstanding share of OncoMed common stock owned immediately prior to the closing of the Merger (except for any dissenting shares): (1) a number of our ADSs determined by reference to an exchange ratio, and (2) one contingent value right (a "CVR"), representing the right

to receive contingent payments if specified milestones are achieved within agreed time periods, subject to and in accordance with the terms and conditions of the Contingent Value Rights Agreement (the "CVR Agreement"), dated April 23, 2019, by and among Computershare, as rights agent, and us.

Except in limited circumstances, the CVRs may not be transferred, pledged, hypothecated, encumbered, assigned or otherwise disposed of.

Milestone Events and Payments

The CVR milestones relate to Mereo BioPharma 5 (formerly OncoMed)'s etigilimab and Navi therapeutic candidates, though the milestone relevant to etigilimab can no longer be achieved and no payments will become due or payable to CVR holders in relation to etigilimab.

The contingent payments would become payable to the rights agent, for subsequent distribution to the holders of the CVRs, upon the achievement of a milestone relating to NAVI as follows:

The NAVI Milestones

A cash payment will be made to CVR holders if, (1) within eighteen months following the closing of the Merger, we or any of our subsidiaries enters into a definitive partnership agreement, collaboration agreement, joint venture agreement, profit sharing agreement, license or sublicense agreement, asset sale agreement, stock sale agreement, investment agreement or similar agreement duly approved by our Board with one or more third parties regarding Navi, and (2) within five years of the closing of the Merger, we or any of our subsidiaries actually receives certain eligible cash milestone payments.

On January 13, 2020, we entered into a global license agreement with OncXerna for the development and commercialization of Navi. Eligible cash milestone payments pursuant to the NAVI Agreement (as defined in the CVR Agreement) will include each cash milestone payment payable to our Company or one or more of our subsidiaries pursuant to a NAVI Agreement (or any agreement contemplated by such NAVI Agreement), except for any (i) royalty or similar sales-based payment that is measured, in whole or in part, by reference to the quantity of Navi that is produced or sold or the revenues (or a formula that makes reference to such revenues) derived therefrom and (ii) for the avoidance of doubt only, any fees for service, research and development funding, reimbursement of intellectual property filing, prosecution, litigation and maintenance-related expenses or reimbursement of manufacturing expenses received from a counterparty pursuant to a NAVI Agreement.

If a NAVI Milestone is achieved, holders of CVRs would be entitled to receive an amount in cash equal to 70% of the aggregate principal amount actually received by us or one or more of our subsidiaries (other than NAVI Sub), net of (A) any tax (including any applicable value added or sales taxes and including any tax which would be payable but for the utilization of a relief), (B) 50% of any expenditure by us or our subsidiaries pursuant to the budget set forth on a confidential schedule to the CVR Agreement, and (C) any other reasonable cost or expense attributable to the receipt of such payment (including (i) any costs, reasonable out-of-pocket fees, expenses or charges we incurred in excess of the commitments provided for in the budget set forth on a confidential schedule to the CVR Agreement, (ii) any costs, reasonable out-of-pocket fees, expenses or charges we incurred under the NAVI Agreement, and (iii) any costs, reasonable out-of-pocket fees, expenses or charges we incurred, or for which we are responsible, in connection with the preparation, negotiation and execution of the relevant NAVI Agreement, in each case to the extent such costs, out-of-pocket fees, expenses or charges have not been previously accounted for in the calculation of a prior NAVI Milestone payment).

The NAVI milestone payments are subject to a cash consideration cap, pursuant to which the aggregate principal amount of all cash payments made to holders of CVRs by us shall in no case exceed $79.7 million. If the aggregate principal amount to be paid to holders of CVRs by us pursuant to the CVR Agreement would, together with the aggregate principal amount of any prior such cash payments, otherwise exceed $79.7 million, then the applicable NAVI Milestone payment will be appropriately reduced.

If a NAVI Milestone occurs at any time prior to the fifth anniversary of the closing of the Merger, being April 23, 2024, and on each such occurrence, then, thirty days following the achievement thereof, we are obligated to notify the rights agent and pay the amounts owed pursuant to the NAVI Agreement.

The receipt of the upfront milestone payment of $4.0 million by us under the Navi License Agreement with OncXerna in January 2020 resulted in a payment to CVR holders of approximately 1.2 cents per CVR, a total of approximately $0.5 million, after deductions of costs, charges and expenditures.

The receipt of the milestone payment of $2.0 million by us under the Navi License Agreement with OncXerna in February 2022 resulted in a payment to CVR holders of approximately 2.3 cents per CVR, a total of approximately $0.9 million, after deductions of costs, charges and expenditures.

Novartis Agreements

In July 2015, three of our wholly-owned subsidiaries, Mereo BioPharma 3 Limited, Mereo BioPharma 2 Limited, and Mereo BioPharma 1 Limited (the "Subsidiaries"), entered into asset purchase agreements (the "Purchase Agreements"), to acquire from Novartis rights to setrusumab, acumapimod, and leflutrozole (the "Compounds"), respectively, and certain related assets (together with the Compounds, the "Novartis Assets").

Under the Purchase Agreements, we have agreed to make tiered royalty payments to Novartis based on annual worldwide net sales of product candidates that include the Compounds (the "Acquired Novartis Product Candidates"), at percentages ranging from the high single digits to low double digits. In the event that the parties agree or it is otherwise determined in accordance with the Purchase Agreements that we require third-party intellectual property rights to exploit the Acquired Novartis Product Candidates, we are entitled to offset a specified percentage of amounts paid to such third parties in consideration for such intellectual property rights against the royalties due to Novartis. The royalty payments are payable for a period of ten years after the first commercial sale of an Acquired Novartis Product. We further agreed that in the event of a change in control that involves the transfer, license, assignment or lease of all or substantially all of a Subsidiary's assets, including a Compound and related assets, we will pay Novartis a percentage of the proceeds of such transaction, with the majority of the proceeds being retained by us. No payment, however, is required with respect to any transaction of Mereo BioPharma Group plc involving its equity interests, a merger or consolidation of it, or a sale of any of its assets.

We also entered into a sublicense agreement with Novartis (the "Sublicense Agreement"), pursuant to which Novartis granted us an exclusive, worldwide, royalty-bearing sublicense for certain therapeutic antibody product candidates directed against sclerostin (the "Antibody Product Candidates"), including setrusumab. Under the Sublicense Agreement, we have agreed to pay Novartis royalties in the low single digits on worldwide net sales of Antibody Product Candidates. Royalties will be payable on a country-by-country basis until the later of expiration of the last valid claim of the licensed patents covering the Antibody Product Candidates in a country and ten years after the first commercial sale of the Antibody Product Candidates in such country, with a maximum royalty term of 12 years after the first commercial sale of the Antibody Product Candidates in such country. We have also agreed to pay Novartis up to $3.25 million in development and regulatory milestones, and to use commercially reasonable efforts to develop and commercialize an Antibody Product. The Sublicense Agreement will expire on the earlier of the termination of the agreement under which Novartis is granting us a sublicense (the "Original License Agreement") and, on a product-by-product and country-by-country basis, the expiration of the royalty term with respect to such Antibody Product Candidate in such country. The Original License Agreement has a perpetual term and may be terminated for breach or upon a change in control of the licensing party. We may terminate the Sublicense Agreement upon written notice to Novartis and either party may terminate the Sublicense Agreement for the other party's uncured material breach or bankruptcy.

Novartis Loan Note

On February 10, 2020, we entered into a £3.8 million convertible loan note instrument with Novartis pursuant to which we issued 3,841,479 unsecured convertible loan notes (the "Novartis Loan Note") with a maturity date of February 10, 2023, and warrants to purchase 1,449,614 ordinary shares, exercisable until February 2025.

On February 10, 2023, we amended the Novartis Loan Note, extending the maturity date to February 10, 2025. Pursuant to the amendment and a new warrant instrument, interest accrued to the amendment date was paid in cash, and warrants to purchase 2,000,000 ordinary shares at an exercise price of £0.150 per ordinary share were issued and are exercisable until February 10, 2028.

Agreements relating to June 2020 Private Placement

On June 3, 2020, we entered into a securities purchase agreement (the "June 2020 Purchase Agreement") with a number of new and existing principally U.S.-based institutional and accredited investors (the "June 2020 Private Placement") pursuant to which we received $70.0 million (£56.0 million) comprising: the allotment of ordinary shares at a subscription price of $19.4 (£15.5) million utilizing the pre-existing share authorities of the Company, and the subscription for Tranche 1 convertible loan notes ("Loan Notes") in an aggregate principal amount of $50.6 million (£40.5 million).

Following the passing of resolutions at our General Meeting on June 30, 2020, the Loan Notes automatically converted into ordinary shares of £0.003 each in the capital of the Company except that no new ordinary shares were issued which would result in any person holding in excess of 9.99 percent of the aggregate voting rights in the Company as a result of the relevant conversion. Accordingly, the automatic conversion resulted in Loan Notes in an aggregate principal amount of £21.8 million (together with accrued interest) converting into 125,061,475 ordinary shares on June 30, 2020. As of December 31, 2022, Loan Notes in an aggregate principal amount of £6.2 million remained outstanding and convertible into ordinary shares or ADSs in accordance with their terms.

The Purchasers also received warrants entitling the holders to subscribe for an aggregate of 161,048,366 new ordinary shares. As of December 31, 2022, there were 144,943,535 warrants outstanding to purchase ordinary shares at an exercise price of £0.348 per ordinary share, exercisable until June 30, 2023 and subject to the terms of the warrants. In accordance with the terms of the warrants, holders may elect to exercise their warrants on a cashless basis.

Cooperation Agreement with Rubric Capital Management LP

On October 28, 2022, Mereo entered into a cooperation agreement (the "Cooperation Agreement") with Rubric Capital Management LP, the Company's largest shareholder. Pursuant to the Cooperation Agreement, four new directors, Dr. Annalisa Jenkins, Dr. Daniel Shames, Mr. Marc Yoskowitz and Mr. Justin Roberts, were subsequently appointed to the Company's Board of Directors on November 10, 2022. Concurrent with these appointments taking effect, directors Dr. Peter Fellner, Dr. Brian Schwartz, Dr. Abdul Mullick and Ms. Anne Hyland resigned from the Board.

Manufacturing

We do not own or operate manufacturing facilities for the production of our product candidates, nor do we have plans to develop our own manufacturing operations in the foreseeable future. We have entered into manufacturing agreements with a number of drug substance, drug product, and other manufacturers and suppliers for alvelestat, etigilimab, acumapimod and leflutrozole and we intend to enter into additional manufacturing agreements as necessary. Following our license of alvelestat, we acquired certain clinical trial materials and we subsequently outsourced production of further clinical supplies to our own manufacturing suppliers. We also outsource certain product formulation trials. We expect that drug product pre- validation and validation batches will be manufactured to satisfy regulatory requirements where we progress product candidates to late-stage trials.

We intend to enter into contractual relationships for the manufacture of commercial supplies for setrusumab, alvelestat and etigilimab, if approved for commercial sale. Any batches of product candidates for commercialization will need to be manufactured in facilities, and by processes, that comply with the requirements of the FDA, the EMA, and the regulatory agencies of other jurisdictions in which we are seeking approval. We employ internal resources to manage our manufacturing contractors and ensure they are compliant with current good manufacturing practices.

Commercialization, Sales and Marketing

We do not have our own marketing, sales, or distribution capabilities. In order to commercialize our product candidates, if approved for commercial sale, we must either develop a sales and marketing infrastructure or collaborate with third parties that have sales and marketing experience. In December 2020, we entered into a license and collaboration agreement with Ultragenyx for setrusumab. For our other current and future product candidates we intend to take strategic decisions on whether to further develop them, potentially through to approval, directly commercializing globally or in certain territories, or to seek a partner for further development, co-development and/or commercialization. For product candidates we intend to commercialize or co-commercialize, we must either establish a sales and marketing organization with technical expertise and supporting distribution capabilities in major markets or potentially outsource aspects of these functions to third parties or partners.

Competition

We compete directly with other biopharmaceutical and pharmaceutical companies that focus on the treatment of solid tumor cancers and hematologic cancers, OI, AATD, AECOPD or male infertility. We may also face competition from academic research institutions, governmental agencies and other various public and private research institutions. We expect to face increasingly intense competition as new technologies become available. Any product candidates, including setrusumab, alvelestat, etigilimab, acumapimod and leflutrozole that we or our partners successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

We consider setrusumab's current closest potential competitors in development for the treatment of OI to be Amgen and UCB's anti-sclerostin antibody, romosozumab (Evenity), which was approved for osteoporosis in the United States in April 2019 and in December 2019 in Europe. In addition, Jiangsu Hengrui has commenced Phase 1 development of an anti-sclerostin antibody for osteoporosis in China, and Transcenta Holding has licensed the Chinese rights to the anti-sclerostin antibody blosozumab from Eli Lilly and Company ("Lilly") and plans to develop it for osteoporosis. Baylor College of Medicine has conducted a Phase 1 open label trial of fresolimumab, a TGF-B inhibitor, in adult OI patients, and Sanofi is conducting a Phase 1 trial of SAR439459, a related TGF-B inhibitor, in adult OI patients. Amgen has also conducted two studies of denosumab (Prolia) an anti-resorptive agent in pediatric patients with OI, however, both studies were terminated.

We consider alvelestat's current closest potential competitors for the treatment of severe AATD to be alpha-1- proteinase inhibitors that are administered intravenously in AAT augmentation therapy. Currently, there are four inhibitors on the market in the United States and the EU: Prolastin-C from Grifols, S.A. ("Grifols"), Aralast from Shire plc, now a subsidiary of Takeda Pharmaceutical Company Ltd ("Shire"), Zemaira from CSL Limited ("CSL"), and Glassia from Kamada Ltd. ("Kamada"). Kamada is also developing an inhaled version of augmentation therapy which is in Phase 3, and has a recombinant alpha-1 antitrypsin in early development. InhibRx, Inc. ("InhibRx") has completed a Phase 1 trial of INBRX-101, a recombinant human alpha-1 antitrypsin Fc fusion protein (rhAAT-Fc) for replacement therapy, and plans to initiate a potential registration study for potential accelerated approval. Apic Bio, Inc. ("Apic Bio") is in the early stages of developing a dual function vector (df-AAV) gene-therapy approach for AATD silencing the mutant Z-AAT protein and augmenting wildtype M-AAT production. Wave Life Sciences is in early stages of development of RNA base-editing oligonucleotide (WVE-0006) to restore wild-type protein in lung and liver disease, a program that has been recently partnered with GSK. Intellia Therapeutics is in early stages of developing CRISPR/Cas9 -based insertion of normal SERPINA1 gene, targeting lung disease (NTLA-3001). Peak Bio acquired an oral NE inhibitor, PHP-303 from Ph Pharma in March 2022. Peak Bio plans to conduct a Phase 2 proof-of-concept clinical trial in patients with severe AATD with trial initiation, potentially, in 2023 once they have received the necessary funding. Vertex Pharmaceuticals Inc. ("Vertex") has a small molecule corrector program for AATD in a Phase 1 trial focused on the liver disease, following Phase 2 trials with two other molecules with the same mechanism of action that were discontinued due to toxicity and efficacy. Centessa (previously Z-factor) was previously in a Phase 1trial with ZF874 protein folding corrector for Z-AATD but this has been terminated. Biomarin is in early stages of development of a small molecule corrector (BMN 349). There are no therapies with regulatory approval for Bronchiolitis Obliterans Syndrome ("BOS") following SCT or lung transplant. We consider alvelestat's closest potential competitors to be the Janus Kinase (JAK1) inhibitor, itacitinib, and JAK2 inhibitor, ruxolitinib, (Incyte Corporation) in Phase 1/Phase2 studies in lung transplant-associated and SCT-associated BOS, respectively; AI Therapeutics inhaled formulation of sirolimus (LAM-001) in Phase 1 for BOS in lung transplant; Isopogen allogeneic bone marrow derived Mesenchymal Stem Cells for Chronic Lung Allograft Dysfuntion (CLAD) in Phase 1 (NCT02709343); and liposomal inhaled cyclosporin-A (Zambon) in Phase 2 in BOS following SCT and in Phase 3 global pivotal trials in BOS associated with lung transplant. In other disease indications, we consider alvelestat's closest potential competitors to be Santhera Pharmaceuticals ("Santhera") which has in-licensed the inhaled NE inhibitor POL6014 and has completed a multiple ascending dose study, in the initial indication of CF; and CHF-6333 is an inhaled human NE inhibitor that has completed a Phase 1 trial by Chiesi Farmaceutici S.p.A. ("Chiesi") for the treatment of non-cystic fibrosis bronchiectasis and CF.

We consider etigilimab's current closest potential competitors to include other anti-TIGIT agents being developed by companies including Roche, Merck, iTeos and GSK, Beigene/Novartis, Seattle Genetics, Inc., Arcus/Gilead and Compugen amongst others. In addition, there are other combinations of existing cancer therapies available commercially for example, Yervoy and Opdivo and Opidivo or Keytruda in combination with chemotherapy agents. There are a number of bispecific antibodies with an anti-TIGIT arm in development including a Phase 3 program in NSCLC being developed by AstraZeneca. There are also a number of other agents in development to other immuno-oncology targets that could compete with an anti-TIGIT approach, for example anti-LAG3.

For acumapimod, although we are not aware of any approved therapies for the treatment of AECOPD, there are a wide range of established therapies available for COPD as well as a number of product candidates in development, with Verona Pharma plc ("Verona Pharma"), GlaxoSmithKline plc. ("GlaxoSmithKline" or "GSK"), and AstraZeneca each conducting Phase 2/3 trials on drugs for the treatment of COPD. In addition, Pulmatrix, Inc. ("Pulmatrix") has PUR1800, a narrow-spectrum kinase inhibitor (NSKI) that completed a Phase 1b trial in COPD. We consider acumapimod's current closest potential competitor in development for the treatment of AECOPD to be Verona Pharma's nebulized and inhaled ensifentrine (RPL554), a PDE3 / PDE4 dual inhibitor that is currently being developed as a bronchodilator and anti-inflammatory agent for COPD, Asthma and Cystic Fibrosis patients. In August 2022 Verona announced positive results (FEV1 and AECOPD exacerbation frequency) from two Phase 3 trials (ENHANCE-1 and ENHANCE-2) in COPD.

We consider leflutrozole's current closest potential competitors for the treatment of male infertility due to HH are Follicle Stimulating Hormone (FSH), injectable recombinant follitropin alpha (Gonal-F, Serono) which is FDA approved for male infertility. Injectable Human Chorionic Gonadotropin (HCG) is not approved for male infertility, but is used 'off-label.' AZD-5904 (myeloperoxidase inhibitor) from the AstraZeneca and St George Street Capital collaboration is in a Phase 1b trial for idiopathic male infertility.]

We may face increasing competition for additional new product acquisitions from pharmaceutical companies as new companies emerge with a similar business model and other more established companies focus on acquiring product candidates to develop their pipelines. Many of our competitors have significantly greater name recognition, financial, manufacturing, marketing, drug development, technical and human resources than we do. Mergers and acquisitions in the biopharmaceutical and pharmaceutical industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining top qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials and in acquiring technologies complementary to, or necessary for, our programs.

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

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize product candidates that are safer, more effective, less expensive, more convenient or easier to administer or have fewer or less severe side effects than any product candidates that we may develop. Our competitors may also obtain FDA, EMA or other regulatory approval for their product candidates more rapidly than we may obtain approval for our own product candidates, which could result in our competitors establishing a strong market position before we are able to enter the market. Even if setrusumab, alvelestat, etigilimab, acumapimod or leflutrozole achieve marketing approval, they may be priced at a significant premium over competing product candidates if any have been approved by then, potentially reducing our market opportunity. For more information, please see “Risk Factors—Risks Related to Commercialization—We operate in a highly competitive and rapidly changing industry, which may result in others acquiring, developing, or commercializing competing product candidates before or more successfully than we do.”

Intellectual Property

We have acquired or exclusively licensed our intellectual property portfolio from Mereo BioPharma 5 (formerly OncoMed), Novartis and AstraZeneca. We strive to protect and enhance the proprietary technologies, inventions and improvements that we believe are important to our business, including seeking, maintaining and defending patent rights, whether developed internally or acquired or licensed from third parties. Our policy is to seek to protect our proprietary position by, among other methods, pursuing and obtaining patent protection in the United States and in jurisdictions outside of the United States related to our proprietary technology, inventions, improvements, platforms and our product candidates that are important to the development and implementation of our business.

Our intellectual property is held by our wholly owned subsidiaries. As of December 31, 2022, our patent portfolio comprises approximately 600 issued patents and approximately 140 pending patent applications on a global basis.

Individual patents extend for varying periods depending on the date of filing of the patent application or the date of patent issuance and the legal term of patents in the countries in which they are obtained. Generally, patents issued for regularly filed applications in the United States are granted a term of 20 years from the earliest effective non-provisional filing date. In addition, in certain instances, a patent term can be extended to recapture a portion of the USPTO delay in issuing the patent as well as a portion of the term effectively lost as a result of the FDA regulatory review period. However, as to the FDA component, the restoration period cannot be longer than five years and the total patent term including the restoration period must not exceed 14 years following FDA approval. The duration of foreign patents varies in accordance with provisions of applicable local law, but typically the duration of foreign issued patents is also 20 years from the earliest effective filing date.

However, the actual protection afforded by a given patent varies on a product-by-product basis and from country to country, dependent on many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent.

In addition to patent protection, we also rely upon trademarks, trade secrets and know-how, and continuing technological innovation, to develop and maintain our competitive position. We seek to protect our proprietary information, in part, using confidentiality agreements with our collaborators, employees and consultants and invention assignment agreements with our employees. We also have confidentiality agreements or invention assignment agreements with our collaborators and selected consultants. These agreements are designed to protect our proprietary information and, in the case of the invention assignment agreements, to grant us ownership of technologies that are developed through a relationship with a third party. These agreements may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our collaborators, employees and consultants use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

Our commercial success will also depend in part on not infringing upon the proprietary rights of third parties. It is uncertain whether the issuance of any third-party patent would require us to alter our development or commercial strategies, or our product candidates or processes, obtain licenses or cease certain activities. Our breach of any license agreements or failure to obtain a license to proprietary rights that we may require to develop or commercialize our product candidates may have an adverse impact on us. If third parties have prepared and filed patent applications prior to March 16, 2013, in the United States that also claim technology to which we have rights, we may have to participate in interference proceedings in the USPTO, to determine priority of invention. For more information, please see “Risk Factors—Risks Related to Intellectual Property.”

Setrusumab (BPS-804/UX143)

As of December 31, 2022, we have 124 patents globally (including four issued U.S. patents) and 25 patent applications globally (including a pending U.S. patent application) relating to setrusumab and its use for the treatment of OI. A first patent family includes three issued U.S. patents and 86 corresponding issued foreign patents that relate to the setrusumab antibody, nucleic acids encoding setrusumab, processes for producing setrusumab, and setrusumab’s use as a medicament. Patents emanating from this first patent family expire in 2028 (not accounting for any available patent term extension). We also have two additional patent families, including an issued U.S. patent and 34 issued foreign patents that relate to methods of using anti-sclerostin antibodies, including setrusumab, for the treatment of OI. Patents emanating from these additional patent families expire in 2037 (not accounting for any available patent term extension). Beyond these patents and patent applications, we jointly own with Ultragenyx one additional patent family relating to dosing regimens for the use of anti-sclerostin antibodies, including setrusumab, in the treatment of OI; we expect any patents emanating from this patent family to expire in 2042 (not accounting for any available patent term extension). In December 2020, we entered into a license and collaboration agreement with Ultragenyx for setrusumab for OI, under which Ultragenyx have exclusive rights under all setrusumab patent families outside of Europe. See “—Licensing Agreement with Ultragenyx for setrusumab.”

On February 3, 2023, Ultragenyx, Mereo BioPharma 3 Limited, UCB Pharma SA (“UCB”) and Amgen Inc. (“Amgen”) entered into a non-exclusive worldwide, royalty-free license to research, develop, and commercialize setrusumab in osteogenesis imperfecta under certain UCB/Amgen-owned patent rights related to anti-sclerostin compounds and their uses.

Alvelestat (MPH-966)

As of December 31, 2022, our patent portfolio relating to our product candidate alvelestat consisted of three issued U.S. patents, no pending U.S. patent applications, 36 issued or allowed foreign patents and two pending foreign patent applications. These patents have all been licensed under our agreement with AstraZeneca. See “Business—Material Agreements—Licensing Agreement with AstraZeneca.” These issued patents and patent applications, if issued, include claims directed to 2-pyridone derivatives as NE inhibitors and their uses as well as claims to polymorphs of the tosylate salt of a 5-pyrazolyl-2-pyridone derivative, with expected expiry dates between 2024 and 2030.

Our patent portfolio relating to our product candidate alvelestat also includes one pending international patent application filed under the PCT, three pending U.S. patent applications and seventeen pending foreign patent applications which have been filed subsequent to the license agreement with AstraZeneca. These patent applications, if issued, include claims directed to dosing regimes of alvelestat and methods of treatment using alvelestat with expected expiry dates between 2040 and 2042.

Etigilimab (MPH-313)

As of December 31, 2022, our patent portfolio relating to our therapeutic candidate etigilimab consisted of four granted U.S. patents and two pending U.S. patent applications, as well as corresponding patent applications in major foreign jurisdictions.

The patent portfolio relating to our therapeutic candidate etigilimab contains one core patent family that covers the product per se as well as medical uses thereof. This patent family currently consists of two granted U.S. patents, fifty-five granted or allowed foreign patents and fifteen pending foreign patent applications. Patents that issue from this core family are generally expected to expire in 2036.

The portfolio also includes a second patent family that relates to specific methods of treatment using etigilimab. This patent family currently consists of two granted U.S. patents, one US pending patent application, and 5 granted or allowed foreign patents and 5 pending foreign patent applications. Any patents that issue from this family are generally expected to expire in 2037.

The portfolio also includes two PCT patent applications and one US provisional patent application. Any patents that issue from these families are generally expected to expire between 2042 and 2043.

Navicixizumab (OMP-305B83)

As of December 31, 2022, our patent portfolio relating to Navi consisted of 21 issued or allowed U.S. patents and two pending U.S. patent applications, as well as corresponding patents or patent applications in major foreign jurisdictions.

The patent portfolio relating to Navi contains two core patent families, both of which cover the product per se as well as medical uses thereof. Patents and patent applications, if issued, in these core families are expected to expire between 2030 and 2032.

The portfolio also includes several other patent families including issued U.S. and foreign patents and pending applications that relate to specific methods of treatment using Navi. Patents and patent applications, if issued, in these families are expected to expire between 2030 and 2039. Navi was licensed by the Group to OncXerna Inc. in January 2020 pursuant to the terms of a global licensing agreement. See “—Licensing Agreement for Navicixizumab.”

Acumapimod (BCT-197)

As of December 31, 2022, our patent portfolio relating to our product acumapimod consisted of 14 issued or allowed U.S. patents, 2 pending U.S. patent applications, 293 issued or allowed foreign patents and 51 pending foreign applications. These issued patents and patent applications, if issued, include claims directed to 5-membered heterocycle-based p38 kinase inhibitors, the use of a pyrazole derivative in the treatment of AECOPD, dosage regimens of acumapimod, the use of acumapimod in the treatment of specific patient subpopulations, methods of producing specific polymorphs of acumapimod and synthetic methods of production of acumapimod with expected expiry dates between 2024 and 2039.

Leflutrozole (BGS-649)

As of December 31, 2022, our patent portfolio relating to our product leflutrozole consisted of four issued U.S. patents and 92 issued foreign patents. These issued patents and patent applications, if issued, include claims directed to leflutrozole formulations and the use of leflutrozole in treating hypogonadism according to a specific dosing regimen, with expected expiry dates between 2032 and 2037.

Government Regulation

Among others, the FDA, U.S. Department of Health and Human Services Office of Inspector General, CMS and comparable regulatory authorities in state, local and foreign jurisdictions and in other countries impose substantial and burdensome requirements upon companies involved in the clinical development, manufacture, marketing and distribution of drugs such as those we are developing. These agencies and other federal, state and local entities regulate, among other things, the research and development, testing, manufacture, quality control, safety, effectiveness, labeling, storage, record keeping, approval, advertising and promotion, distribution, post-approval monitoring and reporting, sampling and export and import of our product candidates.

U.S. Government Regulation

In the United States, the FDA regulates drugs under the FDCA and its implementing regulations, and biological product candidates ("biologics"), under both the FDCA and the PHSA and its implementing regulations.

The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties.

The process required by the FDA before a drug or biologic may be marketed in the United States generally involves the following:

- completion of pre-clinical laboratory tests, animal studies and formulation studies in compliance with the FDA's Good Laboratory Practice ("GLP") regulations and other applicable regulations;
- submission to the FDA of an investigational new drug application (an "IND"), which must become effective before human clinical trials may begin;
- approval by an independent Institutional Review Board ("IRB") at each clinical site before each trial may be initiated;
- Good Clinical Practice ("GCP") requirements to evaluate the safety, purity, potency and/or efficacy of the product candidate for its intended use;
- submission to the FDA of an NDA or BLA after completion of all pivotal trials;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current Good Manufacturing Practice ("cGMP") requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- satisfactory completion of potential FDA audits of clinical trials sites and the sponsor's clinical trial records to assure compliance with GCPs and the integrity of the clinical data; and
- payment of user fees, if applicable, and FDA review and approval of the NDA or BLA;

Pre-clinical Studies

Once a product candidate is identified for development, it enters the preclinical testing stage. Pre-clinical studies include laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies to assess potential safety and efficacy. An IND sponsor must submit the results of the pre-clinical tests, together with manufacturing information, analytical data and any available clinical data or literature, among other things, to the FDA as part of an IND. An IND is a request for authorization from the FDA to administer an investigational drug product to humans. An IND will also include a protocol detailing, among other things, the objectives of the clinical trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated, if the trial includes an efficacy evaluation. Some pre-clinical testing may continue even after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence. Clinical holds also may be imposed by the FDA at any time before or during clinical trials due to safety concerns about on-going or proposed clinical trials or non-compliance with specific FDA requirements, and the trials may not begin or continue until the FDA notifies the sponsor that the hold has been lifted.

Clinical Trials

Clinical trials involve the administration of the investigational new drug or biologic to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which among other things, include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives or endpoints of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. While the IND is active, progress reports summarizing the results of the clinical trials and nonclinical studies performed since the last progress report, among other information, must be submitted at least annually to the FDA, and written IND safety reports must be submitted to the FDA and investigators for serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the same or similar drugs, findings from animal or in vitro testing suggesting a significant risk to humans, and any clinically important increased incidence of a serious suspected adverse reaction compared to that listed in the protocol or investigator brochure.

In addition, an IRB must review and approve the plan for a clinical trial. This can be a central or local IRB. In the case of a central IRB a single IRB will be the source of record for all sites in a trial; otherwise, a local IRB at each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution. 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. In addition, some clinical trials are overseen by an independent group of qualified experts organized by the sponsor, known as a data safety monitoring board or committee. Depending on its charter, this group may determine whether a trial may move forward at designated check points based on access to certain data from the trial. Information about certain clinical trials must also be submitted within specific timeframes to the National Institutes of Health for public dissemination on their website, www.clinicaltrials.gov.

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

- Phase 1: The product candidate is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness.
- Phase 2: The product candidate is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- Phase 3: The product candidate is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well- controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.

Post-approval trials, sometimes referred to as Phase 4 studies, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of a BLA or NDA.

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 cGMPs. 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 product. In addition, 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.

Rare Pediatric Disease Priority Review Voucher Program

In 2012, Congress authorized the FDA to award priority review vouchers to sponsors of certain rare pediatric disease product applications. This program is designed to encourage development of new drug and biological products for prevention and treatment of certain rare pediatric diseases. Specifically, under this program, a sponsor who receives an approval for a drug or biologic for a "rare pediatric disease" may qualify for a voucher that can be redeemed to receive a priority review of a subsequent marketing application for a different product.

The sponsor of a rare pediatric disease drug product receiving a priority review voucher may transfer (including by sale) the voucher to another sponsor. The voucher may be further transferred any number of times before the voucher is used, as long as the sponsor making the transfer has not yet submitted the application. The FDA may also revoke any priority review voucher if the rare pediatric disease drug for which the voucher was awarded is not marketed in the U.S. within one year following the date of approval.

For purposes of this program, a "rare pediatric disease" is a (a) serious or life-threatening disease in which the serious or life-threatening manifestations primarily affect individuals aged from birth to 18 years, including age groups often called neonates, infants, children, and adolescents; and (b) rare diseases or conditions within the meaning of the Orphan Drug Act. Congress has only authorized the Rare Pediatric Disease Priority Review Voucher program until September 30, 2024. Consequently, sponsors of marketing applications approved after that date will not receive the voucher unless Congress reauthorizes the Rare Pediatric Disease Priority Review Voucher program before that time. However, even if the program is not reauthorized, if a drug candidate receives Rare Pediatric Disease Designation before October 1, 2024, the sponsor of the marketing application for such drug will be eligible to receive a voucher if the application for the designated drug is approved by the FDA before October 1, 2026.

Orphan Product Designation and Exclusivity

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic product if it is intended to treat a rare disease or condition (generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a drug product available in the United States for treatment of the disease or condition will be recovered from sales of the product). A company must request orphan product designation before submitting an NDA or BLA. If the request is granted, the FDA will publicly disclose the identity of the therapeutic agent and its potential use. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product with orphan status receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product is entitled to orphan-product exclusivity. Orphan-product exclusivity means that the FDA may not approve any other applications for the same product for the same disease or condition for seven years, except in certain limited circumstances. If a product designated as an orphan product ultimately receives marketing approval for disease or condition broader than what was designated in its orphan- product application, it may not be entitled to exclusivity. Orphan exclusivity will not bar approval of another product under certain circumstances, including if a subsequent product with the same active ingredient for the same indication is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand. Further, the FDA may approve more than one product for the same orphan disease or indication, or disease as long as the product candidates contain different active ingredients. Moreover, competitors may receive approval of different product candidates for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity.

Marketing Approval

Assuming successful completion of the required clinical testing, the results of the pre-clinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA or BLA requesting approval to market the product for one or more indications. In most cases, the submission of an NDA or BLA is subject to a substantial application user fee.

In addition, under the Pediatric Research Equity Act of 2003, as amended and reauthorized ("PREA"), certain NDAs, BLAs or supplements to an NDA or BLA must contain data that are adequate to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective, unless the sponsor has received a deferral or waiver. The required assessments must evaluate 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 clinical trials for some or all of the pediatric subpopulations for several reasons, including a finding that the drug is ready for approval for use in adults before pediatric clinical trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric clinical trials begin. The FDA must send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation.

The FDA conducts a preliminary review of all NDAs and BLAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an application for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA reviews an application to determine, among other things, whether the drug is safe and effective (for biologics, the standard is referred to as safe, pure and potent) and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and purity. Under the goals and policies agreed to by the FDA under the Prescription Drug User Fee Act ("PDUFA") for new molecular entity NDAs and original BLAs, the FDA has 10 months from the filing date in which to complete its initial review of a standard application and respond to the applicant, and six months from the filing date for an application with priority review. This review typically takes 12 months from the date the NDA or BLA is submitted to the FDA, because the FDA has approximately two months to make a "filing" decision.

The FDA may refer an application for a novel drug or biologic candidate to an advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an application, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an application, the FDA may inspect the sponsor and one or more clinical trial sites to assure compliance with GCP requirements and the integrity of the clinical data submitted in an NDA.

After evaluating the application and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter, or, in some cases, a complete response letter. A complete response letter indicates that the review cycle of the application is complete, and that the application will not be approved in its present form. A complete response letter, generally details specific conditions that must be met in order to secure approval of the application and may require additional clinical or pre-clinical testing in order for FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications.

Even if the FDA approves a product, it may limit the approved indications for use of the product, require additional contraindications, warnings or precautions to be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a product's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS, which can materially affect the potential market and profitability of the product. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS. The FDA will not approve the NDA without an approved REMS, if required. A REMS could include medication guides, physician communication plans or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products. The FDA may prevent or limit further marketing of a product based on the results of post- marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes, and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Post-Approval Requirements

Drugs and biologics manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed product candidates and the establishments at which such product candidates are manufactured, as well as new application fees for supplemental applications with clinical data.

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

In addition, manufacturers and other entities involved in the manufacture and distribution of approved product candidates are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP requirements and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in mandatory revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending applications or supplements to approved applications or suspension or revocation of product approvals;
- product seizure or detention or refusal to permit the import or export of product candidates;
- injunctions or the imposition of civil or criminal penalties;
- consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs;
- mandated modification of promotional materials and labeling and the issuance of corrective information; or
- the FDA or other regulatory authorities may issue safety alerts, "Dear Healthcare Provider" letters, press releases or other communications containing warnings or other safety information about the product.

The FDA strictly regulates marketing, labeling, advertising and promotion of product candidates that are placed on the market. Product candidates may be promoted only for the approved indications and in accordance with the provisions of the approved label. Physicians may prescribe legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

Special FDA Expedited Review and Approval

The FDA has various programs, such as Fast Track designation, Breakthrough Therapy designation, accelerated approval, and priority review, which are intended to expedite or simplify the process for the development and FDA review of drugs and biologics that are intended for the treatment of serious or life-threatening diseases or conditions and demonstrate the potential to address unmet medical needs.

To be eligible for a Fast-track designation, the FDA must determine, based on the request of a sponsor, that a product candidate is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address an unmet medical need for such disease or condition. Fast-track designation provides opportunities for frequent interactions with the FDA review team to expedite development and review of the product. The FDA may also review sections of the NDA or BLA for a Fast-Track-designated product on a rolling basis before the complete application is submitted, if the sponsor and FDA agree on a schedule for the submission of the application sections, and the sponsor pays any required user fees upon submission of the first section of the NDA or BLA.

In addition, a sponsor can request designation of a product as a “Breakthrough Therapy.” A Breakthrough Therapy is defined as a drug or biologic that is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life- threatening disease or condition, and preliminary clinical evidence indicates that the drug or biologic may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development.The designation includes all of the Fast Track program features, as well as more intensive FDA interaction and guidance beginning as early as Phase 1 and an organizational commitment to expedite the development and review of the product candidate, including involvement of senior managers.

Product candidates studied for their safety and effectiveness in treating serious or life-threatening illnesses and that have the potential to provide meaningful therapeutic benefit over existing treatments may be eligible for accelerated approval upon a determination the product has an effect on 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 (“IMM”) that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA generally require a sponsor of a product receiving accelerated approval to perform confirmatory to verify and describe the predicted clinical benefit. Products receiving accelerated approval may be subject to expedited withdrawal procedures if the sponsor fails to conduct the required confirmatory trials in a timely manner or if such trials fail to verify the predicted clinical benefit. In addition, the FDA currently requires as a condition of accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

Once an NDA or BLA is submitted for a product intended to treat a serious condition, the FDA may assign a priority review designation to the application if the FDA determines that the product candidate, if approved, would provide a significant improvement in safety or effectiveness. The FDA will attempt to direct additional resources to the evaluation of an NDA or BLA designated for priority review in an effort to facilitate the review. The FDA endeavors to review NDAs for new molecular entities and original BLAs with priority review designations within six months of the filing date as compared to ten months under its current review goals

Fast track designation, breakthrough therapy designation, priority review, and accelerated approval do not change the standards for approval but may expedite the development or approval process. Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. Furthermore, fast-track designation, breakthrough-therapy designation, accelerated approval and priority review do not change the standards for approval and may not ultimately expedite the development or approval process.

Foreign Government Regulation

Our product candidates are subject to similar laws and regulations imposed by jurisdictions outside of the United States, and, in particular, the EU, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws and implementation of corporate compliance programs and reporting of payments or other transfers of value to healthcare professionals.

Non-clinical Studies and Clinical Trials

Similarly to the United States, the various phases of non-clinical and clinical research in the European Union, or EU, are subject to significant regulatory controls.

Non-clinical studies are performed to demonstrate the health or environmental safety of new chemical or biological substances. Non-clinical studies (pharmaco-toxicological) must be conducted in compliance with the principles of good laboratory practice, or GLP, as set forth in EU Directive 2004/10/EC (unless otherwise justified for certain particular medicinal products – e.g., radio-pharmaceutical precursors for radio-labelling purposes). In particular, non-clinical studies, both in vitro and in vivo, must be planned, performed, monitored, recorded, reported and archived in accordance with the GLP principles, which define a set of rules and criteria for a quality system for the organizational process and the conditions for non-clinical studies. These GLP standards reflect the Organization for Economic Co-operation and Development requirements.

Clinical trials of medicinal products in the EU must be conducted in accordance with EU and national regulations and the International Conference on Harmonization ("ICH") guidelines on Good Clinical Practices ("GCP") as well as the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. If the sponsor of the clinical trial is not established within the EU, it must appoint an EU entity to act as its legal representative. The sponsor must take out a clinical trial insurance policy, and in most EU member states, the sponsor is liable to provide 'no fault' compensation to any study subject injured in the clinical trial.

The regulatory landscape related to clinical trials in the EU has been subject to recent changes. The EU Clinical Trials Regulation ("CTR") which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. Unlike directives, the CTR is directly applicable in all EU member states without the need for member states to further implement it into national law. The CTR notably harmonizes the assessment and supervision processes for clinical trials throughout the EU via a Clinical Trials Information System, which contains a centralized EU portal and database.

While the Clinical Trials Directive required a separate clinical trial application ("CTA") to be submitted in each member state in which the clinical trial takes place, to both the competent national health authority and an independent ethics committee, much like the FDA and IRB respectively, the CTR introduces a centralized process and only requires the submission of a single application for multi-center trials. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The CTA must include, among other things, a copy of the trial protocol and an investigational medicinal product dossier containing information about the manufacture and quality of the medicinal product under investigation. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed.

The CTR foresees a three-year transition period. The extent to which ongoing and new clinical trials will be governed by the CTR varies. Clinical trials for which an application was submitted (i) prior to January 31, 2022 under the Clinical Trials Directive, or (ii) between January 31, 2022 and January 31, 2023 and for which the sponsor has opted for the application of the Clinical Trials Directive remain governed by said Directive until January 31, 2025. After this date, all clinical trials (including those which are ongoing) will become subject to the provisions of the CTR.

Medicines used in clinical trials must be manufactured in accordance with Good Manufacturing Practice, or GMP. Other national and EU-wide regulatory requirements may also apply.

Marketing Authorization

In order to market our future product candidates in the EU, and many other foreign jurisdictions, we must obtain separate regulatory approvals. More concretely, in the EU, medicinal product candidates can only be commercialized after obtaining a Marketing Authorization ("MA"). To obtain regulatory approval of a product candidate under EU regulatory systems, we must submit a MA application ("MAA"). The process for doing this depends, among other things, on the nature of the medicinal product. There are two types of MAs:

- "Centralized MAs" are issued by the European Commission through the centralized procedure, based on the opinion of the Committee for Medicinal Products for Human Use ("CHMP") of the EMA and are valid throughout the entire territory of the EU. The centralized procedure is mandatory for certain types of medicinal products, such as (i) medicinal products derived from biotechnological processes, (ii) designated orphan medicinal product products, (iii) advanced therapy medicinal products ("ATMPs") (such as gene therapy, somatic cell therapy and tissue engineered products) and (iv) medicinal products containing a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases. The centralized procedure is optional for products containing a new active substance not yet authorized in the EU, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU; and
- "National MAs" are issued by the competent authorities of the EU member states, only cover their respective territory, and are available for product candidates not falling within the mandatory scope of the centralized procedure. Where a product has already been authorized for marketing in an EU member state, this national MA can be recognized in another member state through the mutual recognition procedure. If the product has not received a national MA in any member state at the time of application, it can be approved simultaneously in various member states through the decentralized procedure. Under the decentralized procedure an identical dossier is submitted to the competent authorities of each of the member states in which the MA is sought, one of which is selected by the applicant as the reference member state.

Under the centralized procedure the maximum timeframe for the evaluation of an MAA by the EMA is 210 days, excluding clock stops. In exceptional cases, the CHMP might perform an accelerated review of a MAA in no more than 150 days (not including clock stops). Innovative products that target an unmet medical need and are expected to be of major public health interest may be eligible for a number of expedited development and review programs, such as the Priority Medicines ("PRIME") scheme, which provides incentives similar to the breakthrough therapy designation in the U.S. In March 2016, the EMA launched the PRIME scheme. PRIME is a voluntary scheme aimed at enhancing the EMA's support for the development of medicines that target unmet medical needs. It is based on increased interaction and early dialogue with companies developing promising medicines, to optimize their product development plans and speed up their evaluation to help them reach patients earlier. Product developers that benefit from PRIME designation can expect to be eligible for accelerated assessment but this is however not guaranteed. The benefits of a PRIME designation includes the appointment of a dedicated contact and rapporteur from the CHMP before submission of an MAA, early and proactive dialogue and scientific advice at key development milestones, and the potential to qualify product candidates for accelerated review earlier in the application process. An initial meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies.

Moreover, in the EU, a "conditional" MA may be granted in cases where all the required safety and efficacy data are not yet available. The CMA is subject to conditions to be fulfilled for generating the missing data or ensuring increased safety measures. It is valid for one year and has to be renewed annually until fulfillment of all the conditions. Once the pending studies are provided, it can become a "standard" MA. However, if the conditions are not fulfilled within the timeframe set by the EMA, the MA ceases to be renewed.

Under the above described procedures, before granting the MA, the EMA or the competent authorities of the EU member states make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy. MAs have an initial duration of five years. After these five years, the authorization may be renewed on the basis of a reevaluation of the risk-benefit balance.

Adaptive pathways

The EMA has an adaptive pathways program which allows for early and progressive patient access to a medicine. The adaptive pathways concept is an approach to medicines approval that aims to improve patients' access to medicines in cases of high unmet medical need. To achieve this goal, several approaches are envisaged: identifying small populations with severe disease where a medicine's benefit-risk balance could be favorable; making more use of real-world data where appropriate to support clinical trial data; and involving health technology assessment bodies early in development to increase the chance that medicines will be recommended for payment and ultimately covered by national healthcare systems. The adaptive pathways concept applies primarily to treatments in areas of high medical need where it is difficult to collect data via traditional routes and where large clinical trials would unnecessarily expose patients who are unlikely to benefit from the medicine. The approach builds on regulatory processes already in place within the existing EU legal framework. These include: scientific advice; compassionate use; the conditional approval mechanism (for medicines addressing life-threatening conditions); patient registries and other pharmacovigilance tools that allow collection of real-life data and development of a risk-management plan for each medicine.

The adaptive pathways program does not change the standards for the evaluation of benefits and risks or the requirement to demonstrate a positive benefit-risk balance to obtain MA. In February 2017, setrusumab was accepted into the adaptive pathways program.

Data and marketing exclusivity

In the EU, new product candidates authorized for marketing, or reference product candidates, generally receive eight years of data exclusivity and an additional two years of market exclusivity upon MA. If granted the data exclusivity period prevents generic or biosimilar applicants from relying on the pre-clinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar MA in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. The market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the EU until 10 years have elapsed from the initial authorization of the reference product in the EU. The overall 10-year market exclusivity period can be extended to a maximum of eleven years if, during the first eight years of those 10 years, the MA holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. However, there is no guarantee that a product will be considered by the EU's regulatory authorities to be a new chemical or biological entity, and products may not qualify for data exclusivity.

There is a special regime for biosimilars, or biological medicinal products that are similar to a reference medicinal product but that do not meet the definition of a generic medicinal product, for example, because of differences in raw materials or manufacturing processes. For such products, the results of appropriate preclinical or clinical trials must be provided, and guidelines from the EMA detail the type of quantity of supplementary data to be provided for different types of biological product. There are no such guidelines for complex biological products, such as gene or cell therapy medicinal products, and so it is unlikely that biosimilars of those products will currently be approved in the EU. However, guidance from the EMA states that they will be considered in the future in light of the scientific knowledge and regulatory experience gained at the time.

Orphan Medicinal Products

The criteria for designating an "orphan medicinal product" in the EU are similar in principle to those in the United States. A medicinal product can be designated as an orphan if its sponsor can establish that: (1) the product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically-debilitating condition, (2) either (a) affecting not more than five in 10,000 persons in the EU when the application is made, or (b) that the product without the benefits derived from the orphan status, would generate sufficient return to justify the necessary investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized for marketing in the EU or, if such method exists, the product will be of significant benefit to those affected by that condition.

Orphan designation must be requested before submitting an MAA. Orphan designation entitles a party to incentives such as reduction of fees or fee waivers, protocol assistance, and access to the centralized procedure. Upon grant of a MA for an orphan medicinal product are entitled to a 10 year period of market exclusivity for the approved indication. During this market exclusivity period, the competent authorities cannot accept another application for a MA, or grant a MA, or accept an application to extend a MA for a similar medicinal product for the same indication. The period of market exclusivity is extended by two years for orphan medicinal products that have also complied with an agreed pediatric investigation plan ("PIP").

This period of orphan market exclusivity may, however, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for which it received orphan drug destination, i.e. the prevalence of the condition has increased above the threshold or it is judged that the product is sufficiently profitable not to justify maintenance of market exclusivity. Additionally, MA may be granted for another similar product for the same indication at any time if (i) the applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior; (ii) the applicant consents to a second orphan medicinal product application; or (iii) the applicant cannot supply enough orphan medicinal product.

Pediatric Development

In the EU MAA for new medicinal product candidates have to include the results of studies conducted in the pediatric population, in compliance with a PIP, agreed with the EMA's Pediatric Committee ("PDCO"). The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the drug for which MA is being sought. The PDCO can grant a deferral of the obligation to implement some or all of the measures of the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults. Further, the obligation to provide pediatric clinical trial data can be waived by the PDCO when these data are not needed or appropriate because the product is likely to be ineffective or unsafe in children, the disease or condition for which the product is intended occurs only in adult populations, or when the product does not represent a significant therapeutic benefit over existing treatments for pediatric patients. Once the MA is obtained in all member states of the EU and study results are included in the product information, even when negative, the product is eligible for a six-month supplementary protection certificate extension (if any is in effect at the time of approval) or, in the case of orphan medicinal products, a two-year extension of orphan market exclusivity.

Similar to the United States, both MA holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA, the European Commission and/or the competent regulatory authorities of the member states. The holder of a MA must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance ("QPPV") who is responsible for the establishment and maintenance of that system, and oversees the safety profiles of medicinal products and any emerging safety concerns. Key obligations include expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports, or PSURs.

All new MAA must include a risk management plan ("RMP") describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the product. The RMP must be updated any time new information on the medicinal product becomes available which has a significant impact on the content of the RMP. The regulatory authorities may also impose specific obligations as a condition of the MA. Such risk-minimization measures or post-authorization obligations may include additional safety monitoring, more frequent submission of PSURs, or the conduct of additional clinical trials or post-authorization safety studies.

The advertising and promotion of medicinal products is also subject to laws concerning promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. All advertising and promotional activities for the product must be consistent with the approved summary of product characteristics, and therefore all off-label promotion is prohibited. Direct-to-consumer advertising of prescription medicines is also prohibited in the EU. Although general requirements for advertising and promotion of medicinal products are established under EU directives, the details are governed by regulations in each member state and can differ from one country to another.

The aforementioned EU rules are generally applicable in the European Economic Area, or EEA, which consists of the 27 EU member states plus Norway, Liechtenstein and Iceland.

Failure to comply with EU and member state laws that apply to the conduct of clinical trials, manufacturing approval, MA of medicinal products and marketing of such products, both before and after grant of the MA, manufacturing of pharmaceutical products, statutory health insurance, bribery and anti-corruption or with other applicable regulatory requirements may result in administrative, civil or criminal penalties. These penalties could include delays or refusal to authorize the conduct of clinical trials, or to grant MA, product withdrawals and recalls, product seizures, suspension, withdrawal or variation of the MA, total or partial suspension of production, distribution, manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties.

Regulation in the United Kingdom

Since the end of the Brexit transition period on January 1, 2021, Great Britain (England, Scotland and Wales) has not been directly subject to EU laws, however under the terms of the Ireland/Northern Ireland Protocol, EU laws generally apply to Northern Ireland. The EU laws that have been transposed into U.K. law through secondary legislation remain applicable in Great Britain. However, under the Retained EU Law (Revocation and Reform) Bill 2022, which is currently before the U.K. parliament, any retained EU law not expressly preserved and "assimilated" into domestic law or extended by ministerial regulations (to no later than June 23, 2026) will automatically expire and be revoked by December 31, 2023. However, new legislation such as the EU CTR is not applicable in Great Britain.

Under the Medicines and Medical Devices Act 2021, the Secretary of State or an ‘appropriate authority’ has delegated powers to amend or supplement existing regulations in the area of medicinal products and medical devices. This allows new rules to be introduced in the future by way of secondary legislation, which aims to allow flexibility in addressing regulatory gaps and future changes in the fields of human medicines, clinical trials and medical devices.

Since January 1, 2021, the Medicines and Healthcare products Regulatory Agency (“MHRA”), has been the U.K.’s standalone medicines and medical devices regulator. As a result of the Northern Ireland protocol, different rules will apply in Northern Ireland than in England, Wales, and Scotland, together, Great Britain, or GB; broadly, Northern Ireland will continue to follow the EU regulatory regime, but its national competent authority will remain the MHRA.

The MHRA has introduced changes to national licensing procedures, including procedures to prioritize access to new medicines that will benefit patients, including a 150-day assessment and a rolling review procedure. All existing EU MAs for centrally authorized products were automatically converted or grandfathered into U.K. MAs, effective in GB (only), free of charge on January 1, 2021, unless the MA holder opted-out. In order to use the centralized procedure to obtain a MA that will be valid throughout the EEA, companies must be established in the EEA. Therefore since Brexit, companies established in the U.K. can no longer use the EU centralized procedure and instead an EEA entity must hold any centralized MAs. In order to obtain a U.K. MA to commercialize products in the U.K., an applicant must be established in the U.K. and must follow one of the U.K. national authorization procedures or one of the remaining post-Brexit international cooperation procedures to obtain an MA to commercialize products in the U.K.. The MHRA may rely on a decision taken by the European Commission on the approval of a new (centralized procedure) MA when determining an application for a GB authorization; or use the MHRA's decentralized or mutual recognition procedures which enable MAs approved in EU member states (or Iceland, Liechtenstein, Norway) to be granted in GB.

There will be no pre-MA orphan designation. Instead, the MHRA will review applications for orphan designation in parallel to the corresponding MAA. The criteria are essentially the same, but have been tailored for the market, i.e., the prevalence of the condition in GB, rather than the EU, must not be more than five in 10,000. Should an orphan designation be granted, the period or market exclusivity will be set from the date of first approval of the product in GB.

The U.K. regulatory framework in relation to clinical trials is derived from existing EU legislation (as implemented into U.K. law, through secondary legislation). On January 17, 2022, the MHRA launched an eight-week consultation on reframing the U.K. legislation for clinical trials. The consultation closed on March 14, 2022 and aims to streamline clinical trials approvals, enable innovation, enhance clinical trials transparency, enable greater risk proportionality, and promote patient and public involvement in clinical trials. The outcome of the consultation is being closely watched and will determine whether the U.K. chooses to align with the CTR or diverge from it to maintain regulatory flexibility.

These developments, or the perception that any related developments could occur, have had and may continue to have a material adverse effect on global economic conditions and the stability of global financial markets, and may significantly reduce global market liquidity and restrict the ability of key market participants to operate in certain financial markets. Any of these factors could depress economic activity and restrict our access to capital, which could have a material adverse effect on our business, financial condition and results of operations and reduce the price of our common stock.

The uncertainty regarding new or modified arrangements between the U.K. and other countries following the withdrawal may have a material adverse effect on the movement of personnel, goods, information or data between the U.K. and members of the EU and the United States, including the interruption of or delays in imports into the U.K. of goods originating within the EU and exports from the U.K. of goods originating there. For example, shipments into the U.K. of medicinal product substance manufactured for us in the EU may be interrupted or delayed and thereby prevent or delay the manufacture in the U.K. of drug product. Similarly, shipments out of the U.K. of drug product to the United States or the EU may be interrupted or delayed and thereby prevent or delay the delivery of drug product to clinical sites. Such a situation could hinder our ability to conduct current and planned clinical trials and have an adverse effect on our business.

Other U.S. Healthcare Laws

In addition to FDA restrictions on marketing of pharmaceutical and biologic product candidates, other U.S. federal and state healthcare regulatory laws restrict business practices in the pharmaceutical and biotechnology industry, which include, but are not limited to, state and federal anti-kickback, false claims, data privacy and security and physician payment and pricing transparency laws.

The U.S. federal Anti-Kickback Statute prohibits, among other things, any person or entity from knowingly and willfully offering, paying, soliciting, receiving or providing any remuneration, directly or indirectly, overtly or covertly, to induce or in return for purchasing, leasing, ordering, or arranging for or recommending the purchase, lease or order of any good, facility, item or service reimbursable, in whole or in part, under Medicare, Medicaid or other federal healthcare programs. The term "remuneration" has been broadly interpreted to include anything of value. The Anti-Kickback Statute has been interpreted to apply to arrangements, such as those between pharmaceutical manufacturers on the one hand and prescribers, purchasers, formulary managers and beneficiaries on the other. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases, or recommendations may be subject to scrutiny if they do not meet the requirements of a statutory or regulatory exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal

under the U.S. federal Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by- case basis based on a cumulative review of all facts and circumstances. Several courts have interpreted the statute's intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the statute has been violated.

Additionally, 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 anti-kickback laws, which establish similar prohibitions and in some cases may apply to items or services reimbursed by any third-party payor, including commercial insurers, or to self-pay patients.

The federal false claims and civil monetary penalties laws, including the civil FCA, prohibit any person or entity from, among other things, knowingly presenting, or causing to be presented, a false, fictitious or fraudulent claim for payment to, or approval by, the federal government, knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. federal government. A claim includes "any request or demand" for money or property presented to the U.S. government. Actions under the civil FCA may be brought by the Attorney General or as a qui tam action by a private individual in the name of the government Several pharmaceutical and other healthcare companies have been prosecuted under these laws for, among other things, allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of product candidates for unapproved, or off-label, uses. The government may also assert that a claim including items or services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil FCA. Many states also have similar fraud and abuse statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

HIPAA created additional federal criminal statutes that prohibit, among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

In addition, there has been a trend of increased federal and state regulation of payments made to physicians and certain other healthcare providers. The Physician Payments Sunshine Act requires applicable manufacturers to report certain payments and "transfers of value" provided to physicians defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain other non-physician practitioners (physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists, anesthesiology assistants and certified nurse midwives), and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Applicable manufacturers must submit reports by the 90th day of each subsequent calendar year. In addition, certain states require implementation of compliance programs and compliance with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, impose restrictions on marketing practices and/or tracking and reporting of gifts, compensation and other remuneration or items of value provided to physicians and other healthcare professionals and entities.

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Ensuring that internal operations and business arrangements with third parties comply with applicable healthcare laws and regulations involve substantial costs.

Violations of any of these laws may be punishable by criminal and civil sanctions, including fines and civil monetary penalties, the possibility of exclusion from federal healthcare programs (including Medicare and Medicaid), disgorgement and corporate integrity agreements, which impose, among other things, rigorous operational and monitoring requirements on companies. Similar sanctions and penalties, as well as imprisonment, also can be imposed upon executive officers and employees of such companies. Given the significant size of actual and potential settlements, it is expected that the government authorities will continue to devote substantial resources to investigating healthcare providers' and manufacturers' compliance with applicable laws.

Privacy and Data Protection Laws in Europe

Numerous state, federal and foreign laws, regulations and standards govern the collection, use, access to, confidentiality and security of health-related and other personal information, and could apply now or in the future to our operations or the operations of our partners. In the United States, numerous federal and state laws and regulations, including data breach notification laws, health information privacy and security laws and consumer protection laws and regulations govern the collection, use, disclosure, and protection of health-related and other personal information. In addition, certain foreign laws govern the privacy and security of personal data, including health-related data. For example, we are subject to European laws relating to our and our suppliers', partners' and subcontractors' collection, control, processing and other use of personal data (i.e., any data relating to an identifiable living individual, whether that individual can be identified directly or indirectly). We are subject to the data protection laws in those jurisdictions where we are established and processing personal data. We are also subject to such laws, when outside the EU or U.K. (as the case may be), where we process personal data relating to individuals in the EU or U.K. "in the context of" an establishment in those markets, where we specifically target goods or services to EU or U.K. residents or where we monitor the behavior of individuals in the EU or U.K. (e.g., undertaking clinical trials). We and our suppliers, partners and subcontractors process personal data including in relation to our employees, employees of customers, clinical trial patients, healthcare professionals and employees of suppliers including health and medical information. The data privacy regime in the EU includes the GDPR, the e-Privacy Directive and the national laws and regulations implementing or supplementing each of them. In the U.K., we are subject to the U.K. Data Protection Act 2018 UK GDPR, along with U.K. regulations implementing the e-Privacy Directive. The U.K.'s data protection regime, while currently closely aligned with the EU's, may diverge over time. The UK courts also recognize a civil tort for misuse of private information, distinct from a claim for breach of confidence, which may engender some exposure. Additionally, in the EU and U.K., there are strict regulations on electronic marketing communications and the use of cookies and related technologies, with which we are required to adhere.

The GDPR and UK GDPR impose comprehensive data privacy compliance obligations in relation to our collection, processing, sharing, disclosure, transfer and other use of personal data, including a principal of accountability and the obligation to demonstrate compliance through policies, procedures, training and audit. In addition, some of the personal data we process in respect of clinical trial participants is considered special category or sensitive personal data under the GDPR and UK GDPR, and subject to additional compliance obligations. We may be subject to diverging requirements under EU member state laws and UK law, such as whether consent can be used as the legal basis for processing of clinical trial data and the roles, responsibilities and liabilities as between CROs and sponsors. As these laws develop, we may need to make operational changes to adapt to these diverging rules, which could increase our costs and adversely affect our business.

We are also subject to EU and U.K. laws on personal data export, as we may transfer personal data from the EU or U.K. to other jurisdictions which are not considered by the European Commission or U.K. Government, respectively, to offer adequate protection of personal data. Recent legal developments in Europe have created complexity and uncertainty regarding such transfers, in particular in relation to transfers to the United States. In 2020, the Court of Justice of the European Union ("CJEU") invalidated the EU-U.S. Privacy Shield (the "Privacy Shield"), which had been a well-recognized cross-border data transfer framework. Subsequent regulatory decisions have taken a restrictive approach to international data transfers. In the wake of that judgment, referred to as Schrems II, the European Commission has issued new "model clauses" for companies to use to transfer personal data, which take into account concerns expressed by the CJEU. In the U.K., the Information Commissioner has issued an addendum to the new "model clauses", which is intended to allow for the use of the "model clauses" for ex-U.K. transfers, along with its own international data transfer agreement. We expect EU and U.K. data protection authorities to more closely scrutinize international data transfers going forwards, along with the diligence undertaken in respect of any international transfers and the protections taken to secure personal data. At present, the precise conditions upon which data may be lawfully transferred from the EEA to inadequate jurisdictions such as the U.S., subject to the EU "model clauses" (and so-called "binding corporate rules") remains unclear, as companies are now required to undertake transfer impact assessments and, where appropriate, apply supplementary measures to ensure that such mechanisms provide adequate protections for EU data. In March 2022, the US and EU announced a new regulatory regime intended to replace the invalidated regulations; however, this new EU-US Data Privacy Framework has not been implemented beyond an executive order signed by President Biden on October 7, 2022 on Enhancing Safeguards for United States Signals Intelligence Activities. European court and regulatory decisions subsequent to the CJEU decision of July 16, 2020 have taken a restrictive approach to international data transfers.

There are costs and administrative burdens associated with compliance with the GDPR and UK GDPR and the resultant changes in the EU and EEA member states' national laws. Any failure to comply with global privacy laws carries with it the risk of significant penalties and sanctions, Penalties for certain breaches of the GDPR or UK GDPR are up to the greater of 20 million euros / 17.5 million pounds sterling or 4% of global annual turnover. In addition to fines, a breach of the GDPR or UK GDPR may result in regulatory investigations, reputational damage, orders to cease/ change our data processing activities, enforcement notices, assessment notices (for a compulsory audit) and/ or civil claims (including class actions).These laws or new interpretations, enactments or supplementary forms of these laws, could create liability for us, could impose additional operational requirements on our business, could affect the manner in which we use and transmit patient information and could increase our cost of doing business. Claims of violations of privacy rights or contractual breaches, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business.

Privacy and security laws, regulations, and other obligations are constantly evolving, may conflict with each other to complicate compliance efforts, and can result in investigations, proceedings, or actions that lead to significant civil and/or criminal penalties and restrictions on data processing.

Coverage and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any pharmaceutical or biological product for which we obtain regulatory approval. In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use our product candidates unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our product candidates. Sales of any product candidates for which we receive regulatory approval for commercial sale will therefore depend, in part, on the availability of coverage and adequate reimbursement from third-party payors. Third-party payors include government authorities, managed care plans, private health insurers and other organizations.

In the United States, the process for determining whether a third-party payor will provide coverage for a pharmaceutical or biologic product typically is separate from the process for setting the price of such product or for establishing the reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors may limit coverage to specific product candidates on an approved list, also known as a formulary, which might not include all of the FDA-approved product candidates for a particular indication. A decision by a third-party payor not to cover our product candidates could reduce physician utilization of our product candidates once approved and have a material adverse effect on our sales, results of operations and financial condition. Moreover, a third-party payor's decision to provide coverage for a pharmaceutical or biologic product does not imply that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. Additionally, coverage and reimbursement for product candidates can differ significantly from payor to payor. One third-party payor's decision to cover a particular medical product or service does not ensure that other payors will also provide coverage for the medical product or service, or will provide coverage at an adequate reimbursement rate. As a result, the coverage-determination process will require us to provide scientific and clinical support for the use of our product candidates to each payor separately and will be a time-consuming process.

In the EU, governments set the price of product candidates through their health technology assessment, and reimbursement rules and control of national health care systems that fund a large part of the cost of those product candidates to consumers. Member states are free to restrict the range of pharmaceutical products for which their national health insurance systems provide reimbursement, and to control the prices and reimbursement levels of pharmaceutical products for human use. Some jurisdictions operate positive and negative list systems under which product candidates may only be marketed once a reimbursement price has been agreed to by the government. Member states may approve a specific price or level of reimbursement for the pharmaceutical product, or alternatively adopt a system of direct or indirect controls on the profitability of the company responsible for placing the pharmaceutical product on the market, including volume-based arrangements, caps and reference pricing mechanisms. To obtain reimbursement or pricing approval, some of these countries might compare the new product to an existing standard of care, including other treatments aimed at the same disease, if they exist. Health technology assessments, including cost-effectiveness evaluations, may be conducted in order to assess the medical value or added clinical benefit of a therapy. Countries may also conduct budget-impact assessments for a new therapy. In some cases, tendering is used to decide which therapy will be reimbursed and made available for a group of patients where more than one treatment exists. Countries might also require further studies or in-use evidence to be developed, or create coverage with evidence generation under some form of so-called managed access agreements. Some countries allow for a company to set the price, which is then agreed in negotiation with the country authorities, who might then monitor sales for that product and re-assess or re-evaluate when a certain statutory health insurance expenditure threshold is reached. Other countries might set their

price based on prices in a selected country or group of countries under international or external reference pricing systems. If an agreement cannot be reached, confidential discounts might be negotiated between the manufacturer and the healthcare system authorities. The downward pressure on health care costs in general, particularly prescription product candidates, has become very intense. As a result, increasingly high barriers are being erected to the entry of new product candidates. In addition, in some countries, legally permissible cross- border imports from low-priced markets within the EU single market exert a commercial pressure on pricing within a country.

The containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of pharmaceutical or biological product candidates have been a focus in this effort. Third-party payors are increasingly challenging the prices charged for medical product candidates and services, examining the medical necessity and reviewing the cost-effectiveness of pharmaceutical or biological product candidates, medical devices and medical services, in addition to questioning safety and efficacy. If these third-party payors do not consider our product candidates to be cost effective compared to other available therapies, they may not cover our product candidates after approval, if any, or, if they do, the level of payment may not be sufficient to allow us to sell our product candidates at a profit.

Healthcare Reform

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medical product candidates. For example, the ACA, among other things, increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program; introduced a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for product candidates that are inhaled, infused, instilled, implanted or injected; extended the Medicaid Drug Rebate Program to utilization of prescriptions of individuals enrolled in Medicaid- managed care plans; imposed mandatory discounts for certain Medicare Part D beneficiaries as a condition for manufacturers' outpatient drugs coverage under Medicare Part D; subjected manufacturers to new annual fees based on pharmaceutical companies' share of sales to federal healthcare programs; created a new Patient Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research and established a Center for Medicare and Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending. Since its enactment, there have been judicial, executive and Congressional challenges to certain aspects of the ACA On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In March 2021, the American Rescue Plan Act of 2021 was signed into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, beginning January 1, 2024.

Moreover, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed product candidates, which have resulted in several Congressional inquiries and proposed bills designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for pharmaceutical and biologic product candidates.

On August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023), and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the Department of Health and Human Services to implement many of these provisions through guidance, as opposed to regulation, for the initial years. For that and other reasons, it is currently unclear how the IRA will be effectuated.

Individual states in the United States have also become increasingly active in implementing state laws and regulations addressing pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine which drugs and suppliers will be included in their healthcare programs Furthermore, there has been increased interest by third party payors and governmental authorities in reference pricing systems and publication of discounts and list prices.

On December 13, 2021, EU Regulation No 2021/2282 on Health Technology Assessment ("HTA") amending Directive 2011/24/EU, was adopted. While the Regulation entered into force in January 2022, it will only begin to apply from January 2025 onwards, with preparatory and implementation-related steps to take place in the interim. Once the Regulation becomes applicable, it will have a phased implementation depending on the concerned products: oncology and advanced therapy medicinal products ("ATMPs") as of 2025, orphan medicinal products as of 2028 and 2030 for all other medicinal products. This Regulation intends to boost cooperation among EU member states in assessing health technologies, including new medicinal products, and providing the basis for cooperation at the EU level for joint clinical assessments in these areas, using methodologies adapted to the specificities of the type of product in question. The Regulation will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the most potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU 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.

We expect that additional state, federal or foreign healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare product candidates and services, which could result in reduced demand for our product candidates once approved or additional pricing pressures.

Employees

As of December 31, 2022, 2021 and 2020, Mereo had 36, 49, and 38 employees, respectively. As at December 31, 2022, 27 employees are located in the United Kingdom and 9 employees are located in the United States.

All of our employees are engaged in either general and administrative or research and development functions. None of our employees are covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

Legal Proceedings

There are no governmental, legal or arbitration proceedings (including any such proceedings which are pending or threatened of which we are aware) that may have, or have had in the recent past (covering the 12 months immediately preceding the date of this annual report), significant effects on our financial position or profitability.

4.C. Organizational Structure

Mereo BioPharma Group plc was formed as a private limited company organized under the laws of England and Wales on March 10, 2015 and re-registered as a public limited company on June 3, 2016.

As at December 31, 2022, Mereo BioPharma Group plc has the following wholly-owned direct or indirect subsidiaries:

Legal Name of Subsidiary	Jurisdiction of Organization
Mereo BioPharma 1 Limited	United Kingdom
Mereo BioPharma 2 Limited	United Kingdom
Mereo BioPharma 3 Limited	United Kingdom
Mereo BioPharma 4 Limited	United Kingdom
Mereo BioPharma Ireland Limited	Ireland
Mereo US Holdings Inc.	Delaware
Mereo BioPharma 5, Inc.	Delaware
Navi Subsidiary, Inc.	Delaware

4.D. Property, Plants and Equipment

Mereo's principal office is located at 4th Floor, One Cavendish Place, London W1G 0QF, United Kingdom, where Mereo leases approximately 7,400 square feet of office space. Mereo leases this office space under a lease that terminates on June 24, 2026.

Item 4A. Unresolved Staff Comments

None.

Item 5. Operating And Financial Review And Prospects

5.A. Operating Results

The following discussion of our financial condition and results of operations should be read in conjunction with Mereo's audited consolidated financial statements and related notes included elsewhere in this annual report. The following discussion is based on Mereo's financial information prepared in accordance with IFRS as issued by the IASB, which may differ in material respects from generally accepted accounting principles in other jurisdictions, including generally accepted accounting principles in the United States. The following discussion includes forward-looking statements that involve risks, uncertainties, and assumptions. Mereo's actual results may differ materially from those anticipated in these forward-looking statements as a result of many factors, including but not limited to those described under "Item 3. Key Information—D. Risk Factors" and elsewhere in this annual report.

Overview

We are a biopharmaceutical company focused on the development of innovative therapeutics for rare diseases. We have developed a robust portfolio of clinical stage product candidates. Our two rare disease product candidates are setrusumab for the treatment of osteogenesis imperfecta (OI) and alvelestat for the treatment of severe alpha-1-anti-trypsin deficiency (AATD-LD) and Bronchiolitis Obliterans Syndrome (BOS) following allogenic stem cell transplant. Our partner, Ultragenyx, has initiated a pivotal Phase 2/3 pediatric and young adult study (5-25 years old) for setrusumab in OI, with the Phase 3 transition expected in mid-2023, and intends to initiate a study in pediatric patients under age five in the first half of 2023.

We announced successful completion of a Phase 2 study for alvelestat in AATD-LD in May 2022 which demonstrated statistically significant changes in biomarkers of lung function at different time points up to 12 weeks. Further, we recently announced that Fast Track designation has been granted by the U.S. Food and Drug Administration (FDA) for alvelestat in AATD, along with additional program updates. In March 2023, we announced the outcome of the end-of-Phase 2 discussions with the FDA and the EMA (Scientific Advice) and based on clear recommendations from both Agencies, we are designing a single, global, Phase 3 study evaluating the 240 mg dose of alvelestat versus placebo in patients with AATD-LD to support applications for full marketing approvals in both the U.S. and EU. Alvelestat is also in an ongoing Phase 2 investigator-led study in AATD, including in patients who may be on augmentation therapy, with data expected in the third quarter of 2023. Following successful completion of a Phase 1b investigator-led study in BOS patients following allogenic stem cell transplant, a Phase 2 study was initiated in the second half of 2022.

Our lead oncology product candidate, etigilimab (an anti-TIGIT antibody), has completed a Phase 1a dose escalation clinical trial in patients with advanced solid tumors and has been evaluated in a Phase 1b study in combination with nivolumab in select tumor types. We have completed enrollment in an open label Phase1b/2 basket study (the ACTIVATE study) evaluating etigilimab in combination with nivolumab in three rare tumors, sarcoma, uveal melanoma and germ cell cancer, three gynecological carcinomas, cervical, ovarian and endometrial carcinomas, and tumors with high mutation burden, along with a Phase 1b/2 study in clear cell ovarian cancer with a partner.

We plan to develop our product candidates through the next key clinical milestone and then partner where it makes sense strategically to do so, but also in select cases for our rare disease product candidates, to develop them through regulatory approval and potentially commercialization.

Our second oncology product, navicixizumab for the treatment of late line ovarian cancer has completed a Phase 1b study and was partnered in January 2020 for further development with OncXerna Inc. ("OncXerna") on a global basis. In February 2022, we received a milestone payment of $2.0 million (£1.5 million) under the license agreement with OncXerna. An associated payment was made to the former shareholders of Mereo BioPharma 5, Inc. under the Contingent Value Rights Agreement ("CVR") of a total of $0.9 million (£0.7 million), after deductions of costs, charges and expenditures. The milestone received and the associated CVR payment were recorded within "Other income and expense" in the Company's consolidated statement of comprehensive (loss)/income.

We plan to partner or sell our other two product candidates, acumapimod for the treatment of AECOPD and leflutrozole for the treatment of infertility and HH in obese men, recognizing the need for greater resources to take these product candidates to market.

In the first half of 2022, we conducted a comprehensive strategic review of our portfolio and capital allocation strategy. This review included a detailed evaluation of current market conditions, the status of our three ongoing programs, an analysis of recent emerging clinical data, our overall cost base and contractual commitments, consideration of obligations in our existing partnership agreements, and feedback from potential new partners and shareholders. In the fourth quarter of 2022 we provided an update to our operating plan, which included a targeted reduction in the employee base of up to 40% and a significant reduction in other costs. Our updated plan maintains the ability to progress our core programs, deliver on multiple near-term milestones and optimize value for shareholders. We will retain the core capabilities and key personnel needed to advance our two core rare disease programs, setrusumab and alvelestat, and to generate value from our assets. The updated plan extends our cash runway into 2026.

We do not have any approved product candidates and, as a result, have not generated any revenue from product sales. Our ability to generate revenue sufficient to achieve profitability will depend on successful development and eventual commercialization of our product candidates either directly or with partners, if approved. Since our inception, we have incurred significant operating losses. For the year-ended December 31, 2022 we had a net loss of £34.2 million, including a £7.8 million gain on changes in fair value of financial instruments. For the years ended December 31, 2021 and 2020, we had a net profit of £12.7 million, including a £40.0 million gain on changes in fair value of financial instruments, and a net loss of £163.6 million, including a £109.8 million loss on changes in fair value of financial instruments, respectively. As of December 31, 2022, we had an accumulated net loss of £331.2 million (£297.0 million as of December 31, 2021).

We expect to continue to incur significant expenses and operating losses for the foreseeable future as we advance the clinical and manufacturing development of our product candidates and seek regulatory approval. If approved, we also expect to incur significant commercialization expenses related to product manufacturing, marketing, sales, and distribution.

We also expect to incur expenses in connection with the in-license or acquisition of additional rare disease product candidates and the potential clinical development of any such product candidates.

Additionally, we anticipate losing our foreign private issuer status and expect to incur increased costs associated with being a U.S. domestic filer, including expenses related to more frequent financial reporting, preparation of financial statements in accordance with US GAAP, compliance with U.S. federal proxy rules, and additional resources and services we will require in order to comply with Nasdaq and SEC rules and requirements applicable to U.S. domestic filers.

We are organized into a single operating segment following management's view of the business as a single portfolio of product candidates. Research and development expenses are monitored at a product level; however, decisions over resource allocation are made at an overall portfolio level. Our financing is managed and monitored on a consolidated basis.

Financial Operations Overview

Revenue

The Company's ordinary business activities are the development of product candidates to key clinical milestones and either strategically partnering them or further developing such product candidates through regulatory approval and potentially commercialization. The Company may enter into a range of different agreements with third parties, including, but not limited to: (i) licensing agreements where the global rights to a product candidate are licensed to a partner; and (ii) collaboration agreements where rights to a product candidate are licensed to a partner but the Company retains certain rights, for example to further develop or commercialize the product candidate in specified geographical territories. Under both licensing and collaboration agreements, rights to product candidates are provided to a partner typically in exchange for consideration in the form of upfront payments and/or development, regulatory, commercial or other similar milestones, and royalties on commercial sales, should regulatory approval be obtained for the product candidates. Where the Company has performed significant development activities for its product candidates, income from agreements with third parties are considered to be proceeds derived from the Company's ordinary activities and therefore represent revenue.

Revenue includes income from licensing and collaboration agreements. Consideration received up front is recognized at the point in time in which the right to use an intangible asset is transferred. Income from development, regulatory, commercial or similar milestones is recognized when considered highly probable that a significant reversal will not occur.

Intangible assets out-licensed under a license or collaboration agreement are recorded within "Cost of revenue" in the Company's consolidated statement of comprehensive income/(loss) based on an allocation of cost or value of the rights that have been out-licensed. Payments to third parties arising as a direct consequence of the income recognized are also recorded within "Cost of revenue" in the Company's consolidated statement of comprehensive income/(loss).

We do not currently have any approved product candidates. Accordingly, we have not generated any commercial sales revenue during the period. In the future, we expect to be able to generate revenues if we are able to obtain regulatory approval and commercialize one or more of our product candidates or through the recognition of milestones and other potential revenues from out-licensing or partnering arrangements for any of our product candidates.

Research and Development Expenses

Research and development expenses include:

- employee-related expenses, such as salaries, share-based compensation, and other benefits, for Mereo's research and development personnel;
- costs for production of drug substance and drug product and development of Mereo's manufacturing processes by CMOs;
- fees and other costs paid to CROs, consultants, and other suppliers to conduct Mereo's clinical trials and pre-clinical and non-clinical studies; and
- costs of facilities, materials, and equipment related to drug production and Mereo's clinical trials and pre-clinical and non-clinical studies.

Our direct research and development expenses are allocated on a product-by-product basis. We allocate employee-related expenses for our research and development personnel and other related expenses to specific product candidate development programs.

Product candidates in a later stage of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later stage clinical trials as well as preparation for potential specific post-authorization evidence generation that might be demanded by regulatory authorities. As we continue to advance the clinical development of our product candidates, we expect that our research and development expense will include costs associated with laying the groundwork for price reimbursement and manufacturing in Europe, and input into development and regulatory plans with our partner, Ultragenyx, for setrusumab; regulatory interactions following the completion of our Phase 2 study in AATD-LD for alvelestat; and the completion of the Phase 1b portion of the Phase1b/2 basket study for etigilimab.

The successful development, approval, and commercialization of our product candidates is highly uncertain. At this time, we cannot reasonably estimate the nature, timing, and estimated costs of the efforts that will be necessary to complete the development of, or the period, if any, in which material net cash inflows may commence from any of our product candidates.

Our future expenditure on developing our product candidates is therefore highly uncertain. This is due to numerous risks and uncertainties associated with developing our product candidates, including the uncertainty of:

- the scope, rate of progress, and expense of our research and development activities;
- the progress and results of our clinical trials and our pre-clinical and non-clinical studies;
- the terms and timing of regulatory approvals, if any;
- establishment of arrangements with our third-party manufacturers to obtain manufacturing supply;
- protection of our rights in its intellectual property portfolio;
- launch of commercial sales of any of our product candidates, if approved, whether alone or in collaboration with others;
- third party strategic relationships for clinical development and/or commercialization of our non-core product candidates and performance of our strategic partners under these arrangements;
- the sale, if any, of one or more of our non-core disease product candidates;
- acceptance of any of our product candidates, if approved, by patients, the medical community and payors at our desired pricing levels;
- competition with other therapies; and
- continued acceptable safety profile of any of our product candidates following approval.

Any of these variables with respect to the development of our product candidates or any other future candidate that we may develop could result in a significant change in the costs and timing associated with their development. For example, if the FDA, the EMA, or another regulatory authority were to require us to conduct pre-clinical studies and clinical trials beyond those that we currently anticipate will be required for the completion of clinical development or if we experience significant delays in enrollment in any clinical trials, we could be required to expend significant additional financial resources and time on the completion of our clinical development programs. We may never succeed in obtaining regulatory approval for any of our product candidates.

Administrative Expenses

Our administrative expenses principally consist of salaries and related benefits, including share-based compensation, for personnel in our executive, finance and other administrative functions. Other general and administrative costs include facility-related costs, professional services fees for auditing, tax and general legal services, costs to maintain, protect and enforce our intellectual property, costs related to our requirements of being a public company listed on Nasdaq, costs incurred relating to the issue of equity to the extent not capitalized and the costs associated with the cancellation of admission of our ordinary shares to trading on the AIM market of London Stock Exchange plc in December 2020.

Finance Income

Finance income consists of interest earned on short-term cash deposits.

Finance Costs

Finance costs comprise interest on convertible loan notes, finance charges on lease liabilities and discounting on provision for deferred cash consideration. For further information on the terms of our convertible loan notes see “—Liquidity and Capital Resources—Indebtedness”.

Changes in Fair Value of Financial Instruments

The fair value changes in financial instruments are recognized in the statement of comprehensive loss.

Net Foreign Exchange Gain/(Loss)

Our functional currency is pound sterling. We initially record transactions in foreign currencies at the rate prevailing on the date the transaction first qualifies for recognition. Net foreign exchange gain/(loss) consists of the difference arising on settlement or translation of our foreign currencies, which are primarily held in U.S. dollars.

Taxation

As a U.K. resident trading entity, we are subject to U.K. corporate taxation. Due to the nature of our business, we have generated losses since formation. As at December 31, 2022, 2021 and 2020, we had cumulative carry-forward tax losses of £125.8 million, £122.6 million and £136.9 million, respectively. The availability to carry forward and offset these tax loss carry forwards against future operating profits is subject to certain restrictions. As a company that carries out extensive research and development ("R&D") activities, we benefit from the U.K. HMRC R&D small and medium-sized enterprise tax credit regime and are able to surrender some of our trading losses that arise from our research and development activities for a cash rebate. To date, a cash rebate of up to 33.35% of eligible R&D expenditure has been available, but the cash rebate will reduce to a maximum of 27% for R&D intensive companies where at least 40% of their total expenditure in on qualifying R&D, or to 18.6% of eligible R&D expenditure for other companies with effect from April 1, 2023 pursuant to changes made by the Finance Act 2023. Certain subcontracted qualifying research expenditures are eligible for a cash rebate, though the rate of the cash rebate will reduce with effect from April 1, 2023 from up to 21.67% of the subcontracted expenditures to 17.53% for R&D intensive companies or 12.09% for other companies. Qualifying expenditures largely comprise employment costs for research staff, subcontracted CRO and CMO costs, consumables and certain internal overhead cost incurred as part of research projects. We may not be able to continue to claim payable R&D tax credits in the future because we may no longer qualify as a small or medium-sized company.

In the event we generate revenues in the future, we may also benefit from the U.K. "patent box" regime that allows profits attributable to revenues from patents or patented product candidates to be taxed at an effective rate of 10%. This relief applies to profits earned following election into the regime.. When taken in combination with the enhanced relief available on our R&D expenditures, we expect a long-term lower rate of corporation tax to apply to us. If, however, there are unexpected adverse changes to the U.K. R&D tax credit regime or the "patent box" regime, or for any reason we are unable to qualify for such advantageous tax legislation, or we are unable to use net operating loss and tax credit carry forwards and certain built-in losses to reduce future tax payments, our business, results of operations, and financial condition may be adversely affected.

As of December 31, 2022, the Company had U.S. federal tax losses to be carried forward of approximately £74.6 million (2021: £65.6 million), of which £67.7 million can be carried forward indefinitely and £6.9 million which will begin to expire in 2023. As of December 31, 2022, the Company had U.S. state tax losses to be carried forward of approximately £4.0 million which begin to expire in 2027.

Critical Accounting Judgments and Estimates

Our consolidated financial statements have been prepared in accordance with IFRS as issued by the IASB. In the application of our accounting policies, we are required to make judgments, estimates, and assumptions about the value of assets and liabilities for which there is no definitive third-party reference. The estimates and associated assumptions are based on historical experience and other factors that we consider to be relevant. Actual results may differ from these estimates. We review our estimates and assumptions on an ongoing basis. Revisions to accounting estimates are recognized in the period in which the estimate is revised if the revision affects only that period or in the period of the revisions and future periods if the revision affects both current and future periods.

Further details relating to critical accounting judgments and estimates can be found in the consolidated financial statements, incorporated herein by reference.

Results of Operations

The following table sets forth Mereo's results of operations for the years ended December 31, 2022 and 2021.

	Year ended December 31		Change	
	2022	2021		%
	£'000s	£'000s	£'000s	%
Revenue	—	36,464	(36,464)	(100)%
Cost of revenue	936	(17,908)	18,844	(105)%
Research and development expenses	(24,962)	(23,559)	(1,403)	6%
Administrative expenses	(19,543)	(15,933)	(3,610)	23%
Operating loss	(43,569)	(20,936)	(22,633)	108%
Finance income	696	1	695	*
Finance costs	(3,361)	(4,022)	661	(16)%
Changes in fair value of financial instruments	7,805	40,039	(32,234)	(81)%
Gain/(loss) on disposal of intangible assets	—	113	(113)	(100)%
Net foreign exchange gain/(loss)	1,525	(954)	2,479	*
Other income and expenses	811	—	811	*
(Loss)/profit before tax	(36,093)	14,241	(50,334)	*
Taxation	1,897	(1,516)	3,413	*
(Loss)/profit attributable to equity holders of the parent	(34,196)	12,725	(46,921)	*
Currency translation of foreign operations	(1,828)	(191)	(1,637)	*
Total comprehensive (loss)/income attributable to equity holders of the parent	(36,024)	12,534	(48,558)	*

* Percentage change not meaningful

Comparison of Years Ended December 31, 2022 and 2021

Revenue

Revenue was nil for the year ended December 31, 2022 compared to £36.5 million for the year ended December 31, 2021.

In January 2021, the Company's licensing and collaboration agreement with Ultragenyx for the development and commercialization of setrusumab for OI became effective. Under the terms of the agreement, Ultragenyx will lead future global development of setrusumab in both pediatric and adult patients. We granted Ultragenyx an exclusive license to develop and commercialize setrusumab in the US and rest of the world, excluding Europe and the U.K. where we retain commercial rights. Each party will be responsible for post-marketing commitments in their respective territories.

Ultragenyx made an upfront payment of £36.5 million ($50 million) to Mereo in January 2021 and will fund global development of the program until approval and has agreed to pay a total of up to $254 million upon achievement of certain clinical, regulatory and commercial milestones. Ultragenyx will pay tiered double digit percentage royalties to us on net sales outside of Europe and the U.K. and we will pay a fixed double digit percentage royalty to Ultragenyx on net sales in Europe and the U.K.

Cost of revenue

Cost of revenue for the year ended December 31, 2022 was a credit of £0.9 million compared to £17.9 million of expense for the year ended December 31, 2021.

In 2021, cost of revenue was comprised of £9.5 million, representing the carrying value of the setrusumab rights granted to Ultragenyx under the licensing and collaboration agreement, and £8.4 million in relation to our 2015 agreement with Novartis, under which the Company pays a percentage of proceeds, subject to certain exceptions. Under the terms of this agreement, we made a payment of £7.2 million to Novartis for the year-ended December 31, 2021. The payment included a deduction for costs of £2.4 million which was deferred to be recognized in the statement of comprehensive income when the associated costs are incurred. For the year ended December 31, 2022, £0.9 million of these deductions were recognized in cost of revenue compared to £1.1 million for the year ended December 31, 2021.

Research and development ("R&D") Expenses

The following table sets forth our R&D expenses by product development program for the years ended December 31, 2022 and 2021.

	Year ended December 31		Change	
	2022	2021		
	£'000s	£'000s	£'000s	%
Setrusumab (BPS-804/UX143)	3,356	3,597	(241)	(7)%
Alvelestat (MPH-966)	5,430	5,303	127	2%
Etigilimab (MPH-313)	15,802	13,499	2,303	17%
Leflutrozole (BGS-649)	58	157	(99)	(63)%
Acumapimod (BCT-197)	50	94	(44)	(47)%
Navicixizumab ("Navi")	—	15	(15)	(100)%
Other	1	63	(62)	(98)%
Unallocated costs	265	831	(566)	(68)%
Total R&D expenses	**24,962**	**23,559**	**1,403**	**6%**

Total R&D expenses increased by £1.4 million, or 6%, from £23.6 million in 2021 to £25.0 million in 2022.

R&D expenses relating to etigilimab increased by £2.3 million. The increase was due to the costs associated with additional patients and the duration of treatment for patients responding to therapy in 2022 compared to 2021 in the open label Phase 1b/2 basket study in combination with an anti-PD-1 in a range of tumor types. R&D expenses relating to alvelestat increased £0.1 million, or 2%, primarily reflecting the end of study related costs for the Phase 2 proof-of-concept study in AATD-LD. Partially offsetting the increases, R&D expenses relating to setrusumab decreased by £0.2 million, or 7%. Setrusumab R&D expenditure in 2022 comprised activities associated with laying the groundwork for price reimbursement in Europe, and input into development, regulatory and manufacturing plans with our partner, Ultragenyx, as the global development of the program is funded by Ultragenyx pursuant to our licensing and collaboration agreement.

Administrative expenses

Administrative expenses increased by £3.6 million, or 23%, from £15.9 million in 2021 to £19.5 million in 2022.

The increase was primarily driven by additional costs incurred in connection with the Schedule 13D filings and subsequent Cooperation Agreement with Rubric Capital, and increased share-based payment expenses, partially offset by a reduction in other professional fees.

Finance income and costs

Total finance costs decreased from £4.0 million in 2021 to £3.4 million in 2022. The decrease is primarily related to a reduction in the interest on the June 2020 Private Placement convertible loan notes of £0.9 million following conversion of certain loan notes in 2022.

Finance income increased by £0.7 million from nil to £0.7 million as a result of interest income on short-term deposits.

Changes in fair value of financial instruments

The total change in fair value of financial instruments for 2022 was a gain of £7.8 million, a decrease of £32.2 million compared to a gain of £40.0 million in 2021. The gain resulted from a £7.6 million (2021: £39.5 million) unrealized gain on Warrants in respect of the June 2020 Private Placement and a £0.2 million (2021: £0.5 million) unrealized gain on warrants issued to our former lenders in connection with the loan facility. The unrealized gain in the warrant instruments in both 2022 and 2021 primarily resulted from a decline in the market price of our ADSs as of December 31, 2022 compared to December 31, 2021, and as of December 31, 2021 compared to December 31, 2020.

Net foreign exchange gain/(loss)

The net foreign exchange gain for 2022 was £1.5 million compared to a loss of £1.0 million in 2021, a change of £2.5 million. The net foreign exchange gain is primarily related to the translation of non-functional currency balances, primarily denominated in U.S. dollars.

Taxation

The income tax benefit for 2022 was £1.9 million. The income tax benefit represents eligible cash rebates paid or receivable from the tax authorities in the jurisdictions within which we operate for eligible types of research and development

activities and associated expenditure (the “R&D tax credit”) and and income taxes paid in the prior year for which a carryback claim has been made to offset against taxable income in the prior year.

The income tax charge for 2021 was £1.5 million. The income tax charge arises primarily from a £40.0 million unrealized gain resulting from changes in the fair value of warrant instruments.

Currency translation of foreign operations

The currency translation of foreign operations for the year ended December 31, 2022 was £1.8 million compared to £0.2 million for the year ended December 31, 2021. The £1.6 million change is primarily related to the devaluation of the pound sterling to the U.S. dollar in the 2022 compared to 2021.

Comparison of the Years Ended December 31, 2021 and 2020

For information relating to the comparison of the years ended December 31, 2021 and 2020, see "Item 5. Operating and Financial Review and Prospects" in our annual report on Form 20-F for the fiscal year ended December 31, 2021 filed with the SEC on March 31, 2022.

5.B. Liquidity and Capital Resources

Overview

Under the current business plan and cash flow forecasts, and in consideration of our ongoing research and development efforts and our general corporate funding requirements, we anticipate that our current on-hand cash resources will extend into 2026. However, we will need additional external funding to complete our development plans and potentially commercialize selected rare disease products. We plan to fund our operations through cash on hand and a combination of non-dilutive funding sources, public or private equity or debt financings or other sources.

We do not currently have any approved product candidates and as a result, have not generated any revenue from product sales. As a result, to date, we have financed our operations primarily through the issuances of our equity securities, convertible debt and warrants. Through these offerings, we raised $183 million (£137.9 million) We also received an upfront payment of $50 million under the license and collaboration agreement with Ultragenyx for setrusumab in 2021.

Contractual Obligations

As further described above under "—A. Operating Results—Asset Purchase Agreements with Novartis" and "—A. Operating Results—License Agreement with AstraZeneca," under various agreements with Novartis and AstraZeneca, Mereo has agreed to make milestone payments and pay royalties. The amount, timing, and likelihood of such payments are not known and will remain uncertain for the foreseeable future.

In addition, Mereo enters into contracts in the ordinary course of business with CROs, CMOs, and other vendors to assist in the performance of its research and development activities and other services and products for operating purposes. The contracts with CROs generally provide for termination on notice, and therefore are cancelable contracts. We have manufacturing commitments with CMOs of £0.9 million as of December 31, 2022.

Cash Flows

Comparison of Years Ended December 31, 2022 and 2021

The table below summarizes our cash flows (used in) from operating, investing and financing activities for the years ended December 31, 2022 and 2021. Year Ended December 31,

	Year Ended December 31,	
	2022	2021
	£'000s	£'000s
Net cash used in operating activities	(38,820)	(5,239)
Net cash from/(used) in investing activities	1,497	(421)
Net cash (used in)/from financing activities	(784)	77,652
Net (decrease)/increase in cash and cash equivalents	(38,107)	71,992

Operating Activities

Net cash used in operating activities for the year ended December 31, 2022 was £38.8 million, an increase of £33.6 million from £5.2 million in 2021. The increase was primarily driven by the receipt of upfront payments from Ultragenyx of £36.5 million, offset by associated payments to Novartis of £7.2 million in 2021. Further, in 2021, we received R&D tax credits from the U.K. tax authorities of £2.8 million compared to a tax payment of £1.5 million in 2022. In 2021, these operating cash inflows primarily offset the operating expenditures of the Company, whereas in 2022, similar cash inflows did not occur.

Investing Activities

Net cash from investing activities for the year ended December 31, 2022 was £1.5 million, an increase from a cash outflow of £0.4 million in 2021. The increase was primarily driven by interest earned on short term deposits of £0.7 million and milestone receipt of £1.5 million from OncXerna following the global licensing arrangement for navicixizumab, offset by payments to CVR holders of £0.7 million.

Financing Activities

Net cash used in financing activities for the year ended December 31, 2022 was £0.8 million, a decrease of £78.4 million, compared to cash inflow of £77.7 million in 2021. The decrease is primarily attributable to £78.4 million net proceeds from the Public Offering in February 2021.

Comparison of the Years Ended December 31, 2021 and 2020

For information relating to the comparison of the years ended December 31, 2021 and 2020, see "Item 5. Operating and Financial Review and Prospects" in our annual report on Form 20-F for the fiscal year ended December 31, 2021 filed with the SEC on March 31, 2022.

Operating and Capital Expenditure Requirements

As of December 31, 2022, we had an accumulated loss of £331.2 million. We expect to continue to report significant operating losses for the foreseeable future as we continue our research and development efforts and seek to obtain regulatory approval of our product candidates and any future product we develop. See also "Risk Factors—Risks Related to Our Business and Industry—If we do not obtain adequate and timely funding, we may not be able to continue as a going concern".

We expect to continue to incur expenses in connection with our ongoing development activities related to our product candidates, our outsourced manufacturing activities and other associated costs including the management of our intellectual property portfolio. We also expect to continue to incur costs associated with operating as a U.S. public company listed on Nasdaq.

These costs will increase further if we:

- seek to develop additional product candidates;
- seek regulatory approvals for any of our product candidates that successfully completes clinical trials;
- potentially establish a sales, marketing, and distribution infrastructure and scale-up manufacturing capabilities to commercialize or co-commercialize any product candidates for which we may obtain regulatory approval and chose to commercialize directly;
- expand our intellectual property portfolio;
- add further clinical, scientific, operational, financial, legal and management information systems, and personnel, including personnel to support our development and to support our operations as a U.S. public company listed on Nasdaq;
- lose our foreign private issuer status in the future; or
- experience any delays or encounter any issues from any of the above, including but not limited to failed studies, complex results, safety issues, or other regulatory challenges.

We expect that our existing cash and short-term deposits will enable us to fund our currently committed clinical trials, operating expenses and capital expenditure requirements into 2026. We have based these estimates on assumptions that may prove to be wrong, and we may use our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with the development of our product candidates and any future product candidates and because the extent to which we may enter into collaborations with third parties for development of any of our product candidates is unknown, we are unable to estimate the amounts of increased capital outlays and operating expenses associated with completing the research and development of our product candidates. Our future capital requirements will depend on many factors, including:

- The costs for our activities related to our ongoing collaboration with Ultragenyx for setrusumab for the treatment of adults and children with OI; and potential future clinical trials for alvelestat in AATD and other potential indications;
- the costs and timing of manufacturing clinical supplies of our product candidates;
- the costs, timing, and outcome of regulatory review of our product candidates, including post-marketing studies that could be required by regulatory authorities;
- the costs, timing, and outcome of potential future commercialization activities, including manufacturing, marketing, sales, life cycle management and distribution, for our product candidates that we commercialize directly;
- the timing and amount of revenue, if any, received from commercial sales of our product candidates;
- the costs and timing of preparing, filing, and prosecuting patent applications; maintaining and enforcing our intellectual property rights; and defending any intellectual property-related claims, including any claims by third parties that we are infringing, misappropriating or otherwise violating their intellectual property rights;
- the sales price and availability of adequate third-party coverage and reimbursement for our product candidates;
- the effect of competitors and market developments;
- the performance of our collaborators and partners under the existing agreements on setrusumab and navicixizumab;
- the extent to which we are able to acquire new product candidates or enter into licensing or collaboration arrangements for our product candidates, although we currently have no commitments or agreements to complete any such transactions;
- milestone and deferred payments under Mereo's license and option agreement with AstraZeneca; and
- tax liabilities or other assessments and our ability to claim R&D tax credits or other reliefs.

Our revenues, if any, will be derived from development milestones or sales of any product candidates that we are able to successfully develop, receive regulatory approval for, and commercialize in future years. In the meantime, we will need to obtain substantial additional funds to achieve our business objective.

Adequate additional funds may not be available to us on acceptable terms, or at all. If we raised additional funds through collaborations, strategic alliances, or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us.

Any future debt financing or preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends and may require the issuance of warrants, which could potentially dilute your ownership interests.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest may be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a shareholder. If we are unable to raise additional funds through partnerships, debt or equity financings when needed, we may be required to delay, limit, reduce, or terminate our product development programs or any future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Indebtedness

Former Credit Facility

As of December 31, 2022, the former lenders, Silicon Valley Bank and Kreos Capital V (UK) Limited, have warrants outstanding to purchase a total of 1,243,908 ordinary shares at an exercise price of £2.95 per share and a total of 1,243,908 ordinary shares at an exercise price of $0.4144 per share.

June 2020 Private Placement

On June 3, 2020, we entered into a securities purchase agreement (the "June 2020 Purchase Agreement") with a number of new and existing principally U.S based institutional and accredited investors (the "June 2020 Private Placement") pursuant to which we received $70.0 million (£56.0 million) comprising: the allotment of ordinary shares at a subscription price of $19.4 million (£15.5 million) utilizing the pre-existing share authorities of the Company, and the subscription for Tranche 1 convertible loan notes ("Loan Notes") in an aggregate principal amount of $50.6 million (£40.5 million).

Following the passing of resolutions at our General Meeting on June 30, 2020, the Loan Notes automatically converted into ordinary shares of £0.003 each in the capital of the Company except that no new ordinary shares were issued which would result in any person holding in excess of 9.99 percent. of the aggregate voting rights in the Company as a result of the relevant conversion. Accordingly, the automatic conversion resulted in Loan Notes in an aggregate principal amount of £21.8 million (together with accrued interest) converted into 125,061,475 ordinary shares on June 30, 2020.

As of December 31, 2022 Loan Notes in an aggregate principal amount of £6.2 million remained outstanding and convertible into ordinary shares or ADSs in accordance with their terms (2021: £12.4 million).

Novartis Notes

On February 10, 2020, we entered into a £3.8 million convertible loan note instrument relating to the issue of 3,841,479 Novartis Loan Note. The Novartis Loan Note is convertible at any time at a fixed price of £0.265 per ordinary share until February 10, 2023. In addition, on February 10, 2020, in connection with the Novartis Loan Note, we entered into a warrant instrument with Novartis to issue 1,449,614 ordinary shares at an exercise price of £0.265 per ordinary share. These warrants are exercisable until February 10, 2025.

On February 10, 2023, we amended the Novartis Loan Note, extending the maturity date to February 10, 2025. Pursuant to the amendment and a new warrant instrument, interest accrued to the amendment date was paid in cash, and warrants to purchase 2,000,000 ordinary shares at an exercise price of £0.150 per ordinary share were issued and are exercisable until February 10, 2028.

Contingent Value Rights ("CVR") arrangement

As a consequence of the License Agreement with OncXerna, and in accordance with the terms and conditions of the Contingent Value Rights Agreement for former stockholders of Mereo BioPharma 5 (formerly OncoMed), dated April 23, 2019, by and among Mereo and Computershare Inc., as rights agent, (the "CVR Agreement"), holders of contingent value rights ("CVRs") pursuant to the CVR Agreement will be entitled to receive certain eligible cash milestone payments made to Mereo under the License Agreement relating to Navi. The receipt of the upfront milestone payment of $4.0 million by us in January 2020 resulted in a payment to CVR holders of approximately 1.2 cents per CVR, a total of approximately $0.5 million (after deductions of costs, charges and expenditures). Future milestone payments occurring prior to the fifth anniversary of the closing of the Merger, April 23, 2024, are also subject to a cash consideration cap, pursuant to which the aggregate principal amount of all cash payments made to holders of CVRs under the CVR Agreement shall in no case exceed $79.7 million.

Mereo accounts for the CVR arrangement as contingent consideration at fair value. As at December 31, 2022, the fair value of the contingent consideration is estimated to be nil. The estimated contingent consideration payable is based on a risk-adjusted, probability-based scenario. Under this approach, the likelihood of future payments being made to the former shareholders of Mereo BioPharma 5 under the CVR arrangement is considered. The estimate could materially change over time in line with the development plan and subsequent commercialization of the Navi product, if approved.

5.C. Research and Development, Patents and Licenses, etc.

As a development stage company, most of our business operations are focused on research and development. Please refer to "Item 4. Information On the Company—B. Business Overview—Our Strategy and –Intellectual Property". For a description of the Company's research and development policies for the last three years see "Item 5. Operating and Financial Review and Prospects—A. Operating Results—Financial Overview—Research and Development Expenses." For a description of Mereo's intellectual property, see "Item 4. Information On the Company—B. Business Overview—Intellectual Property."

5.D. Trend Information

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

5.E. Critical Accounting Estimates

Not applicable.

Item 6. Directors, Senior Management And Employees

6.A. Directors and Senior Management

Executive Officers and Non-Executive Directors

The following table presents information about Mereo's executive officers and non-executive directors, including their ages, as of the date of this annual report:

Name	Age	Position
Executive Officers		
Dr. Denise Scots-Knight	63	Chief Executive Officer and Director
Christine Fox	42	Chief Financial Officer
John Richard	65	Chief Business Officer
Charles Sermon	53	General Counsel
Alexandra (Wills) Hughes-Wilson	51	Chief Patient Access and Commercial Planning
Dr. John Lewicki	71	Chief Scientific Officer
Dr. Suba Krishnan	58	Senior Vice President Clinical Development
Dr. Jackie Parkin	65	Senior Vice President and Therapeutic Head
Non-Executive Directors		
Dr. Jeremy Bender	51	Director
Dr. Anders Ekblom	68	Director
Dr. Pierre Jacquet	56	Director
Dr. Annalisa Jenkins	57	Director
Dr. Deepika R. Pakianathan	58	Director
Justin Roberts	40	Director
Dr. Daniel Shames	77	Director
Marc Yoskowitz	48	Director
Michael S. Wyzga	68	Chairman of the Board and Director

The current business addresses for Mereo's executive officers and directors is c/o Mereo BioPharma Group plc, 4th Floor, One Cavendish Place, London, W1G 0QF, United Kingdom.

The following are brief biographies of Mereo's executive officers and non-executive directors:

Dr. Denise Scots-Knight. Dr. Scots-Knight has served as our Chief Executive Officer since July 2015 and as a member of our Board since our formation. From 2010 until joining us, Dr. Scots-Knight was the Managing Partner of Phase4 Partners Ltd. ("Phase4"), a global life science venture capital firm. Dr. Scots-Knight is currently a board member of Elanco Animal Health Incorporated (NYSE: ELAN). Dr. Scots-Knight previously served as a member of the board of directors of Idenix Pharmaceuticals, Albireo and OncoMed. Dr. Scots-Knight holds a B.Sc. (Hons.) and a Ph.D. from Birmingham University.

Christine Fox. Ms. Fox joined as our Chief Financial Officer in January 2021. From 2015 until joining us, Ms. Fox was the Vice President Finance, External Reporting and most recently Group Financial Controller and Treasurer of Travelport, and prior to that served more than 10 years at KPMG in the U.S. and Switzerland. Ms. Fox is a Certified Public Accountant (CPA) and holds a B.S. in Accounting from Butler University.

J***ohn Richard.*** Mr. Richard has served as our Chief Business Officer, previously titled Head of Corporate Development, since July 2015. Prior to joining us, he was a consultant for Nomura, a global investment bank, and Phase4, and previously served as the head of business development for Sequus Pharmaceuticals Inc., VIVUS Inc. and Genome Therapeutics Corporation. Mr. Richard serves on the boards of Aruna Bio, Inc. and previously served on the boards of Catalyst Biosciences, Vaxart, Inc., Aviragen Therapeutics, Inc., and Targacept, Inc. Mr. Richard holds a B.S. from Stanford University and an MBA from Harvard Business School.

Charles Sermon. Mr. Sermon has served as our General Counsel and Company Secretary since July 2015. From 2010 until joining us, Mr. Sermon was a Partner of Phase4. Mr Sermon serves as a Director on the Board of Trustees of Rainbow Trust Children's Charity. Mr. Sermon trained and qualified as a lawyer with Freshfields in London after completing the Law Society's Final Examination. Mr. Sermon holds an LL.B. (Hons.) from Hull University.

Alexandra (Wills) Hughes-Wilson. Ms. Hughes-Wilson has served as our Chief of Patient Access and Commercial Planning, previously titled Head of Patient Access and Commercial Planning, since March 2018. Prior to joining us, Ms. Hughes-Wilson was Senior Vice President, Chief Patient Access Officer at Swedish Orphan Biovitrum (publ.) AB, a biotechnology company, from 2012 to 2018, and prior to that served as Vice President Health & Market Access Policy EMEA at Genzyme (now Sanofi Genzyme), a biotechnology company. Ms. Hughes-Wilson holds a bachelor's degree in Law and Politics (Hons.) from the University of Durham, U.K.

Dr. John Lewicki. Dr. Lewicki has served as our Chief Scientific Officer since July 2020. He has over 35 years of experience in the biotechnology industry. Dr. Lewicki was President, CEO and a board member of OncoMed from March 2018 to April 2019. Previously, Dr. Lewicki served as Vice President of Research, at Scios Inc. where he co-discovered human B-type natriuretic peptide (BNP). Dr. Lewicki contributed to development of BNP into an FDA-approved treatment (Natrecor) for acute congestive heart failure. Dr. Lewicki received his PhD from the University of California, San Diego. He has co-authored over 80 papers and is co-inventor on over 30 issued US patents.

Dr. Suba Krishnan. Dr Krishnan has served as our SVP Clinical Development since she joined us in December 2020 from Genmab, where, as Global Program Head Immuno-Oncology, she led cross-functional teams in the strategy and execution of multiple first-in-class bispecific antibodies. Dr. Krishnan has held positions of increasing scope, working across all stages of drug development, to evaluate PARP-inhibitors, ADCs and IO agents, and filing for approvals of nivolumab in second-line bladder cancer and pembrolizumab in small cell lung cancer. Earlier, Dr. Krishnan was Assistant Professor, Pediatric Hematology, Columbia University, and held the Sickle Cell Scholar position at Thomas Jefferson University. Dr. Krishnan completed her MBBS at the Armed Forces Medical College in Pune, India and trained in Pediatric Hematology/Oncology at Columbia University.

Dr. Jackie Parkin. Dr. Parkin is our SVP and Therapeutic Head, leading clinical development of alvelestat for alpha-1 antitrypsin deficiency (AATD) lung disease and collaborations for studies in COVID-19 and Bronchiolitis Obliterans Syndrome (BOS). She is also responsible for acumapimod in AECOPD and leflutrozole in male hypogonadism. Dr. Parkin previously served as Vice President for Clinical Development at GlaxoSmithKline, leading immuno-inflammatory and infectious diseases. Prior to GSK, Dr. Parkin was a Clinical Senior Lecturer in Immunology at the St Bartholomew's and Royal London Hospital, caring for patients with HIV infection.

Dr. Jeremy Bender. Dr. Bender has served on our board since October 2020. Dr. Bender is Chief Executive Officer of DayOne Biopharmaceuticals, Inc. (NASDAQ: DAWN). Previously he served as Vice President of Corporate Development at Gilead Sciences, Inc., where he was responsible for development and negotiation of partnerships, alliances, joint ventures, equity investments, licensing agreements and M&A transactions. Dr. Bender joined Gilead from Tizona Therapeutics, Inc., where he was Chief Operating Officer. Prior to Tizona, he was Chief Business Officer of Sutro Biopharma, Inc. Dr. Bender received his undergraduate degree in Biological Sciences from Stanford University and his Ph.D. in Microbiology & Immunology from the University of Colorado. He also holds an M.B.A. from the MIT Sloan School of Management.

Dr. Anders Ekblom. Dr. Ekblom has served on our Board since July 2015. Dr. Ekblom has held a number of executive positions at AstraZeneca, including Executive Vice President Global Drug Development, Executive Vice President Global Medicines Development, Global Head Clinical Development and Chief Executive Officer of AstraZeneca AB Sweden. He currently serves as Chairman of the Board of Elypta AB and Xspray Pharma AB, and on the boards of directors of Alligator Bioscience AB and AnaMar AB. Dr. Ekblom is a board-certified medical doctor and an Associate Professor at the Karolinska Institutet. Dr. Ekblom holds a M.D., Ph.D. and a D.D.S. from Karolinska Institutet.

Dr. Pierre Jacquet. Dr. Jacquet has served on our Board of Directors since September 2021. Dr. Jacquet is currently Managing Director and Vice Chairman of L.E.K. Consulting's Global Healthcare practice. He has served in a variety of leadership roles over 20 years at L.E.K., including Global Head, Healthcare Practice, Global Leadership Team, the Americas management committee, and various partner operating committees. Prior to joining L.E.K. in 2001, Dr. Jacquet was trained as a surgical resident at University of Liège, Belgium and served as a Fellow at the Washington Cancer Institute, where he authored over 40 publications and presentations. In addition to serving on Mereo's Board of Directors, Dr. Jacquet is a Director of Exact Sciences, on the Advisory Board of Life Science Cares, and previously served as a Director of Osprey Pharmaceuticals. He earned a Master of Business Administration from the Darden Graduate School at the University of Virginia, graduated Magna Cum Laude in Medicine from the University of Liège in Belgium and was awarded a Summa Cum Laude Doctor of Philosophy in biomedical sciences from the University of Liège in Belgium.

Dr. Annalisa Jenkins. Dr. Jenkins has served on our Board of Directors since November 2022. Dr. Jenkins served as president and CEO of Dimension Therapeutics, a leading NASDAQ listed gene therapy company that was acquired by Ultragenyx in November 2017. Prior leadership roles have included the head of global research and development at Merck Serono and SVP, Global Development at Bristol Myers-Squibb. Dr. Jenkins is a board member and advisor to a number of public and private health and life science companies globally. She is also a board member of Genomics England and a trustee of The Kings Fund and The British Heart Foundation. Dr. Jenkins graduated with a degree in medicine from St. Bartholomew's Hospital in the University of London and served as a Surgeon Lieutenant Commander in the British Royal Navy.

Dr. Deepika R. Pakianathan. Dr. Pakianathan has served on our Board since April 2019 following completion of the Merger and served as a director of OncoMed since December 2008 until the closing of the Merger. Since 2001, Dr. Pakianathan has been a Managing Member at Delphi Ventures, a venture capital firm focused on biotechnology and medical device investments. Dr. Pakianathan serves on the boards of directors of Karyopharm Therapeutics, Inc., Theravance Biopharma, Inc., and Calithera Biosciences, Inc. Dr. Pakianathan previously served on the boards of directors of Foresite Development Corp II, Alder Biopharmaceuticals, Inc. and Foresite Development Corp I. and Relypsa, Inc. Dr. Pakianathan received a B.Sc. from the University of Bombay, India, a M.Sc. from The Cancer Research Institute at the University of Bombay, India, and an M.S. and Ph.D. from Wake Forest University.

Justin Roberts. Justin Roberts has served on our Board of Directors since November 2022. Mr. Roberts is a Partner at Rubric Capital Management LP, a role he has held since the formation of the company in 2016. Before Rubric he spent seven years at Point72 Asset Management. Mr. Roberts has also held roles at ZS Associates, Moore Capital Management, and began his career at Lehman Brothers as an investment banker in their M&A practice. Mr. Roberts graduated with honors from Johns Hopkins University.

Dr. Daniel Shames. Dr. Shames has served on our Board of Directors since November 2022. Dr. Shames has served as President of Daniel A. Shames Consulting, providing regulatory services to over 100 biotechnology and pharmaceutical clients. Prior to starting his consultancy Dr. Shames spent 12 years at the FDA during which time he was involved in the safety and efficacy review of hundreds of drugs. Most recently Dr. Shames served as Deputy Director, Office of Drug Evaluation III from 2006 to 2008, while also serving as Director of the Division of Gastroenterology and Inborn Error Products. Prior to that he was Director of Reproductive and Urologic Drugs from 2001 to 2006. Before joining the FDA, Dr. Shames founded Carolina Urocorp, operated a private medical practice, and was as Major in the United States Army Medical Corps. Dr. Shames received his undergraduate degree from Brandeis University, his MD from Georgetown University School of Medicine, and did his urology residency at the University of Pennsylvania.

Marc Yoskowitz. Mr. Yoskowitz has served on our Board of Directors since November 2022. Mr. Yoskowitz serves as EVP and Chief Strategy Officer, Life Sciences at Tempus, Inc. Prior to Tempus, Mr. Yoskowitz was Chief Business Officer, Pfizer Essential Health, leading a range of corporate initiatives within the Pfizer portfolio. Prior to Pfizer, he served as SVP, Strategy and Corporate Development at Hospira and was a member of the Executive Committee. Earlier in his career, Mr. Yoskowitz led business development at a specialty pharmaceutical company, spent eight years at McKinsey & Company where he was an Associate Principal, and began his career as an M&A lawyer at Davis, Polk & Wardwell in New York. Mr. Yoskowitz received a bachelor's degree magna cum laude from Washington University in St. Louis and holds a JD from Columbia University School of Law.

Michael S. Wyzga. Mr. Wyzga has served on our Board since April 2019 following completion of the Merger and had served as a director of OncoMed since October 2013 until the closing of the Merger. On May 14, 2020, we entered into the Consulting and Interim Chief Financial Officer Agreement with MSW Consulting Inc. and Michael Wyzga by which Mr.

Wyzga served as Interim Chief Financial Officer from August 1, 2020 to January 4, 2021. Mr. Wyzga is currently the President of MSW Consulting Inc., a strategic consulting group focused in the life sciences area. From December 2011 until November 2013, Mr. Wyzga served as President and Chief Executive Officer and a member of the board of directors of Radius Health, Inc. Prior to that, Mr. Wyzga served in various senior management positions at Genzyme Corporation, including as Chief Financial Officer from July 1999 until November 2011. Mr. Wyzga is a member of the boards of directors of Adagio Therapeutics, Inc. and LogicBio and is Chairman of the board of directors of GenSight Biologics S.A. and of X4 Biologics. Mr. Wyzga previously served as a member of the boards of directors of Exact Sciences Corporation, Idenix Pharmaceuticals, Inc. and Altus Pharmaceuticals, Inc., and as a member of the supervisory board of Prosensa Holding B.V. He received an M.B.A. from Providence College and a B.S. from Suffolk University.

Arrangements Concerning Election of Directors; Family Relationships

We are not a party to, and are not aware of, any voting agreements among our shareholders. In addition, there are no family relationships among our executive officers and directors.

6.B. Compensation

Executive Officer Remuneration

The following table sets forth the remuneration paid during the year ended December 31, 2022.

	Salary (£)	Cash Bonus (1) (£)	All Other Compensation (2) (£)	Total (3) (£)
Dr. Denise Scots-Knight	418,747	226,123	51,106	695,976
Other Executive Officers	2,063,665	762,482	219,818	3,045,965

(1) Amount shown reflects cash bonuses awarded for achievement of performance goals.
(2) Amount shown represents health benefit payments and pension contributions made by us.
(3) Total compensation set out in this table does not include any amounts for the value of options to acquire Mereo ordinary shares or awards granted to or held by current senior management, which is described in "—Equity Compensation Awards to Non-Executive Directors and Executive Officers of Mereo."

Executive Officer Employment Agreements

Dr. Denise Scots-Knight

We entered into an employment agreement with Dr. Scots-Knight on July 29, 2015, as amended and restated on September 3, 2021. This agreement entitles Dr. Scots-Knight to receive an annual base salary and an opportunity to earn an annual discretionary performance-based bonus, subject to the achievement of performance goals determined in accordance with our annual bonus plan. We currently contribute to Dr. Scots-Knight's Self-Invested Personal Pension Scheme an amount equal to 10% of Dr. Scots-Knight's annual salary, provided that she contributes 4% or more of her annual salary to that scheme. In lieu of a pension contribution, we may, at Dr. Scots-Knight's request, pay a pro-rata amount equal to 10% of her base salary as additional compensation. Either party may terminate the employment agreement by giving the other party not less than 12 months' written notice, provided that we may terminate Dr. Scots-Knight at any time with immediate effect for cause or by giving written notice to Dr. Scots-Knight that we will instead pay her basic salary for any remaining notice period. Dr. Scots-Knight's employment agreement also contains restrictive covenants pursuant to which she has agreed to refrain from competing with us or soliciting our key employees for a period of six months following her termination of employment or soliciting our customers for a period of nine months following her termination of employment. The employment agreement includes the provision of accelerated vesting of share options and payments to Dr. Scots-Knight equal to 18 months' annual base salary and Dr. Scots-Knight's target annual bonus in the event of a covered termination during the period commencing on a change in control of the Company and ending 12 months after such change in control.

Christine Fox

We entered into an employment agreement with Ms. Christine Fox on October 20, 2020, as amended on September 3, 2021. The employment agreement entitles Ms. Fox to receive an annual base salary and an opportunity to earn an annual discretionary performance-based bonus, subject to the achievement of performance goals determined in accordance with Mereo's annual bonus plan.

Ms. Fox is also eligible to participate in Mereo's group personal pension scheme and Mereo has agreed to contribute to the pension scheme an amount equal to 10% of Ms. Fox's annual salary provided that she contributes 4% or more of her annual salary to that scheme. In lieu of a pension contribution, Mereo may, at Ms. Fox's request, pay a pro-rata amount equal to 10% of her base salary as additional compensation. Either party may terminate the employment agreement by giving the other party not less than six months' written notice, provided that Mereo may terminate Ms. Fox at any time with immediate effect for cause or by giving written notice to Ms. Fox that Mereo instead pay her basic salary for any remaining notice period. Ms. Fox's employment agreement also contains restrictive covenants pursuant to which she has agreed to refrain from competing with Mereo or soliciting its key employees for a period of six months following her termination of employment or soliciting Mereo customers for a period of nine months following her termination of employment. The employment agreement includes the provision of accelerated vesting of share options and payments to Ms. Fox equal to 12 months' annual base salary and Ms. Fox's target annual bonus in the event of a covered termination during the period commencing on a change in control of the Company and ending 12 months after such change in control.

John Richard

Mr. Richard currently provides services to us pursuant to a revised and restated employment agreement dated September 1, 2019, and a change in control and severance agreement dated September 3, 2021.

Mr. Richard's employment agreement entitles him to receive an annual base salary and an opportunity to earn an annual discretionary performance-based bonus, subject to the achievement of performance goals determined in accordance with our annual bonus plan. Either party may terminate the employment agreement by giving the other party not less than three months' written notice, provided that we may terminate Mr. Richard at any time with immediate effect for cause or by giving written notice to Mr. Richard that we will instead pay his basic salary for any remaining notice period. Mr. Richard's employment agreement also contains restrictive covenants pursuant to which he has agreed to refrain from competing with us or soliciting our key employees or customers for a period of six months following his termination of employment. Mr. Richard's employment agreement includes the provision of accelerated vesting of share options and payments to Mr. Richard equal to 12 months' annual base salary and Mr. Richard's target annual bonus in the event of a covered termination following a change in control of the Company.

Charles Sermon

We entered into an employment agreement with Mr. Sermon on July 29, 2015 as amended on September 3, 2021. This agreement entitles Mr. Sermon to an annual base salary and an opportunity to earn an annual discretionary performance- based bonus, subject to the achievement of performance goals determined in accordance with our annual bonus plan. We have agreed to contribute to Mr. Sermon's Self-Invested Personal Pension Scheme an amount equal to 10% of Mr. Sermon's annual salary provided that he contributes 4% or more of his annual salary to that scheme. In lieu of a pension contribution, we may, at Mr. Sermon's request, pay a pro-rata amount equal to 10% of his base salary as additional compensation. Either party may terminate the employment agreement by giving the other party not less than six months' written notice, provided that we may terminate Mr. Sermon at any time with immediate effect for cause or by giving written notice to Mr. Sermon that we will instead pay his basic salary for any remaining notice period. Mr. Sermon's employment agreement also contains restrictive covenants pursuant to which he has agreed to refrain from competing with us or soliciting our key employees for a period of six months following his termination of employment or soliciting our customers for a period of nine months following his termination of employment. The employment agreement includes the provision of accelerated vesting of share options and payments to Mr Sermon equal to 12 months' annual base salary and Mr Sermon's target annual bonus in the event of a covered termination during the period commencing on a change in control of the Company and ending 12 months after such change in control.

Alexandra (Wills) Hughes-Wilson

Mereo entered into a part-time employment agreement with Ms. Alexandra (Wills) Hughes-Wilson on March 8, 2019, as amended on September 16, 2021. The employment agreement entitles Ms. Hughes-Wilson to an annual base salary and an opportunity to earn an annual discretionary performance-based bonus, subject to the achievement of performance goals determined in accordance with Mereo's annual bonus plan.

Ms. Hughes-Wilson is also eligible to participate in Mereo's group personal pension scheme and Mereo has agreed to contribute to the pension scheme an amount equal to 10% of Ms. Hughes-Wilson annual salary provided that she contributes 4% or more of her annual salary to that scheme. In lieu of a pension contribution, Mereo may, at Ms. Hughes-Wilson's

request, pay a pro-rata amount equal to 10% of her base salary as additional compensation. Either party may terminate the employment agreement by giving the other party not less than six months' written notice, provided that Mereo may terminate Ms. Hughes- Wilson at any time with immediate effect for cause or by giving written notice to Ms. Hughes-Wilson that Mereo instead pay her basic salary for any remaining notice period. Ms. Hughes-Wilson's employment agreement also contains restrictive covenants pursuant to which she has agreed to refrain from competing with Mereo or soliciting its key employees for a period of six months following her termination of employment or soliciting Mereo customers for a period of nine months following her termination of employment. The employment agreement includes the provision of accelerated vesting of share options and payments to Ms Hughes-Wilson equal to 12 months' annual base salary and Ms. Hughes-Wilson's target annual bonus in the event of a covered termination during the period commencing on a change in control of the Company and ending 12 months after such change in control.

Dr. John Lewicki

We entered into an employment agreement with Dr. Lewicki on July 1, 2020, as amended on September 3, 2021. This agreement entitles Dr. Lewicki to receive an annual base salary and an opportunity to earn an annual discretionary performance-based bonus, subject to the achievement of performance goals determined in accordance with our annual bonus plan. Either party can terminate the employment agreement at any time, with or without cause. Dr. Lewicki's employment agreement also contains restrictive covenants pursuant to which he has agreed to refrain from soliciting our key employees for a period of one year following his termination of employment. The employment agreement includes the provision of accelerated vesting of share options and payments to Dr. Lewicki in the event of a covered termination following a change in control of the Company.

During 2020, we also made payments due to Dr. Lewicki pursuant to (i) a Consulting Agreement, dated April 23, 2019, between Dr. Lewicki and OncoMed and (ii) a Severance Agreement, dated October 17, 2018, between Dr. Lewicki and OncoMed.

Dr. Suba Krishnan

We entered into an employment agreement with Dr. Krishnan on December 7, 2020. This agreement entitles Dr. Krishnan to receive an annual base salary and an opportunity to earn an annual discretionary performance-based bonus, subject to the achievement of performance goals determined in accordance with our annual bonus plan. Either party can terminate the employment agreement at any time, with or without cause. Dr. Krishnan's employment agreement also contains restrictive covenants pursuant to which she has agreed to refrain from soliciting our key employees for a period of one year following her termination of employment. The employment agreement includes the provision of accelerated vesting of share options and payments to Dr. Krishnan in the event of a covered termination following a change in control of the Company.

Dr. Jackie Parkin

We entered into an employment agreement with Dr. Parkin on October 26, 2015 as amended on October 12, 2021. This agreement entitles Dr. Parkin to an annual base salary and an opportunity to earn an annual discretionary performance- based bonus, subject to the achievement of performance goals determined in accordance with our annual bonus plan. We have agreed to contribute to Dr. Parkin's Self-Invested Personal Pension Scheme an amount equal to 10% of Dr. Parkin's annual salary provided that she contributes 4% or more of her annual salary to that scheme. In lieu of a pension contribution, we may, at Dr. Parkin's request, pay a pro-rata amount equal to 10% of her base salary as additional compensation. Either party may terminate the employment agreement by giving the other party not less than six months' written notice, provided that we may terminate Dr. Parkin at any time with immediate effect for cause or by giving written notice to Dr. Parkin's that we will instead pay her basic salary for any remaining notice period. Dr. Parkin's employment agreement also contains restrictive covenants pursuant to which she has agreed to refrain from competing with us or soliciting our key employees for a period of nine months following her termination of employment or soliciting our customers for a period of six months following her termination of employment. The employment agreement includes the provision of accelerated vesting of share options and payments to Dr. Parkin equal to 12 months' annual base salary and Dr. Parkin's target annual bonus in the event of a covered termination during the period commencing on a change in control of the Company and ending 12 months after such change in control.

Equity Compensation Awards to Non-Executive Directors and Executive Officers of Mereo

The following table summarizes: (i) the outstanding number of options and awards under the equity incentive plans; and (ii) the number of shares granted to executive officers and non-executive directors, as of December 31, 2022:

Name Dr. or Ph.D or MBBS	Ordinary Shares (including those represented by ADSs)	Ordinary Shares Underlying Options	Exercise Price Per Ordinary Share (£)	ADSs Underlying Options and Deferred RSUs	Exercise Price Per ADS ($)	Grant Date	Expiration Date
Dr. Denise Scots-Knight		1,544,745	1.29			September 25, 2015	September 25, 2025
				87,500	5.40	May 20, 2019	May 20, 2029
				87,500	3.00	July 23, 2019	July 23, 2029
				175,000	1.84	February 20, 2020	February 20, 2030
				520,000	2.72	February 1, 2021	February 1, 2031
				1,100,000	1.40	January 14, 2022	January 14, 2032
	1,078,274						
Christine Fox				170,000	3.32	January 19, 2021	January 19, 2031
				220,000	1.40	January 14, 2022	January 14, 2032
John Richard		772,371	1.29			September 25, 2015	September 25, 2025
		50,000	2.21			June 1, 2016	June 1, 2026
				27,500	5.40	May 20, 2019	May 20, 2029
				27,500	3.00	July 23, 2019	July 23, 2029
				85,000	1.84	February 20, 2020	February 20, 2030
				140,000	2.72	February 1, 2021	February 1, 2031
				220,000	1.40	January 14, 2022	January 14, 2032
	386,158						
Charles Sermon		772,371	1.29			September 25, 2015	September 25, 2025
				27,500	5.40	May 20, 2019	May 20, 2029
				27,500	3.00	July 23, 2019	July 23, 2029
				85,000	1.84	February 20, 2020	February 20, 2030
				150,000	2.72	February 1, 2021	February 1, 2031
				275,000	1.40	January 14, 2022	January 14, 2032
	685,849						
Alexandra (Wills) Hughes-Wilson		30,769	3.25			May 2, 2018	May 2, 2028
		9,231	3.25			May 2, 2018	May 2, 2028
				18,000	5.40	May 20, 2019	May 20, 2029
				18,000	3.00	July 23, 2019	July 23, 2029
				50,000	1.84	February 20, 2020	February 20, 2030
				100,000	2.72	February 1, 2021	February 1, 2031
				160,000	1.40	January 14, 2022	January 14, 2032
	38,250						
Dr. John Lewicki				100,000	2.77	August 12, 2020	August 12, 2030

Name Dr. or Ph.D or MBBS	Ordinary Shares (including those represented by ADSs)	Ordinary Shares Underlying Options	Exercise Price Per Ordinary Share (£)	ADSs Underlying Options and Deferred RSUs	Exercise Price Per ADS ($)	Grant Date	Expiration Date
				100,000	2.72	February 1, 2021	February 1, 2031
				160,000	1.40	January 14, 2022	January 14, 2032
	90,995						
Dr. Suba Krishnan				200,000	3.32	January 19, 2021	January 19, 2031
				180,000	1.40	January 14, 2022	January 14, 2032
Dr. Jackie Parkin		406,240	1.29			October 26, 2015	October 26, 2025
				30,000	5.40	May 20, 2019	May 20, 2029
				50,000	1.84	February 20, 2020	February 20, 2030
				100,000	2.72	February 1, 2021	February 1, 2031
				150,000	1.40	January 14, 2022	January 14, 2032
Dr. Jeremy Bender				22,000	3.32	January 19, 2021	January 19, 2031
				31,500	2.72	February 1, 2021	February 1, 2031
				55,000	1.31	February 1, 2022	February 1, 2032
				38,032	(2)	February 1, 2022	(2)
Dr. Anders Ekblom		216,264	1.29			September 25, 2015	September 25, 2025
				5,500	5.40	May 20, 2019	May 20, 2029
				5,500	3.00	July 23, 2019	July 23, 2029
				11,000	1.84	February 20, 2020	February 20, 2030
				31,500	2.72	February 1, 2021	February 1, 2031
				55,000	1.31	February 1, 2022	February 1, 2032
				44,042	(2)	February 1, 2022	(2)
				1,540	(2)	December 1, 2022	(2)
	189,702						
Dr. Pierre Jacquet				88,393	1.31	February 1, 2022	February 1, 2032
				32,867	(2)	February 1, 2022	(2)
				1,583	(2)	December 1, 2022	(2)
Dr. Annalisa Jenkins				9,167	0.79	December 1, 2022	December 1, 2032
				9,946	(2)	December 1, 2022	(2)
Dr. Deepika R. Pakianathan				5,500	5.40	May 20, 2019	May 20, 2029
				5,500	3.00	July 23, 2019	July 23, 2029
				11,000	1.84	February 20, 2020	February 20, 2030
				31,500	2.72	February 1, 2021	February 1, 2031
				55,000	1.31	February 1, 2022	February 1, 2032
Justin Roberts(1)	83,780,600						
Dr. Daniel Shames				9,167	0.79	December 1, 2022	December 1, 2032
				9,946	(2)	December 1, 2022	(2)
Marc Yoskowitz				9,167	0.79	December 1, 2022	December 1, 2032
				9,946	(2)	December 1, 2022	(2)
Michael S. Wyzga				5,500	5.40	May 20, 2019	May 20, 2029
				5,500	3.00	July 23, 2019	July 23, 2029
				11,000	1.84	February 20, 2020	February 20, 2030
				31,500	2.72	February 1, 2021	February 1, 2031
				55,000	1.31	February 1, 2022	February 1, 2032
				43,524	(2)	February 1, 2022	(2)
				56,342	(2)	June 1, 2022	(2)

(1) Mr. Roberts is a partner of Rubric Capital Management LP, which has ultimate voting and investment power over the ordinary shares and ADSs held by Rubric Capital Management LP. He disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein. Mr. Roberts has waived all remuneration in respect of his appointment as a non-executive director.

(2) Deferred RSUs do not have an exercise price and payment of Deferred RSUs will generally be made 180 days following separation of service.

Mereo has granted or may grant or intend to grant share options and awards under the following seven equity award plans (the "Mereo Share Plans"): (i) the 2015 Plan; (ii) the Share Option Plan; (iii) the LTIP; (iv) the Mereo 2019 DBP; (v) the Mereo 2019 Equity Incentive Plan (the 2019 Plan), (vi) the 2019 NED Equity Incentive Plan (the "2019 NED Plan") (each as defined below).

The 2015 Plan

Prior to the admission of Mereo ordinary shares to trading on the AIM market of the London Stock Exchange plc in June 2016 ("Admission"), Mereo granted options under the 2015 Plan. No further grants have been made under the 2015 Plan since Admission. On December 18, 2020, admission of our ordinary shares to trading on the AIM market of the London Stock Exchange plc was cancelled. The 2015 Plan was amended on December 3, 2020.

Eligibility, Awards and Administration

The 2015 Plan provides for the grant of options to executive directors, non-executive directors, employees and consultants.

Options granted under the 2015 Plan vest in accordance with the vesting schedule set out in each option holder's option agreement, in normal circumstances, between the first and fourth anniversary (or between the first and third anniversary for non-executive directors) of the vesting start date (typically the date of commencement of employment, appointment as a director, or entering into a consultancy agreement with us).

Admission did not automatically accelerate the vesting of options, and unvested options continue to vest in accordance with their original vesting schedule, subject to the rules of the 2015 Plan. The options are not subject to performance conditions other than continued service.

Options are not automatically exercisable on vesting, but upon Admission became exercisable to the extent vested. Options may generally be exercised until the day immediately preceding the tenth anniversary of the date of grant. Options have been granted under the 2015 Plan with an exercise price ranging from £1.43 per Mereo ordinary share to £2.44 per Mereo ordinary share.

Plan Leavers

Options held by option holders who leave their office or employment will lapse immediately, unless the option holder is a Good Leaver (as defined in the plan rules). If the option holder is a Good Leaver, the option may be exercised to the extent vested at the date of cessation of services and for such period as the Mereo Board determines and communicates to the option holder at that time (except upon death, in which case, options may be exercised for a period of one year), after which time they will lapse.

Certain Transactions

Under the 2015 Plan, certain corporate events such as a Takeover or a Trade Sale (as defined in the plan rules) will accelerate the vesting of all unvested options upon the occurrence of such event. Options will then be exercisable for a period of 40 days thereafter, after which they will lapse.

Adjustments

In the event of any capitalization, rights issue, consolidation, subdivision, reduction or any other variation of Mereo's share capital, the number of Mereo ordinary shares subject to an option and the exercise price applying to an option may be varied in such manner as the Mereo Board may determine.

Amendment and Termination

The Mereo Board may, at any time, amend the rules of the 2015 Plan with effect from a current, future or past date by way of a resolution, except that no amendment may be made which would abrogate or adversely affect the subsisting rights of option holders, unless consent from a majority of the affected option holders is obtained (by reference to the number of Mereo ordinary shares subject to options). However, any amendment to benefit the administration of the 2015 Plan, to take account of legislative changes, a Takeover or a Trade Sale (as defined in the plan rules) or to obtain or maintain favorable tax treatment or regulatory treatment may be made by the Mereo Board without the consent of option holders.

The Mereo Share Option Plan (the "Share Option Plan")

The Mereo Board adopted the Share Option Plan on June 9, 2016, and has subsequently amended it. Except where the context indicates otherwise, references to Mereo ordinary shares shall be deemed to include a number of our ADSs representing the right to receive our ordinary shares.

Eligibility, Awards and Administration

The Share Option Plan provides for the grant of options to acquire Mereo ordinary shares to employees and executive directors. Options may be granted to all eligible employees on commencement of employment and may be granted on a periodic basis after that. The Share Option Plan is administered by the Mereo Board who also set the terms and conditions of all options granted under the Share Option Plan, including any vesting and vesting acceleration conditions. Options are granted under the Share Option Plan at the discretion of the Mereo Board.

Vesting and Exercise

Under the Share Option Plan, the Mereo Board may determine the vesting schedule of an option and whether the vesting of an option will be subject to the satisfaction of a performance condition, although options are not currently granted subject to performance conditions other than continued service with Mereo. Once an option has vested, it may be exercised during the period ending on the tenth anniversary of the date of grant, after which time it will lapse. The exercise price of an option may not be less than the greater of: (i) the market value of a share on the date of grant; or (ii) if the shares are to be subscribed, the nominal value of a share. The Mereo Board may determine that an option be settled in cash or by "net exercise" of the option.

Limitation on Awards

No eligible employee may be granted options that, at the time they are granted, would cause the market value of shares subject to the options granted to the employee in respect of a financial year to exceed 400% of the employee's salary.

Plan Leavers

If a participant ceases to hold office or employment with Mereo as a result of dismissal for gross misconduct, any option the participant holds, whether vested or unvested, will lapse.

If a participant ceases to hold office or employment with Mereo for any reason other than dismissal for gross misconduct then: (i) if the option is already vested, it may be exercised within six months from the date of cessation of services if such cessation did not occur as a result of the participant's death, and within 12 months from the date of cessation of services if such cessation occurred as a result of the participant's death; and (ii) if the option is not already vested, it will vest on the normal vesting date as described above, unless the Mereo Board determines that the option will vest on the date of cessation of services. Where an option vests in these circumstances, any performance condition will be taken into account and, unless the Mereo Board determines otherwise, will be pro-rated for time.

Unless the board determines otherwise, options may not be transferred in any way and will lapse immediately on any attempt to do so, except that options may be transferred to a participant's personal representative upon death.

Certain Transactions

Under the Share Option Plan, if certain changes are made in, or events occur with respect to, Mereo ordinary shares (including any variation of share capital, demerger, cancellation of admission, special dividend, rights issue or any other event, which may, in the opinion of the Mereo Board affect the current or future value of Mereo ordinary shares), the number of shares subject to an option or the exercise price of an option may be adjusted as determined by the Mereo Board. In addition, upon such an event, the Mereo Board will determine: (i) whether and to what extent options which have not yet vested will vest; and (ii) the period of time during which any vested option may be exercised.

In the event of certain corporate transactions, including a scheme of arrangement or general offer, the vesting and exercisability of all options will accelerate to the extent determined by the Mereo Board, after which they will be exercisable for one month (or such longer period as determined by the Mereo Board, but not exceeding six months), following which they will lapse. However, if there is an internal reorganization, unless the Mereo Board determines otherwise, an option will generally be exchanged in consideration of the grant of a new option which, as determined by the Mereo Board, is equivalent to the option but relates to shares in a different company (whether the acquiring company or a different company). Any option that does not vest or is not exchanged will lapse immediately.

Amendment and Termination

The Mereo Board may, at any time, amend the rules of the Share Option Plan, except that no amendment may be made: (i) which would be to the material disadvantage of the existing rights of participants unless every participant who may be affected by such amendment has been invited to indicate whether he or she approves the amendment and the amendment is approved by a majority of such participants; or (ii) which would prevent the Share Option Plan from being an employees' share scheme in accordance with the U.K. Companies Act 2006. No options may be granted pursuant to the Share Option Plan after the tenth anniversary of the date of Mereo's Admission.

The Mereo 2019 Equity Incentive Plan (the 2019 EIP)

Our Board adopted the 2019 EIP on April 4, 2019. The Remuneration Committee made minor amendments to the rules of the 2019 EIP on May 16, 2019 and subsequently on February 13, 2020 and January 15, 2021.

Eligibility, Awards and Administration

The 2019 EIP provides for the grant of the following types of awards to executive directors and employees: (i) market value options; (ii) share appreciation rights; (iii) restricted stock / restricted stock unit awards; (iv) performance awards (awards subject to performance conditions) and (v) other share-based awards.

Subject to the terms of the 2019 EIP awards can be granted in respect of ordinary shares, ADSs, cash or a combination thereof. References in this section to ordinary shares will be deemed references to ADSs, as applicable.

The 2019 EIP is administered by the Remuneration Committee unless the Remuneration Committee designates one or more directors as a subcommittee who may act for the Remuneration Committee if necessary. The Board may also choose to administer the 2019 EIP itself.

Vesting Schedule

Awards vest in accordance with the vesting schedule set for the relevant award in its award agreement. Subject to the executive director or employees continued employment, one-fourth of each market value option grant shall vest on the first anniversary of the grant date and the remainder shall vest in equal monthly installments over the three-year period following the first anniversary.

Limitation on Awards

The total number of ordinary shares available for issuance under the 2019 EIP and the 2019 NED EIP is increased on January 1st of each year in an amount equal to the lesser of (i) 5.3% of our issued and outstanding ordinary shares (measured as of January 1st of such year) and (ii) such number of ordinary shares as determined by the Remuneration Committee of the Board, or such other committee as may be designated by the Board, in its discretion.

Leavers

Unvested awards will usually lapse on termination of office or service (including voluntary departure) save for potentially different good leaver treatment. The effect of a participant's termination of office or service on outstanding awards, including whether the awards may be exercised, settled, vested, paid or forfeited, will be determined by the Remuneration Committee and may be set forth in the participant's award agreement.

Certain Transactions

In the event of certain corporate transactions, including a change of control, the Remuneration Committee may determine the appropriate treatment of an award which may include (but is not limited to) it vesting in full, being settled in cash or being varied or replaced so as to relate to other assets (including shares in another company).

The number and type of securities subject to award and any exercise price may also be adjusted for various events that may affect the value of ADSs and for changes in applicable laws, regulations or accounting principles.

Amendment and Termination

The Board may amend, alter, suspend, discontinue or terminate the 2019 EIP or any portion thereof at any time, subject to shareholder approval where required by applicable law or the rules of the stock market or exchange, if any, on which the shares are principally quoted or traded.

However, no such Board action that would materially adversely affect participants' rights under an outstanding award may be taken without such participants' consent, except to the extent that such action is made to cause the 2019 EIP to comply with applicable law, stock market or exchange rules and regulations or accounting or tax rules and regulations or to impose any recoupment provisions on any awards in accordance with the 2019 EIP.

No Award may be granted under the 2019 EIP after the earliest to occur of: (i) the tenth anniversary of the effective date of the 2019 EIP; provided that to the extent permitted by the listing rules of any stock exchange on which we are listed, such ten-year term may be extended indefinitely so long as the maximum number of shares available for issuance under the 2019 EIP have not been issued; (ii) the maximum number of shares available for issuance under the 2019 EIP have been issued; and (iii) our Board terminates the 2019 EIP.

Beginning in the 2021 calendar year, the total number of ordinary shares available for issuance under the 2019 EIP and the 2019 NED EIP is increased on January 1st of each year in an amount equal to the lesser of (i) 5.3% of our issued and outstanding ordinary shares (measured as of January 1st of such year) and (ii) such number of ordinary shares as determined by the Remuneration Committee of the Board, or such other committee as may be designated by the Board, in its discretion.

The Mereo 2019 NED Equity Incentive Plan (the 2019 NED EIP)

Our Board adopted the 2019 NED EIP on April 4, 2019. The Remuneration Committee made minor amendments to the rules of the 2019 NED EIP on May 16, 2019 and subsequently on February 13, 2020 and January 15, 2021.

Eligibility, Awards and Administration

The 2019 NED EIP provides for the grant of the following types of awards to non-executive directors: (i) market value options; (ii) share appreciation rights; (iii) restricted stock / restricted stock unit awards; (iv) performance awards (awards subject to performance conditions) and (v) other share-based awards.

Subject to the terms of the 2019 NED EIP awards can be granted in respect of ordinary shares, ADSs, cash or a combination thereof. References in this section to ordinary shares will be deemed references to ADSs, as applicable.

The 2019 NED EIP is administered by the Remuneration Committee unless the Remuneration Committee designates one or more directors as a subcommittee who may act for the Remuneration Committee if necessary. The Board may also choose to administer the 2019 NED EIP itself.

Vesting Schedule

Awards vest in accordance with the vesting schedule set for the relevant award in its award agreement. In the normal course of events and subject to the non-executive directors holding their current office (or otherwise being employed) through each applicable vesting date, awards over market value option grants shall vest in substantially equal monthly installments over a one-year period following the grant date.

During the year ended December 31, 2022, deferred restricted stock units ("Deferred RSUs") under the 2019 NED EIP were granted to non-executive directors who elected to receive Deferred RSUs over ADSs in lieu of annual cash compensation. The number of Deferred RSUs to be granted were determined by dividing the estimated amount of the annual cash compensation by the average closing trading price of the Company's ADSs over the most recent 30 trading days as of the grant date.

In the normal course of events and subject to the participant holding the participant's current office (or being otherwise employed) through each applicable vesting date, such Deferred RSUs shall vest in substantially equal monthly installments over the year following their grant date. Payment of Deferred RSUs in ADSs will generally be made 180 days following separation of service. No performance conditions apply to such awards.

Limitation on Awards

The total number of ordinary shares available for issuance under the 2019 EIP and the 2019 NED EIP is increased on January 1st of each year in an amount equal to the lesser of (i) 5.3% of our issued and outstanding ordinary shares (measured as of January 1st of such year) and (ii) such number of ordinary shares as determined by the Remuneration Committee of the Board, or such other committee as may be designated by the Board, in its discretion.

Leavers

Unvested awards will usually lapse on termination of office or service (including voluntary departure) save for potentially different good leaver treatment. The effect of a participant's termination of office or service on outstanding awards, including whether the awards may be exercised, settled, vested, paid or forfeited, will be determined by the Remuneration Committee and may be set forth in the participant's award agreement.

Certain Transactions

In the event of certain corporate transactions, including a change of control, the Remuneration Committee may determine the appropriate treatment of an award which may include (but is not limited to) it vesting in full, being settled in cash or being varied or replaced so as to relate to other assets (including shares in another company).

The number and type of securities subject to award and any exercise price may also be adjusted for various events that may affect the value of ADSs and for changes in applicable laws, regulations or accounting principles.

Amendment and Termination

The Board may amend, alter, suspend, discontinue or terminate the 2019 NED EIP or any portion thereof at any time, subject to shareholder approval where required by applicable law or the rules of the stock market or exchange, if any, on which the shares are principally quoted or traded.

However, no such Board action that would materially adversely affect participants' rights under an outstanding award may be taken without such participants' consent, except to the extent that such action is made to cause the 2019 NED EIP to comply with applicable law, stock market or exchange rules and regulations or accounting or tax rules and regulations or to impose any recoupment provisions on any awards in accordance with the 2019 NED EIP.

No Award may be granted under the 2019 NED EIP after the earliest to occur of: (i) the tenth anniversary of the effective date of the 2019 NED EIP; provided that to the extent permitted by the listing rules of any stock exchange on which we are listed, such ten-year term may be extended indefinitely so long as the maximum number of shares available for issuance under the 2019 NED EIP have not been issued; (ii) the maximum number of shares available for issuance under the 2019 NED EIP have been issued; and (iii) our Board terminates the 2019 NED EIP.

Incentive Award Arrangements

We have no incentive award arrangements in place as of the date of this Annual Report.

For a description of the equity incentive plans see "—B. Compensation—Equity Compensation Awards to Non-Executive Directors and Executive Officers of Mereo."

Non-Executive Directors Remuneration

The following table sets forth the remuneration paid during 2022 to the current non-executive directors, all of which was in the form of annual fees and Deferred RSUs:

Name	Annual Fees (£)	Deferred RSU (number)
Dr. Jeremy Bender	3,375	38,032
Dr. Anders Ekblom	3,908	45,582
Dr. Pierre Jacquet	—	34,450
Dr. Annalisa Jenkins	—	9,946
Dr. Deepika R. Pakianathan	45,686	—
Justin Roberts(1)	—	—
Dr. Daniel Shames	—	9,946
Marc Yoskowitz	—	9,946
Michael S. Wyzga	4,167	99,866

(1) Mr. Roberts has waived all remuneration in respect of his appointment as a non-executive director.

Peter Fellner and Brian Schwartz served as non-executive directors until their resignation on November 10, 2022. Between January 1, 2022 and November 10, 2025 Peter Fellner was paid total remuneration of £54,342 and Brian Schwartz was paid £3,283 and received 28,586 Deferred RSUs in lieu of fees. Anne Hyland was appointed as a non-executive director on March 1, 2022 and resigned from the Board on November 10, 2022. Ms. Hyland received 34,758 Deferred RSUs in lieu of the fees for this period. Abdul Mullick was appointed as a non-executive director on May 17, 2022 and resigned from the Board on November 10, 2022. Dr. Mullick received 32,928 Deferred RSUs in lieu of fees.

Deferred restricted stock units ("Deferred RSUs") under the 2019 NED Plan were granted to NEDs who elected to receive Deferred RSUs over ADSs in lieu of annual cash compensation for the year commencing February 1, 2022 ("Plan Year"). Subject to the continued service of the NEDs, the Deferred RSUs vest in substantially equal monthly installments over the Plan Year. Payment of Deferred RSUs in ADSs will generally be made 180 days following separation of service.

The number of Deferred RSUs to be granted were determined by dividing the estimated amount of the annual cash compensation by the average closing trading price of the Company's ADSs over the most recent 30 trading days as of the grant date.

Non-Executive Director Service Contracts

The remuneration of the non-executive directors is determined by the Mereo Board as a whole, based on a review of current practices in other companies. Mereo has entered into service contracts with Mereo's directors for their services, which are subject to a three-month termination period. There are no arrangements under which any non-executive director is entitled to receive compensation upon the early termination of his or her appointment.

Pension, Retirement or Similar Benefits

Mereo operates a defined contribution pension scheme which is available to all employees. Mereo makes payments of up to 10% of basic salary for executives, including Mereo's Chief Executive Officer, into any pension scheme or similar arrangement as the participating executive may reasonably request (or a payment in lieu thereof). Such payments are not counted for the purposes of determining bonuses or awards under the LTIP. The total amount set aside or accrued by Mereo to provide pension, retirement or similar benefits to Mereo's current directors and Mereo's senior management with respect to 2022 was £157,586, which represents contributions made by Mereo in 2022 in respect of a defined contribution scheme.

6.C. Board practices

Composition of the Mereo Board

Our Board currently consists of ten members. Our Board has determined that none of our directors have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of director and that each of these directors is "independent" as that term is defined under the rules of Nasdaq. As a foreign private issuer, we are not required to meet the Nasdaq rule that our board be comprised of a majority of independent directors. However, we currently comply and intend to continue to comply with this requirement. There are no family relationships among any of our directors or senior management.

Insurance and Indemnification

To the extent permitted by the U.K. Companies Act 2006, Mereo is empowered under its Articles to indemnify its directors against any liability they incur by reason of their directorship. Mereo maintains directors' and officers' insurance to insure such persons against certain liabilities. Mereo has entered into a deed of indemnity with each of its directors.

Insofar as indemnification of liabilities arising under the Securities Act may be permitted to the Mereo Board, executive officers, or persons controlling Mereo pursuant to the forgoing provisions, Mereo has been informed that, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

Committees of the Mereo Board

The Mereo Board has four standing committees: an audit and risk committee, a remuneration committee, a nomination and governance committee, and a research and development committee.

Audit and Risk Committee

The audit and risk committee which consists of Deepika R. Pakianathan, Annalisa Jenkins, Michael S. Wyzga and Jeremy Bender, assists the board in overseeing our accounting and financial reporting processes and the audits of our financial statements. Dr. Pakianathan serves as Chair of the committee. The audit and risk committee consists exclusively of members of our board who are financially literate, and Dr. Pakianathan is considered an "audit committee financial expert" as defined by applicable SEC rules and has the requisite financial sophistication as defined under the applicable Nasdaq rules and regulations. Our board has determined that all of the members of the audit and risk committee satisfy the "independence" requirements set forth in Rule 10A-3 under the Exchange Act. The audit and risk committee is governed by a charter that complies with Nasdaq rules.

The audit and risk committee's responsibilities include:

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

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

Remuneration Committee

The remuneration committee which consists of Deepika R. Pakianathan, Justin Roberts and Anders Ekblom, assists the board in determining senior management compensation. Dr. Ekblom serves as Chairman of the committee. Under Nasdaq rules, there are heightened independence standards for members of the remuneration committee, including a prohibition against the receipt of any compensation from us other than standard board member fees. However, foreign private issuers are not required to meet this heightened standard. Nonetheless, our board has determined that Dr. Pakianathan, Mr. Roberts and Dr. Ekblom meet this heightened standard. The remuneration committee is governed by a charter that complies with Nasdaq rules.

The remuneration committee's responsibilities include:

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

Nomination and Corporate Governance Committee

The nomination and corporate governance committee which consists of Michael S. Wyzga, Jeremy Bender, Pierre Jacquet, and Justin Roberts, assists our board in identifying individuals qualified to become members of our board and senior management consistent with criteria established by our board and in developing our corporate governance principles. Mr. Wyzga serves as Chairman of the nomination and corporate governance committee. The nomination and corporate governance committee is governed by a charter that complies with Nasdaq rules.

The nomination and corporate governance committee's responsibilities include:

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

Research and Development Committee

The research and development committee, which consists of Pierre Jacquet, Dr. Daniel Shames, Deepika R. Pakianathan and Anders Ekblom, assists our senior management with oversight and guidance related to strategic research and development matters and provides guidance and makes recommendations to our board regarding strategic research and development matters. Dr. Ekblom serves as Chairman of the research and development committee.

The research and development committee's responsibilities include oversight of:

- our strategic development plans for product candidates, taking into account any regulatory feedback; and
- the acquisition of new product candidates.

In addition, the research and development committee is tasked with keeping informed of strategic issues and commercial changes affecting our development programs and potential product acquisitions.

6.D. Employees

As of December 31, 2022, 2021 and 2020, Mereo had 36, 49, and 38 employees, respectively. As at December 31, 2022, 27 employees are located in the United Kingdom and 9 employees are located in the United States.

All of our employees are engaged in either general and administrative or research and development functions. None of our employees are covered by a collective bargaining agreement.

6.E. Share Ownership

Share Ownership

The total number of ordinary shares of the company beneficially owned by our directors and executive officers including in the form of ADSs, as of the date of this annual report, was 112,636,815 (which includes shares subject to options that are currently exercisable or will be exercisable within 60 days of February 28, 2023) which represents 18.02% of the total number of ordinary shares outstanding as of February 28, 2023. See Item 7.A. below.

Share Options

See "—B. Compensation—Equity Compensation Awards to Non-Executive Directors and Executive Officers of Mereo."

Item 7. Major Shareholders And Related Party Transactions

7.A. Major Shareholders

The following table sets forth information relating to the beneficial ownership of Mereo ordinary shares as of February 28, 2023 by each person known by Mereo to own beneficially 5% or more of the outstanding Mereo ordinary shares.

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

The percentage of Mereo ordinary shares beneficially owned as of February 28, 2023 is computed on the basis of 624,928,519 ordinary shares outstanding as of February 28, 2023. Mereo ordinary shares that a person has the right to acquire within 60 days of February 28, 2023 are deemed outstanding for purposes of computing the percentage ownership of the person holding such rights, but are not deemed outstanding for purposes of computing the percentage ownership of any other person.

Name and Address of Beneficial Owner	Number of Ordinary Shares Beneficially Owned(1)	Percentage of Ordinary Shares Beneficially Owned
5% or Greater Shareholders:		
Rubric Capital Management LP (2)	83,780,600	13.41%
Baker Bros. Advisors LP (3)	69,359,359	9.99%
Suvretta Capital Management, LLC (4)	36,822,190	5.89%
Rock Springs Capital Management LP (5)	31,224,485	5.00%

(1) Ordinary shares figures include ordinary shares represented by ADSs.

(2) Based on information contained in a Statement on Schedule 13G filed by the shareholder on October 28, 2022. The address of the principal business office of Rubric Capital Management LP is 155 East 44th Street, Suite 1630, New York, NY 10017.

(3) Based on information known to Mereo and information contained in a Statement on Schedule 13G filed by the shareholder. Advisors LP on February 14, 2023. The address of the principal business office of Baker Bros. Advisors LP is 860 Washington St, 3rd Floor, New York, NY 10014.

(4) Based upon information contained in a Statement on Schedule 13G filed by the shareholder on February 14, 2023. The address of the principal business office of Suvretta Capital Management, LLC is 540 Madison Avenue, 7th Floor, New York, New York 10022.

(5) Based upon information known to Mereo and information contained in a Statement on Schedule 13G filed by the shareholder on February 14, 2023. The address of the principal business office of Rock Springs Capital Management LP is 650 South Exeter, Suite 1070 Baltimore, MD 21202

On February 12, 2021, we announced the completion of an underwritten public offering of 39,675,000 ADSs, at a public offering price of $2.90 per ADS, which included 5,175,000 additional ADSs issued upon the exercise in full of the underwriters' option to purchase additional ADSs. The aggregate gross proceeds to us from the public offering, before deducting underwriting discounts and commissions and offering expenses were $115.1 million. The net proceeds, after transaction costs, were £78.4 million ($108.2 million).

To our knowledge, and other than changes in percentage ownership as a result of the transaction described above and other than as disclosed in this Annual Report and in our other filings with the SEC, there has been no significant change in the percentage ownership held by the major shareholders listed above since January 1, 2021. The major shareholders listed above do not have voting rights with respect to their ordinary shares or ADSs that are different from the voting rights of other holders of our ordinary shares or ADSs.

As of December 31, 2022, assuming that all of our ordinary shares represented by ADSs are held by residents of the United States, including ADSs held by the entities set forth in the table above, and excluding certain other holders that we know to be non-residents of the United States, we estimate that approximately 92% of our outstanding ordinary shares (including ordinary shares underlying ADSs) were held in the United States. The number of record holders in the United States is not representative of the number of beneficial holders nor is it representative of where such beneficial holders are resident since many of these shares were held by brokers or other nominees.

7.B. Related Party Transactions

The following is a description of related party transactions we have entered into since January 1, 2022, or currently in effect with any member of our board of directors or executive officers and the holders of more than 5% of our ordinary shares or ADSs.

Transactions with Mereo's Executive Officers and Directors

We have entered into employment agreements or consultancy agreements with our executive officers. See "Item 6. Directors, Senior Management and Employees—B. Compensation—Executive Officer Employment Agreements."

Employee Benefit Trust

In 2016, we established an Employee Benefit Trust ("EBT") for the purpose of holding ordinary shares (subsequently ADSs) to satisfy the exercise of options under the Company's share-based incentive schemes.

No funding was loaned to the EBT by the Company during the year ended December 31, 2022 or 2021. During the years ended December 31, 2022 and 2021, no ordinary shares were purchased by the EBT. A total of 15,645 ADSs (2021: 31,205) held by the EBT were used in the year-ended December 31, 2022 to satisfy the exercise of options under the Company's share-based incentive schemes. As of December 31, 2022 the EBT holds 206,606 ADSs (2021: 216,251) along with £17,741 in cash (2021: £17,866).

Indemnity Agreements

We have entered into deeds of indemnity with each of our directors. See "Item 6. Directors, Senior Management and Employees—C. Board practices—Composition of the Mereo Board—Insurance and Indemnification."

Related Person Transaction Policy

Our Board has a written related person transaction policy, which sets forth the policies and procedures for the review and approval or ratification of related person transactions. This policy will cover, any transaction or proposed transactions between us and a related person that are material to us or the related person, including without limitation, purchases of goods or services by or from the related person or entities in which the related person has a material interest, indebtedness, guarantees of indebtedness and employment by us of a related person. In reviewing and approving any such transactions, our audit and risk committee is tasked to consider all relevant facts and circumstances, including, but not limited to, whether the transaction is on terms comparable to those that could be obtained in an arm's length transaction and the extent of the related person's interest in the transaction.

7.C. Interests of Experts and Counsel

Not applicable.

Item 8. Financial Information

8.A. Consolidated Statements and Other Financial Information

See "Item 18. Financial Statements."

Legal Proceedings

There are no governmental, legal or arbitration proceedings (including any such proceedings which are pending or threatened of which Mereo is aware) that may have, or have had in the recent past (covering the 12 months immediately preceding the date of this annual report), significant effects on Mereo's financial position or profitability.

Dividend Policy

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

8.B. Significant changes

Except as disclosed elsewhere in this annual report, there have been no other significant changes since December 31, 2022.

Item 9. The Offer And Listing

9.A.4 Offer and Listing Details

Our ADSs, each representing five of our ordinary shares, nominal value £0.003 per share, have been listed on the Nasdaq Global Market since April 24, 2019. Our ADSs trade under the symbol "MREO." Prior to that date, there was no public trading market for our ADSs. The Company's ordinary shares were previously admitted to trading on the AIM market of London Stock Exchange plc with admission canceled with effect from December 18, 2020.

9.B. Plan of Distribution

Not applicable.

9.C. Markets

Our ADSs are listed on the Nasdaq Global Market under the symbol "MREO".

9.D. Selling Shareholders

Not applicable.

9.E. Dilution

Not applicable.

9.F. Expenses of the Issue

Not applicable.

Item 10. Additional Information

10.A. Share Capital

Not applicable.

10.B. Memorandum and Articles of Association

See Exhibit 1.1 to this Annual Report on Form 20-F for more information.

10.C. Material Contracts

For a description of our material contracts, please see "Item 4. Information on the Company—B. Business Overview—Material Agreements."

10.D. Exchange Controls

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

10.E. Taxation

Material U.S. Federal Income Tax Considerations

The following is a discussion of the material U.S. federal income tax consequences to U.S. Holders (as defined below) of owning and disposing of the ADSs or ordinary shares, but it does not purport to be a comprehensive description of all tax considerations that may be relevant to a particular person's decision to acquire the ADSs or ordinary shares. This discussion applies only to a U.S. Holder that holds the ADSs or ordinary shares as capital assets for U.S. federal income tax purposes. In addition, it does not describe all of the tax consequences that may be relevant in light of the U.S. Holder's particular circumstances, including any estate, gift, alternative minimum or Medicare contribution tax consequences, any U.S. state, local, or non-U.S. tax considerations, and any tax consequences applicable to U.S. Holders subject to special rules, such as:

- banks, insurance companies and other financial institutions;
- real estate investment trusts or regulated investment companies;
- dealers or traders in securities that use a mark-to-market method of tax accounting;
- persons holding our ADSs or ordinary shares as part of a straddle, integrated transaction or similar transaction;
- persons whose functional currency for U.S. federal income tax purposes is not the U.S. dollar;
- entities or arrangements treated as partnerships for U.S. federal income tax purposes and their partners or investors;

- tax-exempt entities, "individual retirement accounts" or "Roth IRAs";
- S corporations;
- former citizens or residents of the United States;
- a person that is subject to special tax accounting rules under section 451(b) of the U.S. Internal Revenue Code of 1986, as amended (the "Code");
- persons that own or are deemed to own 10% or more of our stock by vote or value; or
- persons holding our ADSs or ordinary shares in connection with a trade or business outside the United States.

If a partnership (or other entity that is classified as a partnership for U.S. federal income tax purposes) owns the ADSs or ordinary shares, the U.S. federal income tax treatment of a partner will generally depend on the status of the partner and the activities of the partner and the partnership. Partnerships owning the ADSs or ordinary shares and partners in such partnerships should consult their tax advisers as to the particular U.S. federal income tax consequences of owning and disposing of the ADSs or ordinary shares.

Persons that own or are deemed to own 10% or more of our stock by vote or value should consult their tax advisers regarding the application of the "controlled foreign corporation" rules to their ownership of our ADSs or ordinary shares.

This discussion is based on 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.

We have not sought and do not intend to seek any ruling from the Internal Revenue Service (the "IRS") with respect to the U.S. federal income tax consequences described herein and there can be no assurance that the IRS or a court will not take a contrary position.

As used herein, a "U.S. Holder" is a person that, for U.S. federal income tax purposes, is a beneficial owner of our ADSs or ordinary shares and is:

- an individual who is a citizen or resident of the United States;
- a corporation, or other entity taxable as a corporation, created or organized in or under the laws of the United States, any state therein or the District of Columbia;
- an estate the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust that (i) is subject to the primary supervision of a court within the United States and subject to the control of one or more U.S. persons for all substantial decisions or (ii) has a valid election in effect under applicable U.S. Treasury regulations to be treated as a U.S. person.

U.S. Holders should consult their tax advisers concerning the U.S. federal, state, local and non-U.S. tax consequences of owning and disposing of our ADSs or ordinary shares in their particular circumstances.

For U.S. federal income tax purposes, a beneficial owner of our ADSs generally will be treated as the owner of the underlying ordinary shares represented by such ADSs. Accordingly, gain or loss will generally not be recognized if a U.S. Holder exchanges our ADSs for the underlying ordinary shares.

Passive Foreign Investment Company Rules

Special U.S. tax rules apply to U.S. Holders of stock in a company that are considered to be a passive foreign investment company (a "PFIC"). In general, a non-U.S. corporation will be a PFIC for any taxable year in which (i) 75% or more of its gross income consists of passive income (the "income test") or (ii) 50% or more of the value of its assets (generally determined on a quarterly average basis) consists of assets that produce, or are held for the production of, passive income (the "asset test"). For purposes of the above calculations, a non-U.S. corporation that directly or indirectly owns at least 25% by value of the shares of another corporation is treated as if it held its proportionate share of the assets of the other corporation and received directly its proportionate share of the income of the other corporation. Passive income generally includes interest, dividends, gains from certain property transactions, rents and royalties (other than certain rents or royalties derived in the active conduct of a trade or business). Cash is a passive asset for PFIC purposes. Goodwill (the value of which may be determined by reference to the company's market capitalization) is generally treated as an active asset to the extent attributable to activities intended to produce active income.

Based on our gross income, the average value of our assets, including goodwill, and the nature of the current stage of our business, we believe we were a PFIC for the year ended December 31, 2022. There can be no assurance regarding our PFIC status for the current year or any particular year in the future because PFIC status is factual in nature, depends upon factors not wholly within our control, generally cannot be determined until the close of the taxable year in question and is determined annually. Whether we will be a PFIC in the current or any future taxable year is uncertain because, among other things, we currently own a substantial amount of passive assets, including cash, and because the valuation of our assets that generate non-passive income for PFIC purposes, including our goodwill and other intangible assets, is uncertain and may vary substantially over time. In addition, the composition of our assets and income may vary substantially over time. The average quarterly value of our assets for purposes of determining our PFIC status for any taxable year (to the extent applicable) will generally be determined in part by reference to our market capitalization, which has fluctuated and may continue to fluctuate significantly over time. Accordingly, there can be no assurance that we will not be a PFIC in the current or for any future taxable year. Accordingly, U.S. Holders should invest in our ADSs only if they are willing to bear the U.S. federal income tax consequences associated with investments in PFICs.

If we are a PFIC for any taxable year and any of our non-U.S. subsidiaries or other companies in which we own equity interests were also a PFIC (any such entity, a "Lower-tier PFIC"), U.S. Holders would be deemed to own a proportionate amount (by value) of the shares of each Lower-tier PFIC and would be subject to U.S. federal income tax according to the rules described in the subsequent paragraph on (i) certain distributions by a Lower-tier PFIC and (ii) dispositions of shares of Lower-tier PFICs, in each case as if the U.S. Holders held such shares directly, even though the U.S. Holders had not received the proceeds of those distributions or dispositions.

Generally, if we were a PFIC for any taxable year during which a U.S. Holder holds our ADSs or ordinary shares and the U.S. Holder does not make a valid QEF Election or a mark-to-market election (described below), gain recognized upon a disposition (including, under certain circumstances, a pledge) of our ADSs or ordinary shares by the U.S. Holder will be allocated ratably over the U.S. Holder's holding period for such ADSs or ordinary shares. The amounts allocated to the taxable year of disposition and to years before we became a PFIC will be taxed as ordinary income. The amounts allocated to each other taxable year will be subject to tax at the highest rate in effect for that taxable year for individuals or corporations, as applicable, and an interest charge will be imposed on the resulting tax liability for each relevant taxable year. Further, to the extent that any distribution received by a U.S. Holder on our ADSs or ordinary shares exceeds 125% of the average of the annual distributions received on such securities during the preceding three years or the U.S. Holder's holding period, whichever is shorter (an "excess distribution"), such excess distribution will be subject to taxation in the same manner. If we are a PFIC for any taxable year during which a U.S. Holder owns our ADSs or ordinary shares, we will generally continue to be treated as a PFIC with respect to such U.S. Holder for all succeeding years during which such U.S. Holder owns our ADSs or ordinary shares, even if we cease to meet the threshold requirements for PFIC status. If we are a PFIC for any taxable year but cease to be PFIC for subsequent years, U.S. Holders should consult their tax advisers regarding the advisability of making a "deemed sale" election that would allow them to eliminate the continuing PFIC status under certain circumstances.

To avoid the foregoing rules, a U.S. Holder can make a qualified electing fund election (a "QEF Election") to treat us and each Lower-tier PFIC as a qualified electing fund in the first taxable year that the entity is treated as a PFIC with respect to the U.S. Holder. A U.S. Holder must make the QEF Election for each PFIC by attaching a separate properly completed IRS Form 8621 for that PFIC to the U.S. Holder's timely filed U.S. federal income tax return. A U.S. Holder making a QEF election other than for the first taxable year in which it owns (or is treated as owning) an equity interest in a PFIC would continue to be subject to the rules described in the preceding paragraph with respect to such PFIC, unless the U.S. Holder makes a "deemed sale" election with respect to the PFIC and recognizes gain taxed under the general PFIC rules described above with respect to the PFIC stock's appreciation before the year for which the QEF Election is made.

We will provide the information necessary for a U.S. Holder to make a QEF election with respect to us and we will also use our best efforts to cause each Lower-tier PFIC (as defined below) that we control to provide such information. We intend to provide this information for any taxable year during which our only income is interest income or income from financial investments and for any other taxable year for which we determine that we were a PFIC. However, no assurance can be given that such QEF information will be available for any Lower-tier PFIC that we do not wholly-own. We will post the information necessary to make QEF Elections on our website. If we are a PFIC for any taxable year, the consequences to any U.S. Holder will depend in part on whether the U.S. Holder makes a valid QEF Election or mark-to-market election as described below.

If a U.S. Holder makes a QEF Election with respect to a PFIC, the U.S. Holder will be taxed on its pro rata share of the PFIC's ordinary earnings and net capital gain (at ordinary income and capital gain rates, respectively) for each taxable year that the entity is a PFIC. If a U.S. Holder makes a QEF Election with respect to us, any distributions we pay out of our earnings and profits that were previously included in the U.S. Holder's income under the QEF Election would not be taxable to the U.S. Holder. A U.S. Holder will increase its tax basis in its ADSs or ordinary shares by an amount equal to any income included under the QEF Election and will decrease its tax basis by any amount distributed on the ADSs or ordinary shares that is not included in the U.S. Holder's income. In addition, a U.S. Holder will recognize capital gain or loss on the disposition of ADSs or ordinary shares in an amount equal to the difference between the amount realized and the U.S. Holder's adjusted tax basis in the ADSs or ordinary shares, as determined in U.S. dollars. A. U.S. Holder will not be taxed on the ordinary income and net capital gain under the QEF rules for any year that we are not a PFIC.

Based on the nature of our expected income, the expected composition of our assets, and our business prospects, we do not currently expect to have significant ordinary earnings or net capital gain in any taxable year in which we may be a PFIC. However, it is difficult to predict the nature and composition of our income and assets and the value of our assets in light of the volatile nature of earnings patterns of emerging pharmaceutical or biotechnology companies such as us. Accordingly, U.S. Holders should note that if they make QEF Elections with respect to us and our subsidiaries, they may be required to pay U.S. federal income tax with respect to their ADSs or ordinary shares for any taxable year in which we have a positive amount of earnings or net capital gains even if we do not make any distributions in such year. U.S. Holders should consult their tax advisers regarding the advisability of making QEF Elections in their particular circumstances.

Alternatively, if we are a PFIC for any taxable year and if our ADSs or ordinary shares are "regularly traded" on a "qualified exchange," a U.S. Holder could make a mark-to-market election that will result in tax treatment different from the general tax treatment described in the two preceding paragraphs. Our ADSs and/or ordinary shares will be treated as "regularly traded" in any calendar year in which more than a de minimis quantity of the ADSs and/or ordinary shares are traded on a qualified exchange on at least 15 days during each calendar quarter. NASDAQ, on which the ADSs are listed, is a qualified exchange for this purpose. The Internal Revenue Service has not identified specific non-U.S. exchanges that are "qualified" for this purpose. If a U.S. Holder makes a valid mark-to-market election, the U.S. Holder generally will recognize as ordinary income any excess of the fair market value of its ADSs or ordinary shares at the end of each taxable year over the adjusted tax basis of such ADSs or ordinary shares, and will recognize an ordinary loss in respect of any excess of the adjusted tax basis of its ADSs or ordinary shares over their fair market value at the end of the taxable year (but only to the extent of the net amount of income previously included as a result of the mark-to-market election). If a U.S. Holder makes the election, the U.S. Holder's tax basis in our ADSs or ordinary shares will be adjusted to reflect these income or loss amounts. Any gain recognized on the sale or other disposition of our ADSs or ordinary shares in a year in which we are a PFIC will be treated as ordinary income and any loss will be treated as an ordinary loss (but only to the extent of the net amount of income previously included as a result of the mark-to-market election). If a valid mark-to-market election is made for any year in which we are a PFIC, distributions will be treated as described below under "—Taxation of Distributions" except that the preferential tax rates on dividends paid to non-corporate U.S. Holders will not apply. U.S. Holders will not be able to make a mark-to-market election with respect to Lower-tier PFICs, if any. U.S. Holders should consult their tax advisers as to the availability and desirability of a mark-to-market election in their particular circumstances if we are a PFIC for any taxable year.

If a U.S. Holder owns our ADSs or ordinary shares during any year in which we are a PFIC, the U.S. Holder generally will be required to file annual reports on IRS Form 8621 (or any successor form) with respect to us and any Lower-tier PFIC, generally with the U.S. Holder's U.S. federal income tax return for that year.

U.S. Holders should consult their tax advisers regarding our PFIC status for any taxable year and the potential application of the PFIC rules to an investment in our ADSs or ordinary shares.

Taxation of Distributions

This discussion under "—Taxation of Distributions" is subject to the PFIC rules described in "—Passive Foreign Investment Company Rules" above. Distributions paid on ADSs or ordinary shares, other than certain pro rata distributions of our ordinary shares, will be treated as dividends to the extent paid out of our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. Distributions in excess of our current and accumulated earnings and profits will be treated first as a tax-free return of capital to the extent of the U.S. Holder's basis in the ADSs or ordinary shares and then as capital gain. For any taxable year in which we do not maintain calculations of our earnings and profits under U.S. federal income tax principles, it is expected that any distributions generally will be reported to U.S. Holders as dividends. Dividends will not be eligible for the dividends-received deduction generally available to U.S. corporations under the Code.

Subject to applicable limitations, dividends paid to certain non-corporate U.S. Holders may be eligible for taxation at a preferential tax rate provided that we were not a PFIC for the taxable year in which the dividend is paid or the prior taxable year. Non-corporate U.S. Holders should consult their tax advisers regarding the availability of this preferential rate in the light of the discussion in "—Passive Foreign Investment Company Rules" above and in their particular circumstances.

If dividend payments in respect of our ADSs or ordinary shares are made in a currency other than the U.S. dollar, the amount of the dividend distribution that a U.S. Holder must include in income will be the U.S. dollar value of the payments made in such other currency, determined at the spot U.S. dollar exchange rate on the date the dividend distribution is includible in income, regardless of whether the payment is in fact converted into U.S. dollars. Generally, if the foreign currency received as a dividend is not converted into U.S. dollars on the date of receipt, any gain or loss resulting from currency exchange fluctuations during the period from the date the dividend payment is includible in income to the date the payment is actually converted into U.S. dollars will be treated as ordinary income or loss and will not be eligible for the special tax rate applicable to qualified dividend income. The gain or loss generally will be income or loss from sources within the United States for foreign tax credit limitation purposes. U.S. Holders are urged to consult their tax advisers regarding the tax consequences of receiving, converting or disposing of any non-U.S. currency, received or deemed received as dividends on our ADSs or on the sale or retirement of an ADS or an ordinary share.

Dividends will be included in a U.S. Holder's income on the date of the U.S. Holder's, or in the case of our ADSs, the depositary's, receipt. Dividends generally will be income from non-U.S. sources, which may be relevant in calculating a U.S. Holder's foreign tax credit limitation. Subject to certain conditions and limitations, non-U.S. tax withheld, if any, on dividend may be deducted from such U.S. Holder's taxable income or credited against such U.S. Holder's U.S. federal income tax liability. The limitation on foreign taxes eligible for credit is calculated separately with respect to specific classes of income. For this purpose, dividends that we distribute generally should constitute "passive category income," or, in the case of certain U.S. Holders, "general category income." A foreign tax credit for foreign taxes imposed on distributions may be denied if a U.S. Holder does not satisfy certain minimum holding period requirements. The rules relating to the determination of the foreign tax credit are complex, and U.S. Holders are urged to consult their tax advisors to determine whether and to what extent such U.S. Holder will be entitled to a foreign tax credit.

Sale or Other Taxable Disposition

Except as described under "—Passive Foreign Investment Company Rules" above, a U.S. Holder will generally recognize capital gain or loss on a sale or other taxable disposition of our ADSs or ordinary shares in an amount equal to the difference between the amount realized on the sale or disposition and the U.S. Holder's tax basis in the ADSs or ordinary shares disposed of, in each case as determined in U.S. dollars. A U.S. Holder's initial tax basis in the ordinary shares or ADSs will generally equal the cost of such ordinary shares or ADSs. If a U.S. Holder used foreign currency to purchase the ordinary shares or ADSs, the cost of the ordinary shares or ADSs will be the U.S. dollar value of the foreign currency purchase price on the date of purchase, translated at the spot rate of exchange on that date. Any such gain or loss will be long-term capital gain or loss if at the time of the sale or disposition the U.S. Holder has owned our ADSs or ordinary shares for more than one year. Long-term capital gains recognized by non-corporate U.S. Holders may be subject to a tax rate that is lower than the rate applicable to ordinary income. The deductibility of capital losses is subject to limitations. Any capital gain or loss recognized upon the sale or disposition of ADSs or ordinary shares will generally be treated as U.S.-source income for foreign tax credit limitation purposes. U.S. Holders should consult their tax advisers regarding the proper treatment of gain or loss, the availability of a foreign tax credit, and for U.S. Holders that sell the ADSs or ordinary shares for an amount denominated in a currency other than the U.S. dollar should consult their tax advisers regarding any potential foreign currency gain or loss that may have to be recognized.

Information Reporting and Backup Withholding

In general, payments of dividends and proceeds from the sale or other disposition of our ADSs or ordinary shares that are made within the United States or through certain U.S.-related financial intermediaries may be subject to information reporting and backup withholding, unless (i) in the case of information reporting, the U.S. Holder is a corporation or other "exempt recipient" and (ii) in the case of backup withholding, the U.S. Holder provides a correct taxpayer identification number and certifies that it is not subject to backup withholding. Backup withholding is not an additional tax. The amount of any backup withholding from a payment to a U.S. Holder generally will be allowed as a credit against the U.S. Holder's U.S. federal income tax liability and may entitle it to a refund, provided that the required information is timely furnished to the IRS. U.S. Holders should consult their tax advisers regarding the application of the information reporting and backup withholding rules.

Information with Respect to Foreign Financial Assets

Certain U.S. Holders who are individuals (or certain specified entities) may be required to report information relating to their ownership of our ADSs or ordinary shares, or non-U.S. accounts through which our ADSs or ordinary shares are held, subject to certain exceptions. Penalties and potential other adverse tax consequences may be imposed if a U.S. Holder is required to submit such information to the IRS and fails to do so. U.S. Holders should consult their tax advisers regarding their reporting obligations with respect to our ADSs or ordinary shares.

Material United Kingdom Tax Considerations

The following is a description of the material U.K. tax considerations relating primarily to the ownership and disposal of our ADSs by the U.S. Holders described above. The U.K. tax comments set out below are based on current U.K. tax law as applied in England and Wales, and HMRC practice (which may not be binding on HMRC) as at the date of this summary, both of which are subject to change, possibly with retrospective effect. They are intended as a general guide and, save where otherwise stated, only apply to you if you are not resident in the U.K. for U.K. tax purposes and do not hold our ADSs for the purposes of a trade, profession or vocation that you carry on in the U.K. through a branch, agency or permanent establishment in the U.K. and if you hold our ADSs as an investment for U.K. tax purposes and are not subject to special rules.

This summary does not address all possible tax consequences relating to an investment in our ADSs. In particular it does not cover the U.K. inheritance tax consequences of holding our ADSs. It assumes that DTC has not made an election under section 97A(1) of the Finance Act 1986. It assumes that we do not (and will not at any time) derive 75% or more of our qualifying asset value, directly or indirectly, from U.K. land, and that we are and remain solely resident in the U.K. for tax purposes. This summary is for general information only and is not intended to be, nor should it be considered to be, legal or tax advice to any particular holder. Holders of our ADSs are strongly urged to consult their tax advisers in connection with the U.K. tax consequences of their investment in our ADSs.

U.K. Taxation of Dividends

Mereo will not be required to withhold amounts for or on account of U.K. tax at source when paying a dividend in respect of its ordinary shares.

Holders who hold our ADSs as an investment, who are not resident in the U.K. for U.K. tax purposes and who do not hold their ADSs in connection with any trade, profession or vocation carried on by them in the U.K. through a branch, agency or permanent establishment in the U.K. should not be subject to U.K. tax in respect of any dividends on our ordinary shares.

U.K. Taxation of Capital Gains

An individual holder who is not resident in the U.K. for U.K. tax purposes should not be liable to U.K. capital gains tax on capital gains realized on the disposal of their ADSs unless such holder carries on a trade, profession or vocation in the U.K. through a branch or agency in the U.K. to which ADSs are attributable.

Any such individual holder of our ADSs who is temporarily non-resident for U.K. tax purposes will, in certain circumstances, become liable to U.K. tax on capital gains in respect of gains realized while they were not resident in the U.K.

A corporate holder of our ADSs which is not resident in the U.K. for U.K. tax purposes should not be liable for U.K. corporation tax on chargeable gains realized on the disposal of our ADSs unless it carries on a trade in the U.K. through a permanent establishment in the U.K. to which our ADSs are attributable.

Stamp Duty and Stamp Duty Reserve Tax

The following statements apply to all holders, regardless of their jurisdiction of tax residence.

No stamp duty is payable on the issue of our ordinary shares into a depositary receipt system (such as, Mereo understands, that operated by Citibank) or a clearance service (such as, Mereo understands, DTC). Based on current published HMRC practice and case law, no stamp duty reserve tax (“SDRT”) should be payable on the issue of our ordinary shares into a depositary receipt system or a clearance service. Accordingly, no stamp duty or SDRT should be payable on the creation and issue of our ADSs pursuant to the issue of our ordinary shares to Citibank’s custodian.

Transfers of ordinary shares to, or to a nominee or agent for, a person whose business is or includes issuing depositary receipts or to, or to a nominee or agent for, a person whose business is or includes the provision of clearance services, will generally be regarded by HMRC as subject to stamp duty or SDRT at 1.5% of the amount or value of the consideration or, in certain circumstances, the value of the ordinary shares transferred. In practice, this liability for stamp duty or SDRT is in general borne by such person depositing the relevant shares in the depositary receipt system or clearance service.

No SDRT or stamp duty should be payable on paperless transfers of, or agreements to transfer, our ADSs through the facilities of DTC.

The transfer on sale of ordinary shares by a written instrument of transfer will generally be liable to U.K. stamp duty at the rate of 0.5% of the amount or value of the consideration for the transfer. The purchaser normally pays the stamp duty.

An agreement to transfer ordinary shares outside a depositary receipt system or a clearance service will generally give rise to a liability on the purchaser to SDRT at the rate of 0.5% of the amount or value of the consideration. Such SDRT is payable on the seventh day of the month following the month in which the charge arises, but where an instrument of transfer is executed and duly stamped before the expiry of a period of six years beginning with the date of that agreement, (i) any SDRT that has not been paid ceases to be payable, and (ii) any SDRT that has been paid may be recovered from HMRC, generally with interest.

10.F. Dividends and Paying Agents

Not applicable.

10.G. Statement by Experts

Not applicable.

10.H. Documents on Display

We are subject to certain of the information reporting requirements of the Exchange Act. As a foreign private issuer, we are exempt from the rules and regulations under the Exchange Act prescribing 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, with respect to their purchase and sale of our shares. In addition, we are not required to file reports and financial statements with the SEC as frequently or as promptly as U.S. companies whose securities are registered under the Exchange Act. However, we are required to file with the SEC, within four months after the end of each fiscal year, an annual report on Form 20-F containing financial statements audited by an independent accounting firm. We publish unaudited interim financial information after the end of the second quarter. We furnish this half-year financial information to the SEC under cover of a Form 6-K.

The SEC maintains a website that contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC. The address of this website is http://www.sec.gov. The Company’s website is www.mereobiopharma.com.

10.I. Subsidiary Information

Not applicable.

Item 11. Quantitative And Qualitative Disclosures About Market Risk

We are exposed to a variety of financial risks. Our overall risk management program seeks to minimize potential adverse effects of these financial risks on our financial performance. Further information relating to quantitative and qualitative disclosures about market risk can be found within Note 24 (Financial and capital risk management and fair value measurement) of our annual consolidated financial statements, incorporated by reference into this document.

Interest Rate Risk

We manage interest rate risk by monitoring short and medium-term interest rates and placing cash on deposit for periods that optimize the amount of interest earned while maintaining access to sufficient funds to meet day-to-day cash requirements. Interest payable on our convertible loan notes is fixed. In December 2020, we repaid the outstanding principal and accrued interest of our credit facility in full. Consequently, there is no material exposure to interest rate risk in respect of interest payable.

Credit Risk

We consider all of our material counterparties to be creditworthy. We consider the credit risk for each of our major counterparties to be low. We are, however, dependent on a number of third parties for the delivery of our programs and, where required, we pay upfront deposits and fees in advance of the delivery of services. We continue to assess credit risk as part of its management of these third-party relationships.

Liquidity Risk

We manage our liquidity risk by maintaining adequate cash reserves at highly rated banks and financial institutions and invest in short-term deposits to achieve a competitive rate of return. Our liquid resources are invested regard to the timing of payments to be made in the ordinary course of business and we monitor our funding requirements through preparation of short-term, mid-term, and long-term forecasts, matching the maturity profiles of financial assets and liabilities.

Foreign Currency Risk

Foreign currency risk reflects the risk that the value of a financial commitment or recognized asset or liability will fluctuate due to changes in foreign currency rates. The majority of our operating costs are denominated in pound sterling, U.S. dollars and Euros. Our financial position, as expressed in pound sterling, is exposed to movements in foreign exchange rates, principally against the U.S. dollar and Euro.

We are exposed to foreign currency risk as a result of operating transactions, translation of foreign currency bank accounts and short-term deposits as well as funding arrangements with our subsidiary.

In addition, the assets and liabilities of our subsidiaries are translated into pound sterling at exchange rates in effect at each balance sheet date and operations accounts are translated using the average exchange rate for the relevant period (where the functional currency of the subsidiary is not pound sterling). Foreign currency translation adjustments are accounted for as a component of comprehensive income and reflected in the foreign exchange translation reserve and in comprehensive income on the consolidated statement of changes in equity.

We monitor our exposure to foreign exchange risk. We have not entered into foreign exchange contracts to hedge against foreign exchange fluctuations but maintain cash and short-term deposits in U.S. dollars to cover anticipated forward commitments. For the year ended December 31, 2022, we recorded a net foreign exchange gain of £1.5 million, compared to a loss of £1.0 million loss for the year ended December 31, 2021.

Item 12. Description of Securities Other Than Equity Securities

12.A. Debt Securities

Not applicable.

12.B. Warrants and Rights

Not applicable.

12.C. Other Securities

Not applicable.

12.D. American Depositary Shares

Fees and Charges

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

Service	Fee
Issuance of ADSs (e.g., an issuance of ADS upon a deposit of ordinary shares or upon a change in the ADS(s)-to-ordinary shares ratio), excluding ADS issuances as a result of distributions of ordinary Shares	Up to $5.00 per 100 ADSs (or fraction thereof) issued
Cancellation of ADSs (e.g., a cancellation of ADSs for delivery of deposited property or upon a change in the ADS(s)-to-ordinary shares ratio)	Up to $5.00 per 100 ADSs (or fraction thereof) cancelled
Distribution of cash dividends or other cash distributions (e.g., upon a sale of rights and other entitlements)	Up to $5.00 per 100 ADSs (or fraction thereof) held
Distribution of ADSs pursuant to (i) stock dividends or other free stock distributions, or (ii) exercise of rights to purchase additional ADSs	Up to $5.00 per 100 ADSs (or fraction thereof) held
Distribution of securities other than ADSs or rights to purchase additional ADSs (e.g., upon a spin-off)	Up to $5.00 per 100 ADSs (or fraction thereof) held
ADS Services	Up to $5.00 per 100 ADSs (or fraction thereof) held on the applicable record date(s) established by the depositary
Registration of ADS Transfers (e.g., upon a registration of the transfer of registered ownership of ADSs, upon a transfer of ADSs into DTC and vice versa, or for any other reason)	Up to $5.00 per 100 ADSs (or fraction thereof) transferred
Conversion of ADSs of one series for ADSs of another series (e.g., upon conversion of Partial Entitlement ADSs for Full Entitlement ADSs, or upon conversion of Restricted ADSs (each as defined in the Deposit Agreement) into freely transferable ADSs, and vice versa)	Up to $5.00 per 100 ADSs (or fraction thereof) converted

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

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

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

ADSs. In the case of (i) registration of ADS transfers, the ADS transfer fee will be payable by the holders of ADSs whose ADSs are being transferred or by the person to whom the ADSs are transferred, and (ii) conversion of ADSs of one series for ADSs of another series, the ADS conversion fee will be payable by the holder whose ADSs are converted or by the person to whom the converted ADSs are delivered.

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

PART TWO

Item 13. Defaults, Dividend Arrearages And Delinquencies

None.

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

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, has evaluated the effectiveness of our disclosure controls and procedures (as such term is defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act and regulations promulgated thereunder) as of December 31, 2022, or the Evaluation Date. Based on such evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that, as of the Evaluation Date, our disclosure controls and procedures were effective in recording, processing, summarizing and reporting, on a timely basis, information required to be included in periodic filings under the Exchange Act and that such information is accumulated and communicated to management, including our Chief Executive Officer and Chief Financial Officer, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure.

(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 such term is defined in Rule 13a-15(f) under the Exchange Act.

Our management conducted an assessment of the effectiveness of our internal control over financial reporting based on the criteria set forth in "Internal Control – Integrated Framework (2013)" issued by the Committee of Sponsoring Organizations of the Treadway Commission.

Based on this assessment, our management concluded that, as of December 31, 2022, our internal control over financial reporting was effective.

(c) Attestation Report of the Registered Public Accounting Firm

Not applicable.

(d) Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting (as such term is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) that occurred during the period covered by this annual report that have materially affected, or that are reasonably likely to materially affect, our internal control over financial reporting.

Item 16. [Reserved]

Item 16A. Audit Committee Financial Expert

Our board has determined that Dr. Deepika Pakianathan qualifies to serve as an "audit committee financial expert" as defined under the SEC rules, and has the requisite financial sophistication as defined under the applicable Nasdaq rules and regulations. Dr. Pakianathan also qualifies as an independent director under the corporate governance standards of the Nasdaq listing requirements and the audit committee independence requirements of Rule 10A-3 of the Exchange Act. For more information see "Item 6. Directors, Senior Management and Employees—C. Board Practices—Committees of the Mereo Board—Audit and Risk Committee."

Item 16B. Code of Ethics

Code of Business Conduct and Ethics and Anti-Bribery and Anti-Corruption Policy

We have adopted a Code of Business Conduct and Ethics and an Anti-Bribery and Anti-Corruption Policy applicable to all of our directors, executive officers and employees, including our Chief Executive Officer, Chief Financial Officer, controller or principal accounting officer, or other persons performing similar functions, which is a code of ethics as defined in Item 16B of Form 20-F promulgated by the SEC. The full text of the Code of Business Conduct and Ethics and the Anti-Bribery and Anti-Corruption Policy can be found on our website at www.mereobiopharma.com. Information contained on, or that can be accessed through, our website does not constitute a part of this report and is not incorporated by reference herein. If we make any amendment to the Code of Business Conduct and Ethics or the Anti-Bribery and Anti-Corruption Policy or grant any waivers, including any implicit waiver, from a provision of the code of ethics, we will disclose the nature of such amendment or waiver on our website to the extent required by the rules and regulations of the SEC. Under Item 16B of Form 20-F, if a waiver or amendment of the Code of Business Conduct and Ethics applies to our principal executive officer, principal financial officer, principal accounting officer or controller and relates to standards promoting any of the values described in Item 16B(b) of Form 20-F, we are required to disclose such waiver or amendment on our website in accordance with the requirements of Instruction 4 to such Item 16B.

Item 16C. Principal Accountant Fees and Services

Our consolidated financial statements have been prepared in accordance with IFRS and were audited by BDO LLP, our independent registered public accounting firm registered with the Public Company Accounting Oversight Board in the United States.

BDO LLP has served as our independent registered public accounting firm for the year ended December 31, 2022 and for the year ended December 31, 2021. Ernst & Young LLP served as our independent registered public accounting firm for the year ended December 31, 2020.

The following table provides information regarding fees paid by us to BDO LLP for all services, for the years ended December 31, 2022 and December 31, 2021:

	Year Ended December 31,	
	2022	2021
	(in thousands of pounds)	
Audit fees(1)	479	461
Audit related fees	—	—
Other fees	—	—
Total fees	**479**	**461**

(1) Includes professional services rendered in connection with the audit of our annual financial statements, review of our interim financial statements, review of our registration statement, related consents and audits of our subsidiary accounts.

Audit Committee Pre-Approval Policies and Procedures

Our audit committee's specific responsibilities in carrying out its oversight of the quality and integrity of the accounting, auditing and reporting practices of Mereo include the approval of audit and non-audit services to be provided by the independent auditor before the auditor is engaged to render such services. The audit committee approves in advance the particular services or categories of services to be provided to Mereo during the following yearly period and also sets forth a specific budget for such audit and non-audit services. Additional non-audit services may be pre-approved by the audit committee.

Item 16D. Exemptions From The Listing Standards For Audit Committees

None.

Item 16E. Purchases of Equity Securities By The Issuer And Affiliated Purchasers

In the years ending December 31, 2022 and 2021 Mereo's Employee Benefit Trust ("EBT") purchased no ordinary shares. In December 2020, the EBT converted its ordinary shares into 247,456 ADS's. As at December 31, 2022 a total cash balance of £17,741 was held by the EBT. Mereo utilizes the EBT to hold ADSs to satisfy the exercise of options under the Mereo's share-based incentive schemes.

	Total Number of Ordinary Shares Purchased	Average Price Paid Per Ordinary Share	Total Number of Ordinary Shares Purchased as Part of Publicly Announced Plans or Programs(1)	Maximum Number of Ordinary Shares that May Yet Be Purchased Under the Plans or Programs
Month #1 (October 1, 2018 – October 31, 2018)	131,487	£ 1.90		
Month #2 (December 1, 2018 – December 31, 2018)	31,513	£ 1.80		
Month #3 (May 1, 2019 – May 31, 2019)	1,074,274	£ 0.93		
June 4, 2020	7	£ 0.17		
Total	1,237,274	£ 1.88		

(1) The ordinary shares were not purchased as part of a publicly announced plan or program

Item 16F. Change In Registrant's Certifying Accountant

None

Item 16G. Corporate Governance

Foreign Private Issuer Exemption

As a "foreign private issuer," as defined by the SEC, Mereo is permitted to follow home country corporate governance practices, instead of certain corporate governance practices required by Nasdaq for U.S. domestic issuers. While Mereo intends to follow most Nasdaq corporate governance rules, it intends to follow U.K. corporate governance practices in lieu of Nasdaq corporate governance rules as follows:

- Mereo does not intend to follow Nasdaq Rule 5620(c) regarding quorum requirements applicable to meetings of shareholders. Such quorum requirements are not required under English law. In accordance with the U.K. Companies Act 2006, Mereo's Articles provide alternative quorum requirements that are generally applicable to meetings of shareholders.
- Mereo does not intend to follow Nasdaq Rule 5605(b)(2), which requires that independent directors regularly have scheduled meetings at which only independent directors are present.
- Mereo does not intend to follow Nasdaq Rule 5635, which generally requires an issuer to seek shareholder approval in connection with certain private placements of equity securities. Mereo intends to follow the requirements of the U.K. Companies Act 2006 with respect to any requirement to obtain shareholder approval to authorize Mereo's directors to allot shares and to disapply statutory pre-emption rights prior to any private placements of equity securities.

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

Mereo intends to take all actions necessary for it to maintain compliance as a foreign private issuer under the applicable corporate governance requirements of the Sarbanes-Oxley Act of 2002, the rules adopted by the SEC and the Nasdaq corporate governance rules and listing standards.

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

Mereo Shareholder Rights Under U.K. Law

The rights of the holders of our ordinary shares are governed by the laws of England and Wales and Mereo's Articles. The rights of the holders of our ADSs are governed by the deposit agreement.

Purchase and Redemption Rights

Under the U.K. Companies Act 2006, a public limited company may issue redeemable shares if authorized by its articles of association, subject to any conditions stated therein. No redeemable shares may be issued at a time when there are no issued shares of the company existing which are not redeemable. Mereo is empowered to issue redeemable shares under its Articles.

Under the U.K. Companies Act 2006, a company may redeem shares only if the shares are fully paid and, in the case of public limited companies, only out of: (1) distributable profits; or (2) the proceeds of a new issue of shares made for the purpose of such redemption.

Preemptive Rights

Under the U.K. Companies Act 2006, the issuance of "equity securities" (being (1) shares in a 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 or (2) rights to subscribe for, or to convert securities into, such shares) that are to be paid for wholly in cash must be offered first to the existing holders of Mereo Shares in proportion to the respective nominal values (i.e., par values) of their holdings on the same or more favorable terms, unless an exception applies or a special resolution to the contrary has been passed or the articles of association otherwise provide, in each case in accordance with the provisions of the U.K. Companies Act 2006 and Mereo's Articles. An exclusion of pre-emptive rights can be granted for a maximum of five years from the date that Mereo's directors are granted authority to allot the relevant Mereo ordinary shares, after which shareholders' approval would be required to renew such exclusion.

Inspection Rights

Under English law, a company must retain and keep available for inspection by shareholders, free of charge, and by any other person on payment of a prescribed fee, its register of members. It must also keep available for inspection by shareholders, free of charge, records of all resolutions passed by and minutes of meetings of shareholders for a period of at least ten years from the date of the relevant resolution or meeting, and for a fee, provide copies of such records to shareholders who request them.

Appraisal Rights

There is no mandatory provision in English law for appraisal rights. Such rights could, in theory, be provided for in the articles of association or in a shareholders' agreement. Mereo's Articles do not provide for appraisal/dissenters' rights. However, English law provides dissenters' rights which would permit a shareholder to object to a court of England and Wales in the context of the compulsory acquisition of minority shares.

Votes on Certain Transactions

The U.K. Companies Act 2006 provides for schemes of arrangement, which are arrangements or compromises between a company and any class of shareholders or creditors and used in certain types of reconstructions, amalgamations, capital reorganizations or takeovers. These arrangements require: (1) the approval, at a shareholders' or creditors' meeting convened by order of a court of England and Wales, of a majority in number representing 75% in value of the creditors or class of creditors or members or class of members (as the case may be) present and voting, either in person or by proxy; and (2) the approval of a court of England and Wales.

Amendment of Corporate Governance Documents

Under the U.K. Companies Act 2006, a company incorporated in England and Wales may amend its articles of association by way of a special resolution.

Shareholder Action by Written Consent

Under the U.K. Companies Act 2006, a resolution of the members (or of a class of members) of a public company must be passed at a general meeting of the members. Written resolutions are not permitted.

Notwithstanding the foregoing: (1) English law currently provides that certain matters could be effected by a company otherwise than by passing a resolution where it can be shown that all shareholders of that company have provided unanimous informed consented to the relevant matter; and (2) under the U.K. Companies Act 2006, rights attached to a class of the company's shares may, where the company's articles contain no provision for the variation of the relevant rights, be carried by consent in writing from the holders of at least three-quarters in nominal value of the issued shares of that class.

Shareholder Meetings

The U.K. Companies Act 2006 requires that a public limited company, such as Mereo, must convene an annual general meeting within six months following its accounting reference date.

Subject to the notice requirements of the U.K. Companies Act 2006 outlined below and Mereo's Articles, a general meeting of the shareholders of Mereo may be called by the Mereo Board whenever and at such times and places as it shall determine.

A general meeting may also be convened by the Mereo Board on the requisition of two or more Mereo shareholders who hold at least 5% of the paid-up capital of Mereo carrying voting rights at a general meeting.

General meetings at which special resolutions are proposed and passed generally involve proposals to change the name of the company, permit the company to issue new shares for cash without the shareholders' pre-emptive right, amend the company's articles of association, or carry out other matters where either the company's articles of association or the U.K. Companies Act 2006 prescribe that a special resolution is required.

Other proposals relating to the ordinary course of the company's business, such as the election of directors, would generally be the subject of an ordinary resolution.

Under the U.K. Companies Act 2006, 21 clear days' notice must be given for an annual general meeting and any resolutions to be proposed at that meeting. At least 14 clear days' notice is required for any other general meeting.

In addition, certain matters, such as the removal of directors or auditors, require special notice, which is 28 clear days' notice.

Shareholder Proposals and Shareholder Nomination of Directors

Under the U.K. Companies Act 2006, shareholders of a company may require the directors to call a general meeting of the company and may specify the text of a resolution to be voted on at that meeting if the request is made by two or more shareholders holding at least 5% of the paid-up capital of Mereo carrying voting rights at a general meeting.

In certain circumstances, shareholders may also require the company to circulate to shareholders that are entitled to receive notice of a general meeting, a statement of not more than 1,000 words with respect to (1) a matter referred to in a proposed resolution to be dealt with at that meeting, or (2) other business to be deal with at that meeting. A company is required to circulate a statement once it has received requests to do so from (1) two or more shareholders representing at least 5% of the total voting rights of all shareholders who have a relevant right to vote, or (2) by at least 100 shareholders who have a relevant right to vote and hold shares in the company on which there has been paid up an average sum, per shareholder, of at least £100.

Resolutions to appoint or re-appoint directors to a public limited company such as Mereo must generally be put to shareholders on the basis of one resolution for each nominated director.

Number of Directors

Under the U.K. Companies Act 2006, a public limited company must have at least two directors being natural persons.

Classification of the Board

Under the U.K. Companies Act 2006, a company may not enter into a service contract with a fixed term of more than two years with a director or (where the director is a director of a holding company) with a member of the group consisting of that company and its subsidiaries unless such contract has been approved by an ordinary resolution of the shareholders of the company or (in the case of a director of a holding company) of the shareholders of the holding company. Such a resolution must not be passed unless a memorandum setting out the proposed contract incorporating the provision is made available to members of the company both (1) at the company's registered office for not less than 15 days ending with the date of the meeting; and (2) at the meeting itself.

Removal of Directors

Under the U.K. Companies Act 2006, a company may remove a director without cause at a general meeting by way of an ordinary resolution of shareholders, irrespective of any provision of any agreement or service contract between the director and the company, provided that 28 clear days' notice of the proposed resolution to remove the director is given and certain other procedural requirements under the U.K. Companies Act 2006 are followed (such as allowing the director to make representations against his or her removal either at the meeting or in writing).

Limitation of Director Liability

Under the U.K. Companies Act 2006, any provision (whether contained in a company's articles of association or any contract or otherwise) that purports to exempt a director of a company (to any extent) from any liability that would otherwise attach to him in connection with any negligence, default, breach of duty or breach of trust in relation to the company is void, and any provision where the company is seeking to indemnify a director for such liability is also void except as allowed by the provision of insurance.

Directors and Officers Indemnity

Any provision by which Mereo directly or indirectly provides an indemnity (to any extent) for a director of the company or of an "associated company" (i.e., a company that is a parent, subsidiary or sister company of Mereo) 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 void except as permitted by the U.K. Companies Act 2006, which provides exceptions for Mereo to:

- purchase and maintain director and officer insurance insuring its directors or the directors of an associated company against any liability attaching 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;
- provide a "qualifying third party indemnity," which is an indemnity against liability incurred by Mereo's directors and directors of an associated company to a person other than Mereo or an associated company. Such indemnity must not cover criminal fines, penalties imposed by regulatory bodies, 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 relief from liabilities for such matters; and

- provide a "qualifying pension scheme indemnity," which is an indemnity against liability incurred in connection with the company's activities as trustee of an occupational pension plan. Such indemnity must not cover a fine imposed in criminal proceedings, or sum payable to a regulatory authority by way of a penalty in respect of non-compliance with any requirement of a regulatory nature (however arising), or any liability incurred by the director in defending criminal proceedings in which he or she is convicted.

The U.K. Companies Act 2006 also provides that Mereo may lend a director of Mereo funds to meet expenditure incurred by him in defending any criminal or civil proceedings in connection with any alleged negligence, default, breach of duty or breach of trust by him in relation to Mereo or an associated company, or in connection with an application for certain specified relief, subject to the requirement that the loan must be on terms that it is to be repaid if the defense or the application for relief is unsuccessful.

Derivative Suits and Class Action Suits

Under English law, generally, the company, rather than its shareholders, is the proper claimant in an action in respect of a wrong done to the company or where there is an irregularity in the company's internal management. Notwithstanding this general position, the U.K. Companies Act 2006 provides that (1) a court may allow a shareholder to bring a derivative claim (that is, an action in respect of and on behalf of the company) in respect of a cause of action arising from a director's negligence, default, breach of duty or breach of trust and (2) a shareholder may bring a claim for a court order on the ground that the company's affairs have been or are being conducted in a manner that is unfairly prejudicial to the interests of its shareholders generally or of some of its shareholders, or that an actual or proposed act or omission of the company is or would be so prejudicial.

The U.K. Limitation Act 1980 imposes a limitation period, with certain exceptions, of civil claims. The period is six years in respect of actions in contract and tort, and 12 years for "actions on a specialty," such as a breach of any obligation contained in a deed. The limitation period begins to run from the date on which the action accrued. In the case of contract, this is the date on which the breach of contract occurred, and in tort this is the date on which the damage is suffered.

Conflicts of Interest Transactions

Under English law, a director is under a duty to avoid conflicts of interest, and is obliged to declare his or her interest (whether direct or indirect) in a proposed transaction with the company to the other directors. It is an offense to fail to declare an interest (whether direct or indirect) in an existing transaction with the company.

The duty to avoid a conflict of interest is not infringed if the situation cannot reasonably be regarded as likely to give rise to a conflict of interest or if the matter has been authorized by the directors.

Other U.K. Law Considerations

See "Item 10. Additional Information—B. Memorandum and Articles of Association—Other U.K. Law Considerations" for other applicable corporate governance practices.

Item 16H. Mine Safety Disclosure

Not applicable.

Item 16I. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections.

Not applicable.

PART THREE

Item 17. Financial Statements

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

Item 18. Financial Statements

Our audited consolidated financial statements are included in this annual report beginning at page F-1.

Item 19. Exhibits

EXHIBIT INDEX

Exhibit No.	Description
1.1	Articles of Association of the Company (incorporated herein by reference to Exhibit 3.1 to the Company's Form 6-K, furnished to the SEC on May 17, 2022 (Film No. 22932321)).
2.1	Form of American Depositary Receipt of Mereo BioPharma Group plc (incorporated into this Form 20-F by reference to Exhibit 4.3 to Mereo's Form F-4/A filed March 15, 2019 (File No. 333-229351)).
2.2*	Description of Securities Registered under Section 12 of the Exchange Act.
4.1	Agreement and Plan of Merger and Reorganization, dated December 5, 2018, by and among Mereo BioPharma Group plc, Mereo US Holdings Inc., Mereo MergerCo One Inc. and OncoMed Pharmaceuticals, Inc. (incorporated into this Form 20-F by reference to Exhibit 2.1 to Mereo's Form F-4/A filed March 15, 2019 (File No. 333- 229351)).
4.9†	BCT197 Asset Purchase Agreement, dated July 28, 2015, by and between Mereo BioPharma 1 Limited and Novartis Pharma AG (incorporated into this Form 20-F by reference to Exhibit 10.20 to Mereo's Form F-4 filed January 25, 2019 (File No. 333-229351)).

Exhibit No.	Description
4.9.1	Amendment Agreement for BCT197, dated October 19, 2018, by and between Mereo BioPharma 1 Limited and Novartis Pharma AG (incorporated into this Form 20-F by reference to Exhibit 10.20.1 to Mereo's Form F-4 filed January 25, 2019 (File No. 333-229351)).
4.9.2	Addendum to the Asset Purchase Agreement, dated October 4, 2017, by and between Mereo BioPharma 1 Limited and Novartis Pharma AG (incorporated into this Form 20-F by reference to Exhibit 10.20.2 to Mereo's Form F-4 filed January 25, 2019 (File No. 333-229351)).
4.9.3	Addendum to the Asset Purchase Agreement, dated April 12, 2016, by and between Mereo BioPharma 1 Limited and Novartis Pharma AG (incorporated into this Form 20-F by reference to Exhibit 10.20.3 to Mereo's Form F-4 filed January 25, 2019 (File No. 333-229351)).
4.10†	BGS649 Asset Purchase Agreement, dated July 28, 2015, by and between Mereo BioPharma 2 Limited and Novartis Pharma AG (incorporated into this Form 20-F by reference to Exhibit 10.21 to Mereo's Form F-4 filed January 25, 2019 (File No. 333-229351)).
4.10.1	Amendment Agreement for BGS649, dated October 19, 2018, by and between Mereo BioPharma 2 Limited and Novartis Pharma AG (incorporated into this Form 20-F by reference to Exhibit 10.21.1 to Mereo's Form F-4 filed January 25, 2019 (File No. 333-229351)).
4.10.2	Addendum to the Asset Purchase Agreement, dated August 17, 2017, by and between Mereo BioPharma 2 Limited and Novartis Pharma AG (incorporated into this Form 20-F by reference to Exhibit 10.21.2 to Mereo's Form F-4 filed January 25, 2019 (File No. 333-229351)).
4.11†	BPS804 Asset Purchase Agreement, dated July 28, 2015, by and between Mereo BioPharma 3 Limited and Novartis Pharma AG (incorporated into this Form 20-F by reference to Exhibit 10.22 to Mereo's Form F-4 filed January 25, 2019 (File No. 333-229351)).
4.11.1†	Amendment Agreement, dated August 10, 2018, by and between Mereo BioPharma 3 Limited and Novartis Pharma AG (incorporated into this Form 20-F by reference to Exhibit 10.22.1 to Mereo's Form F-4 filed January 25, 2019 (File No. 333-229351)).
4.11.2	Addendum to the Asset Purchase Agreement, dated December 21, 2016, by and between Mereo BioPharma 3 Limited and Novartis Pharma AG (incorporated into this Form 20-F by reference to Exhibit 10.22.2 to Mereo's Form F-4 filed January 25, 2019 (File No. 333-229351)).
4.12†	Sublicense Agreement, dated July 29, 2015, by and between Mereo BioPharma 3 Limited and Novartis Pharma AG (incorporated into this Form 20-F by reference to Exhibit 10.23 to Mereo's Form F-4 filed January 25, 2019 (File No. 333- 229351)).
4.13†	Exclusive License and Option Agreement, dated October 28, 2017, by and between Mereo BioPharma 4 Limited and AstraZeneca AB (incorporated into this Form 20-F by reference to Exhibit 10.24 to Mereo's Form F-4 filed January 25, 2019 (File No. 333-229351)).
4.14	Form of Deed of Indemnity for members of the board of directors of Mereo BioPharma Group plc (incorporated into this Form 20-F by reference to Exhibit 10.26 to Mereo's Form F-4 filed January 25, 2019 (File No. 333-229351)).
4.15	Form of Contingent Value Rights Agreement by and between Computershare, Inc., as rights agent, and Mereo BioPharma Group plc (incorporated into this Form 20-F by reference to Annex B to Mereo's Form F-4/A filed March 15, 2019 (File No. 333-229351)).
4.17*	Form of Letter of Appointment for members of the board of directors of Mereo BioPharma Group plc.
4.19	Form of Convertible Loan Note Instrument, dated June 3, 2020, relating to Mereo BioPharma Group plc and amended March 29, 2021 (incorporated by reference to Exhibit 10.3 to the registrant's report on Form 6-K filed with the SEC on June 5, 2020 (File No. 001-38452)).
4.20	Form of Warrant Instrument, dated June 3, 2020, relating to Mereo BioPharma Group plc and amended March 29, 2021 (incorporated by reference to Exhibit 10.4 to the registrant's report on Form 6-K filed with the SEC on June 5, 2020 (File No. 001-384520).
4.21	Deed of Consent and Amendment to Convertible Loan Note Instrument, dated December 17, 2020 between Mereo BioPharma Group plc. and the Noteholders named therein (incorporated into this Form 20-F by reference to Exhibit 4.21 to Mereo's 20-F filed March 31, 2021 (File No. 001-38452).

Exhibit No.	Description
4.22	Form of Amended Convertible Loan Note Instrument, dated December 18, 2020 relating to Mereo BioPharma Group plc. (incorporated into this Form 20-F by reference to Exhibit 4.22 to Mereo's 20-F filed March 31, 2021 (File No. 001-38452)
4.23	Form of Amended Convertible Loan Note Instrument, dated February 5, 2021 relating to Mereo BioPharma Group plc. (incorporated into this Form 20-F by reference to Exhibit 4.23 to Mereo's 20-F filed March 31, 2021 (File No. 001-38452)
4.24	Form of Amended Convertible Loan Note Instrument, dated March 29, 2021 relating to Mereo BioPharma Group plc. (incorporated into this Form 20-F by reference to Exhibit 4.24 to Mereo's 20-F filed March 31, 2021 (File No. 001-38452)
4.25	Deed of Consent and Amendment to Warrant Instrument, dated March 29, 2021 between Mereo BioPharma Group plc. and the Alpha-1 Project, Inc. (incorporated into this Form 20-F by reference to Exhibit 4.25 to Mereo's 20-F filed March 31, 2021 (File No. 001-38452)
4.26	Employment Agreement, dated September 1, 2019 between Mereo Biopharma Group plc and John Richard (incorporated by reference to Exhibit 10.1 to the registrant's report on Form 6-K filed with the SEC on September 3, 2019 (File No. 001-38452)).
4.27	Employment Agreement, dated July 1, 2020 between Mereo BioPharma Group plc and John Lewicki. (incorporated into this Form 20-F by reference to Exhibit 4.27 to Mereo's 20-F filed March 31, 2021 (File No. 001-38452)
4.28	Form of Convertible Loan Instrument, dated February 10, 2020 relating to Mereo BioPharma Group plc (incorporated into this Form 20-F by reference to Exhibit 4.28 to Mereo's 20-F filed March 31, 2022 (File No. 001-38452).
4.29	Form of Warrant Instrument, dated February 10, 2020 relating to Mereo BioPharma Group plc (incorporated into this Form 20-F by reference to Exhibit 4.29 to Mereo's 20-F filed March 31, 2022 (File No. 001-38452).
4.30	Deed of Consent and Amendment to Note Instrument, dated November 24, 2020 between Mereo BioPharma Group plc. and Novartis Pharma AG (incorporated into this Form 20-F by reference to Exhibit 4.30 to Mereo's 20-F filed March 31, 2022 (File No. 001-38452).
4.31	Deed of Consent and Amendment to Warrant Instrument, dated November 24, 2020 between Mereo BioPharma Group plc. and Novartis Pharma AG (incorporated into this Form 20-F by reference to Exhibit 4.31 to Mereo's 20-F filed March 31, 2022 (File No. 001-38452).
4.32††	Collaboration and License Agreement, dated December 17, 2020, between Mereo BioPharma 3 Limited and Ultragenyx Pharmaceutical Inc. (incorporated into this Form 20-F by reference to Exhibit 4.32 to Mereo's 20-F filed March 31, 2022 (File No. 001-38452)
4.33	Amended and restated Contract of Employment, dated September 3, 2021, between Mereo BioPharma Group plc and Denise Scots-Knight (incorporated into this Form 20-F by reference to Exhibit 4.33 to Mereo's 20-F filed March 31, 2022 (File No. 001-38452)
4.34	Amended and restated Contract of Employment, dated September 3, 2021, between Mereo BioPharma Group plc and Christine Fox (incorporated into this Form 20-F by reference to Exhibit 4.34 to Mereo's 20-F filed March 31, 2022 (File No. 001-38452)
4.36	Amended and restated Contract of Employment, dated September 3, 2021, between Mereo BioPharma Group plc and Charles Sermon (incorporated into this Form 20-F by reference to Exhibit 4.36 to Mereo's 20-F filed March 31, 2022 (File No. 001-38452)
4.37	Amended and restated Contract of Employment, dated September 16, 2021, between Mereo BioPharma Group plc and Alexandra (Wills) Hughes-Wilson (incorporated into this Form 20-F by reference to Exhibit 4.37 to Mereo's 20-F filed March 31, 2022 (File No. 001-38452)
4.38	Employment Agreement, dated December 7, 2020, between Mereo BioPharma Group plc and Suba Krishnan (incorporated into this Form 20-F by reference to Exhibit 4.38 to Mereo's 20-F filed March 31, 2022 (File No. 001-38452)
4.39	Amended and restated Contract of Employment, dated October 12, 2021], between Mereo BioPharma Group plc and Jackie Parkin (incorporated into this Form 20-F by reference to Exhibit 4.39 to Mereo's 20-F filed March 31, 2022 (File No. 001-38452)
4.40	Form of Change in Control and Severance Agreement for Executives employed by Mereo Biopharma 5, Inc. (incorporated into this Form 20-F by reference to Exhibit 4.40 to Mereo's 20-F filed March 31, 2022 (File No. 001-38452)

4.44	Deferred Compensation Plan for Non-Employee Directors, dated January 31, 2022 (incorporated into this Form 20-F by reference to Exhibit 4.44 to Mereo's 20-F filed March 31, 2022 (File No. 001-38452)
4.45†††	License Agreement, dated January 13, 2020, between OncoMed Pharmaceuticals, Inc., Mereo BioPharma Group plc and Oncologie, Inc. (incorporated into this Form 20-F by reference to Exhibit 4.45 to Mereo's Form 20-F filed March 31, 2021 (File No. 001-38452).
4.46*	Deed of Consent and Amendment to Note Instrument, dated February 9, 2023 between Mereo BioPharma Group plc and Novartis Pharma AG
4.47*	Form of Warrant Instrument, dated February 10, 2023, relating to Mereo BioPharma Group plc
4.48	Form of Performance Based Restricted Stock Unit Award Agreement under the Plans (incorporated into this Form 20-F by reference to Exhibit 4.4 to Mereo's Form S-8 filed January 24, 2023 (File No. 333-269388))
4.49	Form of Restricted Stock Unit Award Agreement under the Plans (incorporated into this Form 20-F by reference to Exhibit 4.5 to Mereo's Form S-8 filed January 24, 2023 (File No. 333-269388))
8.1*	List of Subsidiaries of Mereo BioPharma Group plc

Exhibit No.	Description
10.1	Form of Securities Purchase Agreement, dated June 3, 2020, by and among Mereo BioPharma Group PLC and the several purchasers named therein (incorporated by reference to Exhibit 10.1 to the registrant's report on Form 6-K filed with the SEC on June 5, 2020 (File No. 001-38452)).
10.2	Form of Registration Rights Agreement, dated June 3, 2020, by and between Mereo BioPharma Group PLC and the several purchasers named therein (incorporated by reference to Exhibit 10.2 to the registrant's report on Form 6-K filed with the SEC on June 5, 2020 (File No. 001-38452)).
12.1*	Certification Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
12.2*	Certification Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
13.1*	Certification Pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
13.2*	Certification Pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
15.1*	Consent of BDO LLP, Independent Registered Public Accounting Firm
15.2*	Consent of Ernst & Young LLP, Independent Registered Public Accounting Firm
101	The following materials from this annual report on Form 20-F formatted in XBRL (Extensible Business Reporting Language) are furnished herewith: (i) the Report of Independent Registered Public Accounting Firm, (ii) the consolidated statements of financial position data, (iii) the consolidated statements of comprehensive loss data, (iv) the consolidated statements of changes in shareholders' equity (capital deficiency), (v) the consolidated statements of cash flows, and (vi) the notes to consolidated financial statements, in each case tagged as blocks of text and in detail.
104	Cover Page Interactive Data File

* Filed herewith.

† Portions of this exhibit are subject to a previously filed confidential treatment order pursuant to Rule 406 under the Securities Act.

†† Confidential portions of this exhibit were redacted pursuant to Item 601(b)(10) of Regulation S-K and the Company agrees to furnish supplementally to the Commission a copy of any omissions upon request.

††† Certain portions of this exhibit have been omitted because they are not material and they are the type of information that the Registrant treats as private or confidential.

Table of Contents

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.

MEREO BIOPHARMA GROUP PLC

By: /s/ Denise Scots-Knight
Name: Denise Scots-Knight
Title: Chief Executive Officer

Date: March 28, 2023

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

	Page
Audited Financial Statements	
Report of Independent Registered Public Accounting Firm (BDO LLP; London, United Kingdom; PCAOB ID Number: 1295)	F-2
Report of Independent Registered Public Accounting Firm (Ernst & Young LLP; London, United Kingdom; PCAOB ID Number: 1438)	F-3
Consolidated Statements of Comprehensive (Loss)/income	F-4
Consolidated Balance Sheets	F-5
Consolidated Statements of Cash Flows	F-6
Consolidated Statements of Changes in Equity	F-7
Notes to the Consolidated Financial Statements	F-8

Report of Independent Registered Public Accounting Firm

Shareholders and Board of Directors Mereo BioPharma Group plc London, United Kingdom

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Mereo BioPharma Group plc (the "Company") as of December 31, 2022 and 2021, the related consolidated statements of comprehensive (loss)/income, changes in equity, and cash flows for each of the two 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 two years in the period ended December 31, 2022, in conformity with International Financial Reporting Standards as issued by the International Accounting Standards Board.

Basis for Opinion

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

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

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

/s/ BDO LLP

We have served as the Company's auditor since 2021.
Reading, United Kingdom
March 28, 2023

Report of Independent Registered Public Accounting Firm

To the Shareholders and the Board of Directors of Mereo BioPharma Group plc

Opinion on the Financial Statements

We have audited the accompanying consolidated statements of comprehensive loss, changes in equity, and cash flows of Mereo BioPharma Group plc (the Company) for the year ended December 31, 2020, 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 results of its operations and its cash flows for the year ended December 31, 2020, in conformity with International Financial Reporting Standards as issued by the International Accounting Standards Board.

Adoption of New Accounting Standard

As discussed in Note 2 to the consolidated financial statements, the Company changed its method of accounting for leases in 2019 due to the adoption of IFRS 16 (Leases).

Basis for Opinion

These financial statements are the responsibility of the Company’s management. Our responsibility is to express an opinion on the Company’s financial statements based on our audit. 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 audit 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 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 audit 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 audit included performing procedures to assess the risks of material misstatement of the 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 financial statements. Our audit also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audit provides a reasonable basis for our opinion.

/s/ Ernst & Young LLP
We have served as the Company’s auditor from 2015 to 2021.
Reading, United Kingdom
March 31, 2021

MEREO BIOPHARMA GROUP PLC
CONSOLIDATED STATEMENTS OF COMPREHENSIVE (LOSS)/INCOME

	Notes	Year ended December 31, 2022 £'000s	2021 £'000s	2020 £'000s
Revenue	6	—	36,464	—
Cost of revenue	6	936	(17,908)	—
Research and development expenses		(24,962)	(23,559)	(16,347)
Administrative expenses		(19,543)	(15,933)	(21,222)
Operating loss		**(43,569)**	**(20,936)**	**(37,569)**
Finance income	9	696	1	44
Finance costs	9	(3,361)	(4,022)	(6,383)
Changes in the fair value of financial instruments	9	7,805	40,039	(109,849)
Gain/(loss) on disposal of intangible assets		—	113	(10,872)
Net foreign exchange gain/(loss)		1,525	(954)	(1,821)
Other income and expenses	9	811	—	—
(Loss)/profit before tax	7	**(36,093)**	**14,241**	**(166,450)**
Taxation	10	1,897	(1,516)	2,822
(Loss)/profit for the year, attributable to equity holders of the parent		(34,196**)**	**12,725**	**(163,628)**
Items that may be reclassified subsequently to profit or loss:				
Currency translation of foreign operations		(1,828)	(191)	349
Total comprehensive (loss)/income for the year, attributable to equity holders of the parent		(36,024)	**12,534**	**(163,279)**
Basic (loss)/profit per share for the year (in £)	11	(0.06**)**	0.02	(0.48)
Diluted loss per share for the year (in £)	11	(0.06)	(0.05)	(0.48)

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

MEREO BIOPHARMA GROUP PLC
CONSOLIDATED BALANCE SHEETS

	Notes	As at December 31, 2022 £'000s	2021 £'000s
Assets			
Non-current assets			
Property, plant and equipment	12	1,831	2,530
Intangible assets	13	24,116	24,564
		25,947	27,094
Current assets			
Prepayments		3,125	2,799
R&D tax credits	10	1,296	—
Other taxes receivable	10	614	809
Other receivables	15	762	1,419
Cash and short-term deposits	16	56,334	94,296
		62,131	99,323
Total assets		**88,078**	**126,417**
Equity and liabilities			
Non-current liabilities			
Provisions	18	—	1,320
Convertible loan notes	21	—	14,384
Warrant liability	20	129	8,336
Lease liability	12	1,222	1,754
Other liabilities		182	80
		1,533	**25,874**
Current liabilities			
Trade and other payables	17	3,078	2,499
Accruals		4,491	3,826
Current tax liabilities	10	—	1,522
Provisions	18	4,822	2,803
Convertible loan notes	21	11,085	—
Warrant liability	20	402	—
Lease liability	12	466	622
Other liabilities	6	333	1,269
		24,677	12,541
Total liabilities		**26,210**	38,415
Net assets		**61,868**	88,002
Equity			
Issued capital	22	1,875	1,755
Share premium	22	254,303	247,460
Other capital reserves	22	132,680	129,835
Employee Benefit Trust shares	22	(1,058)	(1,140)
Other reserves	22	7,401	7,401
Accumulated losses	22	(331,164)	(296,968)
Translation reserve		(2,169)	(341)
Total equity		**61,868**	88,002

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

MEREO BIOPHARMA GROUP PLC
CONSOLIDATED STATEMENTS OF CASH FLOWS

	Notes	Year ended December 31, 2022 £'000s	2021 £'000s	2020 £'000s
Operating activities				
(Loss)/profit before tax		(36,093)	14,241	(166,450)
Adjustments to reconcile (loss)/profit before tax to net cash flows:				
Depreciation of property, plant and equipment	12	727	642	1,599
Share-based payments expense	26	3,862	3,302	1,558
Net foreign exchange (gain)/loss		(2,064)	954	1,821
Increase in provisions and other liabilities	18,6	211	1,385	162
Finance income	9	(696)	(1)	(44)
Finance costs	9	2,910	3,797	6,226
Other non-cash movements		647	156	—
Gain on lease modification		—	—	(957)
Fair value remeasurement on warrants	9	(7,805)	(40,039)	109,849
Other income and expenses	9	(811)	—	—
(Gain)/loss on disposal of intangible assets		—	(113)	10,872
Out-license of intangible asset		—	9,457	—
Working capital adjustments				
Decrease/(increase) in receivables and prepayments		695	(589)	141
Increase/(decrease) in trade and other payables and accruals		1,126	(1,256)	(3,551)
Taxation	10	(1,529)	2,825	10,433
Net cash flows used in operating activities		**(38,820)**	**(5,239)**	**(28,341)**
Investing activities				
Acquisition of subsidiary		—	—	(354)
Purchase of property, plant and equipment	12	(10)	(535)	(16)
Proceeds from intangible assets (net of transaction costs)	9	1,484	113	1,821
Interest earned	9	696	1	44
Payments to CVR holders	9	(673)	—	—
Net cash flows (used in)/from investing activities		**1,497**	**(421)**	**1,495**
Financing activities				
Proceeds from issuance of ordinary shares		—	78,532	20,136
Transaction costs on issuance of shares		—	(234)	(1,307)
Proceeds from exercise of employee share options		—	46	—
Proceeds from issuance of convertible loan notes		—	—	44,375
Transaction costs on issuance of convertible loan notes		—	—	(3,598)
Repayment of bank loans		—	—	(19,802)
Transaction costs relates to loans and borrowings		—	—	(81)
Interest paid on bank loan		—	—	(2,900)
Payment of lease liabilities	12	(937)	(692)	(2,086)
Proceeds from TAP agreement	22	153	—	—
Net cash flows (used in)/from financing activities		**(784)**	**77,652**	**34,737**
Net (decrease)/increase in cash and cash equivalents		**(38,107)**	**71,992**	**7,891**
Cash and cash equivalents at January 1		94,296	23,469	16,347
Effect of exchange rate changes		145	(1,165)	(769)
Cash and cash equivalents at December 31		**56,334**	**94,296**	**23,469**

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

MEREO BIOPHARMA GROUP PLC
CONSOLIDATED STATEMENTS OF CHANGES IN EQUITY

	Notes	Issued capital	Share premium	Other capital reserves	Employee Benefit Trust shares	Other reserves	Accumulated losses	Translation reserves	Total
At December 31, 2019		**294**	**121,684**	**59,147**	**(1,305)**	**7,000**	**(146,065)**	**(499)**	**40,256**
Loss for the year		—	—	—	—	—	(163,628)	—	(163,628)
Other comprehensive income		—	—	—	—	—	—	349	349
Total		—	—	—	—	—	(163,628)	349	(163,279)
Share-based payments	26	—	—	1,558	—	—	—	—	1,558
Issuance of share capital, net		347	18,715	—	—	(2,125)	—	—	16,937
Conversion of loan notes and warrants		375	21,386	34,188	—	—	—	—	55,949
Reclassification of loan notes embedded derivative		—	—	33,481	—	—	—	—	33,481
Conversion of warrants		1	—	—	—	126	—	—	127
At December 31, 2020		**1,017**	**161,785**	**128,374**	**(1,305)**	**5,001**	**(309,693)**	**(150)**	**(14,971)**
Profit for the year		—	—	—	—	—	12,725	—	12,725
Other comprehensive income		—	—	—	—	—	—	(191)	(191)
Total		—	—	—	—	—	12,725	(191)	12,534
Share-based payments	26	—	—	3,302	—	—	—	—	3,302
Issuance of share capital, net	22	601	78,609	—	—	—	—	—	79,210
Exercise of share options		—	—	(119)	165	—	—	—	46
Conversion of loan notes and warrants	22	137	7,066	(1,722)	—	2,400	—	—	7,881
At December 31, 2021		**1,755**	**247,460**	**129,835**	**(1,140)**	**7,401**	**(296,968)**	**(341)**	**88,002**
Loss for the year		—	—	—	—	—	(34,196)	—	(34,196)
Other comprehensive income		—	—	—	—	—	—	(1,828)	(1,828)
Total		—	—	—	—	—	(34,196)	(1,828)	(36,024)
Share-based payments	26	—	—	3,862	—	—	—	—	3,862
Exercise of share options		—	—	(82)	82	—	—	—	—
Conversion of loan notes	22	120	6,843	(1,005)	—	—	—	—	5,958
Issuance of warrants	22	—	—	70	—	—	—	—	70
At December 31, 2022		**1,875**	**254,303**	**132,680**	**(1,058)**	**7,401**	**(331,164)**	**(2,169)**	**61,868**

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

MEREO BIOPHARMA GROUP PLC
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS

1. Corporate information

Mereo BioPharma Group plc (the "Company" or "Mereo") is a clinical-stage, United Kingdom ("UK") based biopharmaceutical company focused on rare diseases.

The Company is a public limited company incorporated and domiciled in the UK, and registered in England, with shares publicly traded on the Nasdaq Global Market via American Depositary Shares ("ADSs") under the ticker symbol "MREO". The Company's ordinary shares were previously admitted to trading on the AIM market of London Stock Exchange plc with admission cancelled with effect on December 18, 2020. The Company's registered office is located at Fourth Floor, 1 Cavendish Place, London, W1G 0QF, United Kingdom.

The consolidated financial statements of Mereo BioPharma Group plc and its subsidiaries for the year ended December 31, 2022 were authorized for issue in accordance with a resolution of the Directors on March 28, 2023. The principal activities of the Company are the development and commercialization of innovative therapeutic pharmaceutical products for rare diseases.

2. Significant accounting policies

Basis of preparation

The Company's consolidated financial statements have been prepared in accordance with International Financial Reporting Standards (IFRS) as issued by the International Accounting Standards Board (IASB).

The consolidated financial statements are presented in pound sterling ("£"), which is the presentational currency of the Company. The functional currencies of consolidated subsidiaries are pound sterling and US dollars ("$"). All amounts disclosed in the consolidated financial statements and notes have been rounded to the nearest thousand, unless otherwise stated. The financial statements have been prepared on the historical cost basis, except for the revaluation of certain financial instruments that are measured at fair values at the end of each reporting period, as explained in the accounting policies below.

Basis of consolidation

The consolidated financial information comprises the financial statements of Mereo BioPharma Group plc and its subsidiaries as at December 31, 2022. Subsidiaries are all entities over which the Company has control. The Company controls an entity when the Company is exposed to, or has rights to, variable returns from its involvement with the entity and has the ability to affect those returns through its power over the entity.

Subsidiaries are fully consolidated from the date on which control is transferred to the Company. They are deconsolidated from the date that control ceases. Intercompany transactions, balances and unrealized gains on transactions between subsidiaries are eliminated in preparing the consolidated financial statements. Accounting policies of subsidiaries are consistent with the policies adopted by the Company.

The Company has an employee share trust to facilitate share transactions pursuant to employee share schemes. Although the trust is a separate legal entity from the Company, it is consolidated into the Company's results in accordance with the IFRS 10 rules on special purpose vehicles. The Company is deemed to control the trust principally because the trust cannot operate without the funding the Company provides.

Segmental information

The Company has one operating segment. The Chief Operating Decision Maker ("CODM") is the Chief Executive Officer. The Company has a single portfolio of product candidates, with only direct research and development expenses monitored at a product candidate level. The CODM makes decisions over resource allocation at an overall portfolio level and the Company's financing is managed and monitored on a consolidated basis.

Non-current assets held by the Company are located in the United Kingdom and United States. As at December 31, 2022, less than £0.1 million (2021: £0.1 million) of non-current assets are located in the United States.

Going concern

The going concern basis has been applied in these consolidated financial statements as the Company has adequate resources to meet its liabilities as they fall due for the foreseeable future and at least 12 months from the issuance date of these consolidated financial statements.

The Company expects to incur significant operating losses for the foreseeable future as it continues its research and development efforts, seeks to obtain regulatory approval of its product candidates and pursues any future product candidates the Company may develop.

Until such time as the Company can generate significant revenue from product sales, or other commercial revenues, if ever, or through licensing and/or collaboration agreements for its rare disease or oncology product candidates, the Company will seek to finance its operations through a combination of public or private equity or debt financings or other non-dilutive sources.

Summary of significant accounting policies

a) Revenue

The Company's ordinary business activities are the development of product candidates to key clinical milestones and either strategically partnering them or further developing such product candidates through regulatory approval and potentially commercialization. The Company may enter into a range of different agreements with third parties, including but not limited to: (i) licensing agreements where the global rights to a product candidate are licensed to a partner; and (ii) collaboration agreements where rights to a product candidate are licensed to a partner but the Company retains certain rights, for example to further develop or commercialize the product candidate in specified geographical territories. Under both licensing and collaboration agreements, rights to product candidates are provided to a partner typically in exchange for consideration in the form of upfront payments and/or development, regulatory, commercial or other similar milestones, and royalties on commercial sales, should regulatory approval be obtained for the product candidates. Where the Company has performed significant development activities for its product candidates, income from agreements with third parties are considered to be proceeds derived from the Company's ordinary activities and therefore represent revenue within the scope of IFRS 15, Revenue from Contracts with Customers.

Revenue includes income from licensing and collaboration agreements. Consideration received up front is recognized at the point in time in which the right to use an intangible asset is transferred and further payments received are recognized upon the achievement of specified development, regulatory, commercial or other similar milestones. For agreements with a right to access an intangible asset, revenue is recognized over time, typically on a straight-line basis over the life of the license or collaboration agreement. When there are other performance obligations in such agreements, the consideration is allocated using the residual approach and recognized when the performance obligations are satisfied.

Income from development, regulatory, commercial or similar milestones is recognized when considered highly probable that a significant reversal will not occur. Timing of the recognition of such milestones are considered to be a key judgment, as they are often dependent on third parties. In general, for milestones which are subject to the decisions of third parties (e.g. the acceptance or approval of a filing by a regulatory authority), the Company recognizes milestone income when the decision occurs.

MEREO BIOPHARMA GROUP PLC
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

The Company does not currently have any approved product candidates. Accordingly, no commercial sales revenue was generated during the year.

Intangible assets out-licensed under a license or collaboration agreement are recorded within “Cost of revenue” in the Company’s consolidated statement of comprehensive (loss)/income based on an allocation of cost or value of the rights that have been out-licensed. Payments to third parties arising as a direct consequence of the income recognized are also recorded within “Cost of revenue” in the Company’s consolidated statement of comprehensive (loss)/income.

b) Research and development (R&D) expenses

Expenditure on product development is capitalized as an intangible asset and amortized over the expected useful economic life of the product candidate concerned. Capitalization commences from the point at which technical feasibility and commercial viability of the product candidate can be demonstrated and the Company is satisfied that it is probable that future economic benefits will result from the product candidate once completed. Capitalization ceases when the product candidate receives regulatory approval for launch. No such costs have been capitalized to date.

Expenditure on R&D activities that do not meet the criteria for capitalization, including ongoing costs associated with acquired intellectual property rights and intellectual property rights generated internally by the Company, is recognized in the consolidated statement of comprehensive (loss)/income as incurred. Intellectual property and in-process R&D from asset acquisitions are recognized as intangible assets at cost.

c) Taxation

Tax expense recognized in the consolidated statement of comprehensive (loss)/income comprises the sum of deferred tax and current tax not recognized in other comprehensive income or directly in equity.

Current income tax

Current income tax assets and liabilities are measured at the amount expected to be recovered from or paid to the taxation authorities that are unpaid at the reporting date. Current tax is payable on taxable profit, which differs from profit or loss in the consolidated financial statements. Calculation of current tax is based on tax rates and tax laws that have been enacted, or substantively enacted, by the end of the reporting period in the jurisdictions in which the Company operates.

Amounts receivable in respect of research and development tax credits are recognized in the consolidated financial statements provided there is sufficient evidence that the amounts are recoverable. These credits are recognized within income tax in the consolidated statement of comprehensive (loss)/income.

A provision is recognized for matters in which the tax determination is uncertain but it is considered probable that there will be a future outflow of funds to a tax authority. The provisions are measured at the best estimate of the amount expected to become payable.

Deferred tax

Deferred tax is provided using the liability method on temporary differences between the tax bases of assets and liabilities and their carrying amounts for financial reporting purposes at the reporting date.

Deferred income tax assets are recognized for all deductible temporary differences, carry-forward of unused tax credits and unused tax losses, to the extent that it is probable that taxable profit

will be available against which the deductible temporary differences and the carry-forward of unused tax credits and unused tax losses can be utilized. The carrying amount of deferred income tax assets is reviewed at the end of each reporting period and reduced to the extent that it is no longer probable that sufficient taxable profit will be available to allow all or part of the deferred income tax asset to be utilized. Unrecognized deferred income tax assets are reassessed at the end of each reporting period and are recognized to the extent that it has become probable that future taxable profit will allow the deferred tax assets to be recovered.

Deferred tax assets and liabilities are measured on an undiscounted basis at the tax rates that are expected to apply in the year when the asset or liability is realized, based on tax rates (and tax laws) enacted or substantively enacted at the end of the reporting period.

Deferred tax assets and liabilities are offset when there is a legally enforceable right to set off current tax assets against current tax liabilities and when they relate to income taxes levied by the same taxation authority and the Company intends to settle its current tax assets and liabilities on a net basis.

d) Foreign currencies

Items included in the consolidated financial statements are measured using the currency of the primary economic environment in which the entity operates (“the functional currency”). The consolidated financial statements are presented in pound sterling (“£”), which is the presentational currency of the Company. The functional currencies of consolidated subsidiaries are pound sterling and US dollars (“$”).

Transactions in foreign currencies are initially recorded by the Company at the rate prevailing on the date the transaction first qualifies for recognition. Differences arising on settlement or translation of monetary items as well as gains or losses on the retranslation of foreign currency balances at the period-end are recognized in the consolidated statement of comprehensive (loss)/income.

The results and financial position of subsidiaries that have a functional currency different from the presentational currency of the Company are translated into the presentational currency (pound sterling). The assets and liabilities of such entities are translated into pound sterling at the rate of exchange prevailing at the balance sheet date. Income and expenses are translated at the average rate for the period, which approximates the exchange rates at the dates of the transactions. Fair value adjustments arising on acquisition of such entities are treated as assets and liabilities of the relevant entity and translated into pound sterling at the closing rate. The exchange differences arising on translation for consolidation are recognized in other comprehensive (loss)/income.

e) Property, plant and equipment

Property, plant and equipment is stated at cost, net of accumulated depreciation and accumulated impairment losses, if any. Such cost includes the cost of replacing part of the plant and equipment if the recognition criteria are met. All other repair and maintenance costs are recognized in profit or loss as incurred.

Depreciation is computed using the straight-line method over the estimated useful lives of the related assets. Useful lives of various property, plant and equipment are as follows:

- Leasehold improvements — shorter of lease term or ten years
- Office equipment — five years
- IT equipment — three years

Property, plant and equipment is derecognized upon disposal or when no future economic benefits are expected from its use or disposal. Any gain or loss arising on derecognition of the asset (calculated as the difference between the net disposal proceeds and the carrying amount of the asset) is included in the consolidated statement of comprehensive (loss)/income when the asset is derecognized.

The residual values, useful lives and methods of depreciation of property, plant and equipment are reviewed annually and adjusted prospectively, if appropriate.

f) Business combinations

Business combinations are accounted for using the acquisition method of accounting. At the date of acquisition, the Company initially recognizes the fair value of the identifiable assets acquired, the liabilities assumed and any non-controlling interest in the acquired business.

The consideration transferred is measured at fair value at the date of acquisition. The excess of the consideration transferred over the fair value of net identifiable assets of the business acquired is recorded as goodwill, unless the amount of consideration transferred is less than the fair value of net identifiable assets of the business acquired in which case the difference is recognized directly in the consolidated statement of comprehensive (loss)/income as a bargain purchase. A valuation is performed of assets and liabilities assumed on each acquisition accounted for as a business combination based on the best estimate of fair value.

Where the settlement of any part of cash consideration is deferred, the amounts payable in the future are discounted to their present value. Contingent consideration is classified either as equity or a financial liability and is recognized at fair value on the acquisition date. Amounts classified as a financial liability are subsequently remeasured to fair value in accordance with IFRS 9 (Financial Instruments), with changes in fair value recognized in the consolidated statement of comprehensive (loss)/income as an administrative expense.

Directly attributable acquisition-related costs are expensed as incurred within the consolidated statement of comprehensive (loss)/income.

g) Leases

Effective January 1, 2019, the Company adopted IFRS 16 (Leases) using the modified retrospective approach.

The Company assesses whether a contract is, or contains, a lease at inception of the contract. The Company recognizes a right-of-use asset and a corresponding liability with respect to all lease arrangements in which it is a lessee.

The lease liability is initially measured at the present value of the lease payments that are not paid at the commencement date, discounted using the rate implicit in the lease. If this rate cannot be readily determined, the Company uses its incremental borrowing rate.

Lease payments included in the measurement of the lease liability comprise of fixed lease payments, less any lease incentives receivable.

The lease liability is subsequently measured by increasing the carrying amount to reflect interest on the lease liability (using the effective interest method) and by reducing the carrying amount to reflect the lease payments made. The Company remeasures the lease liability (and makes a corresponding adjustment to the related right-of-use asset) whenever there is a significant change in lease term, lease payments or if the lease contract is modified and the lease modification is not accounted for as a separate lease.

The right-of-use assets comprise the initial measurement of the corresponding lease liability and lease payments made at or before the commencement date, less any lease incentives received and any initial direct costs. They are subsequently measured at cost less accumulated depreciation and impairment losses.

The right-of-use assets are presented within property, plant and equipment. Right-of-use assets are depreciated over the shorter period of lease term and useful life of the underlying asset:

- Right-of-use asset (building) six to nine years
- Right-of-use asset (equipment) one to two years

When the Company is an intermediate lessor, it accounts for the head lease and the sub-lease as two separate contracts. The sub-lease is classified as a finance or operating lease by reference to the right-of-use asset arising from the head lease. Rental income from operating leases is recognized on a straight-line basis over the term of the relevant lease.

h) Intangible assets

Intangible assets are initially recorded at cost which has been determined as the fair value of the consideration paid and payable. Assets that have been acquired through a business combination are initially recorded at fair value. The fair value of consideration is regularly reviewed based on the probability of achieving contractual milestones. Refer to policy on provision for deferred cash consideration below.

Where the consideration paid or payable is in shares, the cost is measured in accordance with IFRS 2 (Share Based Payments).

Intangible assets that are not yet available for use are reviewed for impairment at each reporting date by allocating the assets to the cash-generating units to which they relate. The estimated useful life is the lower of the legal duration and economic useful life. The estimated useful lives of intangible assets are reviewed at least annually.

Intangible assets are amortized from the date they are available for commercial use. No amortization has been recognized to date.

An intangible asset is derecognized on disposal, or when no future economic benefits are expected from use or disposal. Gains or losses arising from derecognition of an intangible asset, measured as the difference between the net disposal proceeds and the carrying amount of the asset, are recognized in profit or loss when the asset is derecognized.

i) Financial instruments

Financial assets and liabilities are recognized in the consolidated balance sheet only when the Company becomes party to the contractual provisions of the instrument.

Financial assets

On initial recognition, a financial asset is classified into one of three primary measurement categories:

- Amortized cost;
- Fair value through other comprehensive income (“FVOCI”); or
- Fair value through profit or loss (“FVTPL”).

The initial classification into a primary measurement category depends on the nature and purpose of the financial asset.

For short-term investments, interest income and impairment gains or losses are recognized directly in the consolidated statement of comprehensive income. The difference between cumulative fair value gains or losses and the cumulative amounts recognized in the consolidated statement of comprehensive (loss)/income is recognized in other comprehensive income until derecognition, when the amounts in other comprehensive income are reclassified to the consolidated statement of comprehensive (loss)/income.

Classification as debt or equity

Debt and equity instruments are classified as either financial liabilities or as equity in accordance with the substance of the contractual arrangements and the definitions of a financial liability and an equity instrument.

Embedded derivatives

An embedded derivative is a component of a hybrid contract that also includes a non-derivative host with the effect that some of the cash flows of the combined instrument vary in a way similar to a stand-alone derivative. Derivatives embedded in hybrid contracts with hosts that are not financial assets within the scope of IFRS 9 (e.g. financial liabilities) are treated as separate derivatives when they meet the definition of a derivative, their risks and characteristics are not closely related to those of the host contracts and the host contracts are not measured at FVTPL.

Convertible loan notes

Convertible loan notes are regarded as compound instruments consisting of a liability component and an equity component. At the date of issue, the fair value of the liability component is estimated using a discount rate for an equivalent liability without the conversion feature. This amount is recorded as a liability on an amortized cost basis using the effective interest method until extinguished upon conversion or at the instrument's maturity date. The difference between the proceeds from the issue of the convertible loan note and the fair value assigned to the liability component is included in equity and not subsequently remeasured. Upon conversion, the amount initially recognized in "Other capital reserves" will be transferred to "Share premium."

Financial liabilities

All financial liabilities are measured subsequently at amortized cost using the effective interest method or at FVTPL.

Borrowings (including interest-bearing loans) are initially recognized at fair value, net of transaction costs incurred. Borrowings are subsequently measured at amortized cost. Any difference between the proceeds (net of transaction costs) and the redemption amount is recognized in profit or loss over the period of the borrowings using the effective interest method. Under the effective interest method, amortization is included as a finance cost in the consolidated statement of comprehensive (loss)/income.

Non-substantial modifications to financial liabilities are measured at amortized cost with the associated gain or loss recognized in the consolidated statement of comprehensive (loss)/income. The gain or loss is computed as the difference between the original contractual cash flows and the modified cash flows, discounted at the original effective interest rate. For substantial modifications, the existing financial liability is derecognized and a new financial liability is established.

Borrowings are derecognized from the balance sheet when the obligation specified in the contract is discharged, cancelled or expired.

The warrant instruments are recorded at fair value, with changes in the fair value recognized in the consolidated statement of comprehensive (loss)/income, where the terms of the warrant instruments allow for cashless exercise.

j) Fair value measurement

Fair value is the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. The fair value measurement is based on the presumption that the transaction to sell the asset or transfer the liability takes place either:

- In the principal market for the asset or liability; or
- In the absence of a principal market, in the most advantageous market for the asset or liability. The principal or the most advantageous market must be accessible by the Company.

The fair value of an asset or a liability is measured using the assumptions that market participants would use when pricing the asset or liability, assuming that market participants act in their economic best interest.

The Company uses valuation techniques that are appropriate in the circumstances and for which sufficient data are available to measure fair value, maximizing the use of relevant observable inputs and minimizing the use of unobservable inputs.

All assets and liabilities for which fair value is measured or disclosed in the consolidated financial statements are categorized within the fair value hierarchy, described as follows, based on the lowest level input that is significant to the fair value measurement as a whole:

- Level 1 — quoted (unadjusted) market prices in active markets for identical assets or liabilities.
- Level 2 — valuation techniques for which the lowest level input that is significant to the fair value measurement is directly or indirectly observable.
- Level 3 — valuation techniques for which the lowest level input that is significant to the fair value measurement is unobservable.

For assets and liabilities that are recognized in the consolidated financial statements on a recurring basis, the Company determines whether transfers have occurred between levels in the hierarchy by reassessing categorization (based on the lowest level input that is significant to the fair value measurement as a whole) at the end of each reporting period.

k) Impairment of non-financial assets

Further disclosures relating to impairment of non-financial assets are also provided in the following notes:

- Disclosures for significant assumptions — Note 3
- Property, plant and equipment — Note 12
- Intangible assets not yet available for use — Notes 13 and 14

At each reporting date, the Company assesses whether there is any indication that an asset may be impaired. If any such indication exists, or when annual impairment testing for an asset is required,

the Company estimates the asset's recoverable amount. An asset's recoverable amount is the higher of an asset's or cash-generating unit's fair value less costs of disposal and its value in use. The recoverable amount is determined for an individual asset, unless the asset does not generate cash inflows that are largely independent of those from other assets or groups of assets. When the carrying amount of an asset or cash-generating unit exceeds its recoverable amount, the asset is considered impaired and is written down to its recoverable amount.

In assessing value in use, the estimated future cash flows are discounted to their present value using a pre-tax discount rate that reflects current market assessments of the time value of money and the risks specific to the asset. In determining fair value less costs of disposal, recent market transactions are taken into account. If no such transactions can be identified, an appropriate valuation model is used. These calculations are corroborated by valuation multiples, quoted share prices for publicly traded companies or other available fair value indicators.

Impairment losses are recognized in the consolidated statement of comprehensive (loss)/income in expense categories consistent with the function of the impaired asset.

An assessment is made at each reporting date to determine whether there is an indication that previously recognized impairment losses no longer exist or have decreased. If such indication exists, the Company estimates the asset's or cash-generating unit's recoverable amount. A previously recognized impairment loss is reversed only if there has been a change in the assumptions used to determine the asset's recoverable amount since the last impairment loss was recognized. The reversal is limited so that the carrying amount of the asset does not exceed its recoverable amount, nor exceed the carrying amount that would have been determined, net of depreciation, had no impairment loss been recognized for the asset in prior years. Such reversal is recognized in the consolidated statement of comprehensive (loss)/income unless the asset is carried at a revalued amount, in which case the reversal is treated as a revaluation increase.

l) Cash and short-term deposits

Cash and short-term deposits in the balance sheet comprise cash at banks and on hand along with short-term deposits with a maturity of three months or less, which are subject to an insignificant risk of changes in value.

m) Provisions

Provisions are recognized when the Company has a present obligation (legal or constructive) as a result of a past event, it is probable that an outflow of resources embodying economic benefits will be required to settle the obligation and a reliable estimate can be made of the amount of the obligation. When the Company expects some or all of a provision to be reimbursed, for example, under an insurance contract, the reimbursement is recognized as a separate asset, but only when the reimbursement is virtually certain. The expense relating to a provision is presented in the consolidated statement of comprehensive (loss)/income net of any reimbursement.

If the effect of the time value of money is material, provisions are discounted using a current pre-tax rate that reflects, when appropriate, the risks specific to the liability. When discounting is used, the increase in the provision due to the passage of time is recognized as a finance cost.

Where contingent payments relate to future use of the in-licensed IP, no liability or provision is recognized for variable amounts to be paid to the vendors based on future events unless such arrangements are onerous. The liability (and corresponding expense in the income statement) to the vendors is recognized as an obligation arises.

n) Provision for deferred cash consideration

Provision for deferred cash consideration consists of future payments which are contractually committed but not yet certain. In respect of products which are not yet approved, such deferred cash consideration excludes potential milestones, royalties or other payments that are deemed to be so uncertain as to be unquantifiable. Deferred cash consideration is recognized as a liability with the amounts calculated as the risk adjusted net present value of anticipated deferred payments. The provision is reviewed at each balance sheet date and adjusted based on the likelihood of contractual milestones being achieved and therefore the deferred payment being settled. Increases in the provision relating to changes in the probability are recognized as an intangible asset. Increases in the provision relating to the unwinding of the time value of money are recognized as a finance expense.

o) Share-based payments

Employees (including executives) and non-executive directors of the Company receive remuneration in the form of share-based payments, whereby employees and non-executive directors render services as consideration for equity instruments (equity settled transactions).

Incentives in the form of shares are provided to employees and non-executive directors under various plans (see Note 26).

In accordance with IFRS 2 Share-based Payments (“IFRS 2”), charges for these incentives are expensed through the consolidated statement of comprehensive (loss)/income on a straight-line basis over their vesting period, based on the Company’s estimate of shares that will eventually vest. The total amount to be expensed is determined by reference to the fair value of the options or awards at the date they were granted. For LTIP shares, the fair value on grant date excludes the impact of any non-market vesting conditions, which are taken into account by adjusting the number of equity instruments included in the measurement of the share-based payment transaction and are adjusted each period until such time as the equity instruments vest.

Equity-settled share-based payment transactions with parties other than employees are measured at the fair value of the goods or services received, except where that fair value cannot be estimated reliably, in which case they are measured at the fair value of the equity instruments granted, measured at the date the entity obtains the goods or the counterparty renders the service.

In accordance with IFRS 2, the cancellation of share options is accounted for as an acceleration of the vesting period and therefore any amount unrecognized that would otherwise have been charged in future accounting periods is recognized immediately. When options are forfeited, the accounting expense for any unvested awards is reversed.

p) Costs of issuing capital

Incremental costs incurred and directly attributable to the offering of equity securities are deducted from the related proceeds of the offering. The net amount is recorded as share premium in the period when such shares are issued. Where such expenses are incurred prior to the offering they are recorded in prepayments until the offering completes. Other costs incurred in such offerings are expensed as incurred and included in general and administrative expenses.

q) Employee Benefit Trust

The Company operates an Employee Benefit Trust (“EBT”), the Mereo BioPharma Group plc Employee Benefit Trust.

The EBT holds ADS’s to satisfy the exercise of options under the Company’s share-based incentive schemes (see Note 26). The EBT is a Jersey-based trust which was initially funded by a loan from the Company, which it utilized to purchase shares in sufficient quantity to fulfill the envisaged awards. The Company will issue ordinary shares to a custodian for conversion by a depositary bank to ADS’s and delivery to the EBT. These ordinary shares will be deducted from the shareholders’ funds on the consolidated balance sheet at their nominal value.

Shares held by the EBT are included in the consolidated balance sheet as a reduction in equity.

r) Pension contribution costs

Payments to defined contribution retirement benefit plans are recognized as an expense when employees have rendered service entitling them to the contributions.

3. Significant judgments, estimates and assumptions

The preparation of these consolidated financial statements requires the management of the Company to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses. The Company bases its estimates and judgments on historical experience and on various other assumptions that it considers to be reasonable. Actual results may differ from these estimates under different assumptions or conditions.

Judgments

a) Revenue

Judgment is required to determine the appropriate accounting for the license and collaboration agreement with Ultragenyx Pharmaceutical, Inc. (“Ultragenyx”). Management has determined that the upfront proceeds from the license and collaboration agreement represent proceeds from the Company’s ordinary business activities and, therefore, represent revenue within the scope of IFRS 15, Revenue from Contracts with Customers. Judgment is also required to determine the portion of the carrying amount of the intangible asset to derecognize, relative to the value retained, as a result of the license and collaboration agreement with Ultragenyx.

b) Impairment of intangible assets and property, plant and equipment

An assessment was made in respect of indicators of impairment in the carrying value of the Company’s intangible assets (see Note 14), right-of-use assets, leasehold improvements, office equipment and IT equipment as at December 31, 2022.

If such an indication exists, the recoverable amount of the asset, being the higher of the asset’s fair value less costs to sell and value in use, is compared to the asset’s carrying value. Any excess of the asset’s carrying value over its recoverable amount is recognized as an impairment in the consolidated statement of comprehensive (loss)/income. The assessment of intangible assets involves a number of significant judgments regarding the likelihood of successful product approval, the costs of attaining approval, the estimated useful life of intangible assets following commercialization and the subsequent commercial profitability of the product once approved.

c) Incremental borrowing rate and lease modification

Future lease payments are discounted using the interest rate implicit in the lease, or, if that rate cannot be readily determined, the incremental borrowing rate. IFRS 16 (Leases) defines the incremental borrowing rate as the rate of interest a lessee would have to pay to borrow over a similar term, and with a similar security, the funds necessary to obtain an asset of similar value to the right-of-use assets in a similar economic environment.

The incremental borrowing rate for the current lease portfolio was determined based on relevant and available information as the interest rate implicit in the lease arrangements cannot be readily determined.

In addition to the determination of an appropriate discount rate, the Company was also required to assess the lease term for qualifying leases. The determination of the lease term is judgmental as for certain qualifying leases held by the Company, the contract includes an extension option beyond the non-cancellable period for which the Company has the right to use the underlying asset. In applying this judgment, the Company considered the period over which it was reasonably certain to make use of the extension option.

In August 2020, a lease for office space was modified to reduce the size of the office space leased. At the time of this lease modification, judgment was applied in determining the new lease term and remeasuring the lease liability by discounting the revised lease payments using a revised incremental borrowing rate. The lease expired in August 2022.

d) Identification and classification of financial instruments

On June 3, 2020, the Company completed a private placement transaction (Note 19) which comprised the issue of ordinary shares, Loan Notes and Warrants. Judgment is applied under IAS 32 (Financial instruments: Presentation) in determining the features of the identified financial instruments on both the transaction date and the date of the general meeting at which Resolutions relating to the private placement were voted on by the Shareholders, to determine the appropriate recognition in accordance with IAS 32. In applying this judgment, management considered the probability of passing the Resolutions at the general meeting and the likelihood of a change of control prior to the passing of the Resolutions, which impact the settlement terms of the financial instruments, and the classification of the financial instruments as liabilities or equity. Management concluded that a change of control event was uncertain and outside of the Company's control, and therefore the conversion feature on the Loan Notes at the transaction date represented a financial liability with an embedded derivative for the conversion option. On the passing of the Resolutions, judgment was applied to determine that the effective terms of the Loans Notes changed and the embedded derivative financial liability representing the conversion option was reclassified to equity at its fair value, with no associated gain or loss recognized in profit or loss.

Estimates and assumptions

a) Deferred consideration

Deferred consideration represents contingent cash consideration and is recognized as a provision at each balance sheet date, to the extent its amount is quantifiable at the inception of the arrangement (see Note 18). The amount provided is based on estimates regarding the timing and progress of the related research and development activities (see Note 24).

Deferred consideration in the form of shares is recognized as a share-based payment when it is probable that shares will be transferred.

b) Fair value of financial instruments

As part of the private placement transaction (see Note 19), the Company performed a valuation of the fair value of the identified financial instruments including the embedded derivative and the warrants on the transaction date and the general meeting date. For qualifying financial instruments, the fair value is reassessed at each balance sheet date. Specific consideration was applied to the estimation of implied share price on the transaction date, the volatility, credit spread and discount rate (see Note 24).

c) Contingent consideration

The Company makes a provision for the estimated fair value of amounts payable to the former shareholders of Mereo BioPharma 5, Inc. under the Contingent Value Rights Agreement ("CVR"), which is accounted for as a contingent consideration liability.

At December 31, 2022, the Company estimates the fair value of the contingent consideration liability to be £nil (2021: nil). Total potential payments under the CVR on a gross, undiscounted basis, are approximately £58.6 million ($80.0 million).

The estimated contingent consideration payable is based on a risk-adjusted, probability-based scenario. Under this approach the likelihood of future payments being made to the former shareholders of Mereo BioPharma 5, Inc. under the CVR is considered. The estimate could materially change over time in line with the development plan and potential subsequent commercialization of the product.

4. Changes in accounting policies

a) New standards, interpretations and amendments adopted from January 1, 2022

In the current year, the Company has applied the below amendments to IFRS issued by the IASB that are effective for an annual period that begins on or after January 1, 2022. Their adoption has not had any material impact on the disclosures or on the amounts reported in these consolidated financial statements:

- Annual Improvements to IFRS Standards 2018-2020 (Amendments to IFRS 1, IFRS 9, IFRS 16 and IAS 41)
- Amendments to IAS 16 – Proceeds before Intended Use
- Amendments to IAS 37 – Onerous Contracts – Cost of Fulfilling a Contract
- Amendments to IFRS 3

b) New standards, interpretations and amendments not yet effective

At the date of authorization of these consolidated financial statements, the Company has not applied the following new and revised IFRS that have been issued but are not yet effective:

Effective January 1, 2023

- Amendments to IFRS 17 – Insurance Contracts
- Amendments to IAS 12 – Deferred tax related to assets and liabilities arising from a single transaction
- Amendments to IAS 8 – Definition of accounting estimates
- Amendments to IAS 1 and IFRS Practice Statement 2 – Disclosure of accounting policies

Effective January 1, 2024

- Amendments to IAS 1 – Classification of liabilities as current or non-current
- Amendments to IAS 1 – Non-current liabilities with covenants
- Amendments to IFRS 16 – Lease liability in a sale and leaseback

The Company does not expect the adoption of these IFRS amendments will have a material impact on the Company in the current or future reporting periods and on foreseeable future transactions.

MEREO BIOPHARMA GROUP PLC
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

5. Group information

Information about subsidiaries

The consolidated financial statements of the Company include:

Name	Principal activities	Country of incorporation	% Equity interest December 31, 2022	% Equity interest December 31, 2021
Mereo BioPharma 1 Limited	Pharmaceutical R&D	UK	100	100
Mereo BioPharma 2 Limited	Pharmaceutical R&D	UK	100	100
Mereo BioPharma 3 Limited	Pharmaceutical R&D	UK	100	100
Mereo BioPharma 4 Limited	Pharmaceutical R&D	UK	100	100
Mereo BioPharma Ireland Limited	Pharmaceutical R&D	Ireland	100	100
Mereo BioPharma 5, Inc.	Pharmaceutical R&D	US	100	100
Navi Subsidiary, Inc.	Pharmaceutical R&D	US	100	100
Mereo US Holdings, Inc.	Holding Company	US	100	100
Mereo BioPharma Group plc Employee Benefit Trust	Employee share scheme	Jersey	—	—

The registered office of Mereo BioPharma 1 Limited, Mereo BioPharma 2 Limited, Mereo BioPharma 3 Limited and Mereo BioPharma 4 Limited is located at Fourth Floor, 1 Cavendish Place, London W1G 0QF. The registered office of Mereo BioPharma Ireland Limited is Rocktwist House, Block 1, Western Business Park, Shannon, County Clare, V14 FW97, Republic of Ireland.

Mereo US Holdings Inc. was incorporated on December 3, 2018 for the sole purpose of effecting the business combination with Mereo BioPharma 5, Inc. (formerly OncoMed Pharmaceuticals, Inc.) on April 23, 2019. The registered office of Mereo US Holdings Inc., Mereo BioPharma 5, Inc. and its wholly owned subsidiary, Navi Subsidiary, Inc., is 251 Little Falls Drive, City of Wilmington, County of New Castle, Delaware 19808, US.

6. Revenue

The Company recognized upfront proceeds of £36.5 million ($50.0 million) from the license and collaboration agreement with Ultragenyx for setrusumab as revenue in the year ended December 31, 2021. The variable consideration relating to future milestones and sales royalties will be recognized in the consolidated statement of comprehensive (loss)/income when the milestones are achieved or the underlying commercial sales are made, in the event regulatory approval is achieved.

As a consequence of the license and collaboration agreement with Ultragenyx and in accordance with terms of the 2015 asset purchase with Novartis, the Company made a payment to Novartis of £7.2 million ($10.0 million). The payment included a deduction for costs of £2.4 million which was deferred and will be recognized in the consolidated statement of comprehensive (loss)/income when the associated costs are incurred. In the year ended December 31, 2022, £0.9 million (2021: £1.1 million) of these deductions were recognized within “Cost of revenue” in the consolidated statement of comprehensive (loss)/income. As of December 31, 2022, the remaining balance to be recognized of £0.3 million (2021: £1.3 million) is included within “Other liabilities” in the consolidated balance sheet. See Note 13 for additional details.

7. (Loss)/profit before tax

(Loss)/Profit before tax is stated after charging:

	Year ended December 31,		
	2022 £'000s	2021 £'000s	2020 £'000s
Fees payable to the Company's Auditor for the audit of the consolidated accounts	371	358	449
Fees payable to the Company's Auditor for other services:			
Audit of subsidiary accounts	49	46	49
Audit related assurance services	59	57	318
Gain on modification of lease	–	–	(957)
Income from sub-lease	–	–	(646)
Depreciation of right-of-use assets	583	570	1,531
Depreciation (excluding right-of-use assets)	144	72	68

Gain on modification of lease, sub-lease income and transaction costs associated with lease modification are included within administrative expenses within the consolidated statement of comprehensive income/(loss).

8. Employees

Total compensation costs for persons employed by the Company (including Directors) during the year was:

	Year ended December 31,		
	2022 £'000s	2021 £'000s	2020 £'000s
Included in research and development expenses:			
Salaries	4,590	4,126	3,046
Social security costs	456	402	397
Pension contributions	78	73	66
Share-based payment expenses	1,083	1,210	446
Included in administrative expenses:			
Salaries	4,478	3,763	4,832
Social security costs	606	418	681
Pension contributions	124	99	89
Share-based payment expenses	2,779	2,092	1,112
Total	**14,194**	**12,183**	**10,669**

Total compensation costs for Directors during the year was:

	Year ended December 31,		
	2022 £'000s	2021 £'000s	2020 £'000s
Salaries and fees	534	810	1,114
Benefits in kind	9	9	14
Pension contributions	42	58	61
Bonus	226	239	538
Total	**811**	**1,116**	**1,727**

During 2022, one Director was a member of a defined contribution pension scheme (2021: one; 2020: one). Further details concerning the remuneration of key management personnel is included in Note 27.

9. Other income/expenses and adjustments

Finance income

	Year ended December 31,		
	2022 £'000s	2021 £'000s	2020 £'000s
Bank interest earned	696	1	5
Gain on short-term investments	—	—	39
Total	**696**	**1**	**44**

Finance costs

	Year ended December 31,		
	2022 £'000s	2021 £'000s	2020 £'000s
Interest on convertible loan notes	(2,660)	(3,549)	(2,241)
Interest on bank loan	—	—	(2,900)
Interest on lease liabilities	(209)	(227)	(1,085)
Discounting of provision on deferred cash consideration	(451)	(225)	(157)
Other	(41)	(21)	—
Total	**(3,361)**	**(4,022)**	**(6,383)**

Changes in the fair value of financial instruments

	Year ended December 31,		
	2022 £'000s	2021 £'000s	2020 £'000s
Changes in the fair value of warrants – private placement	7,593	39,535	(45,977)
Changes in the fair value of warrants – bank loan	212	504	(714)
Changes in the fair value of embedded derivative	—	—	(63,158)
Total	**7,805**	**40,039**	**(109,849)**

Other income and expenses

In February 2022, the Company received a milestone payment of $2.0 million (£1.5 million) under the Navi License Agreement with OncXerna. An associated payment was made to the former shareholders of Mereo BioPharma 5, Inc. under the Contingent Value Rights Agreement ("CVR") of a total of $0.9 million (£0.7 million), after deductions of costs, charges and expenditures, which resulted in other income, net of £0.8 million.

MEREO BIOPHARMA GROUP PLC
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

10. Taxation

	Year ended December 31,		
	2022 £'000s	2021 £'000s	2020 £'000s
UK corporation tax R&D credit	1,296	—	2,822
Tax credit/(charge)	601	(1,516)	—
Total	**1,897**	**(1,516)**	**2,822**

U.K. income tax

The Company is entitled to claim tax credits in the United Kingdom under the U.K. R&D small or medium-sized enterprise ("SME") scheme, which provides additional taxation relief for qualifying expenditure on R&D activities, and includes an option to surrender a portion of tax losses arising from qualifying activities in return for a cash payment from HM Revenue & Customs ("HMRC").

U.S. income tax

During the year-ended December 31, 2022, the Company received £0.8 million related to Alternative Minimum Tax ("AMT") credits, previously recognized as other taxes recoverable within the consolidated balance sheet. The Company generates R&D tax credits for U.S. federal and state purposes. In respect of these R&D tax credits, no deferred tax assets have been recognized in any periods presented. As of December 31, 2022, the Company had an uncertain tax position of £3.1 million, representing approximately 20% of these historic R&D tax losses claimed.

Reconciliation of effective tax rate

	Year ended December 31,		
	2022 £'000s	2021 £'000s	2020 £'000s
(Loss)/profit on ordinary activities before income tax	(36,093)	14,241	(166,450)
Tax on profit at standard U.K rate of 19%	6,857	(2,706)	31,626
Expenses not deductible for income tax purposes (permanent differences)	(965)	(708)	(13,270)
Income not taxable	12	78	4
Temporary timing differences	—	(65)	—
R&D relief uplift	558	1,435	1,214
Losses (unrecognized)	(4,810)	(345)	(14,479)
Foreign tax	422	505	184
Differences in overseas tax rates	323	286	261
Derecognition of deferred tax	—	—	(2,686)
Effects of carryback loss relief	(649)	—	—
Adjustments in respect of prior years	612	—	—
Other	(463)	4	(32)
Tax credit/(charge) for the year	**1,897**	**(1,516)**	**2,822**

Deferred tax

The analysis of unrecognized deferred tax is set out below:

	Year ended December 31,		
	2022 £'000s	**2021 £'000s**	**2020 £'000s**
Losses	47,209	44,683	37,021
Loan relationships	443	73	421
U.S tax credits	12,206	10,557	9,880
R&D capitalization	3,001	—	—
Fixed assets	—	—	414
Share options	434	151	55
Other U.S deferred tax	—	31	86
Other	—	—	137
Temporary differences	51	56	18
Net deferred tax asset (unrecognized)	**63,344**	**55,551**	**48,032**

The analysis of recognized deferred tax is set out below:

	At January 1, 2022	**Recognized in income**	**At December 31, 2022**
Deferred tax liabilities			
Intangible asset and right-of-use asset	(20)	(156)	(176)
Deferred tax asset			
Net operating losses and lease liability	20	156	176
Net deferred tax asset/(liability)	**—**	**—**	**—**

A deferred tax asset on losses has been recognized up to the level of the deferred tax liability, resulting in a net deferred tax liability of £nil.

The remaining deferred tax assets, as set out in the table above, have not been recognized as there is uncertainty regarding when suitable future profits against which to offset the accumulated tax losses will arise.

U.K. deferred tax

The deferred tax assets have not been recognized as there is uncertainty regarding when suitable future profits against which to offset the accumulated tax losses will arise. There is no expiration date for the accumulated tax losses.

The standard rate of corporation tax applied to the reported profit/(loss) before tax is 19% (2021: 19%). The Finance Act 2021, which was substantively enacted on May 24, 2021, included provisions to increase the standard rate of U.K. corporation tax from 19% to 25%, effective from April 1, 2023. As a result, U.K. deferred tax assets and liabilities have been measured at a rate of 25%.

At December 31, 2022, the Company had U.K. tax losses to be carried forward of approximately £125.8 million.

U.S. deferred tax

U.S. deferred tax assets and liabilities are calculated at a blended rate of approximately 21%.

For Mereo BioPharma 5, Inc, with respect to accumulated tax losses carried forward prior to its acquisition by the Company, there is a change of control restriction which will limit the amount available in any one year.

At December 31, 2022, the Company had U.S. federal tax losses to be carried forward of approximately £74.6 million, of which £67.7 million can be carried forward indefinitely and £6.9 million which will begin to expire in 2023. At December 31, 2022, the Company had U.S. state tax losses to be carried forward of approximately £4.0 million which begin to expire in 2027.

MEREO BIOPHARMA GROUP PLC
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

11. Earnings per share

Basic profit/(loss) per share is calculated by dividing the profit/(loss) attributable for the year to ordinary equity holders of the parent by the weighted average number of ordinary shares outstanding during the year. Diluted loss per share is based on dividing the loss attributable for the year, adjusted for the effect of diluted ordinary shares, by ordinary share equivalents, which includes the weighted average number of ordinary shares outstanding and the effect of dilutive ordinary share equivalents.

	Year ended December 31,		
	2022	**2021**	**2020**
Numerator – Basic earnings per share (£'000s):			
(Loss)/profit attributable to equity holders of the parent	(34,196)	12,725	(163,628)
Denominator – Basic earnings per share:			
Weighted average number of ordinary shares	603,196,403	527,818,648	338,953,141
(Loss)/profit per share – basic (£)	(0.06)	0.02	(0.48)
Numerator – Diluted earnings per share (£'000s):			
(Loss)/profit attributable to equity holders of the parent	(34,196)	12,725	(163,628)
Effect of dilutive ordinary shares	—	(38,523)	—
Numerator – Diluted earnings per share	(34,196)	(25,798)	(163,628)
Denominator – Diluted earnings per share:			
Number of ordinary shares used for basic earnings per share	603,196,403	527,818,648	338,953,141
Weighted average effect of dilutive ordinary shares	—	27,457,163	—
Weighted average number of diluted ordinary shares outstanding	603,196,403	555,275,811	338,953,141
Loss per share – diluted (£)	(0.06)	(0.05)	(0.48)

For the years ended December 31, 2022 and 2020, share options, convertible loan notes and warrants were anti-dilutive as they would have decreased the loss per share and were excluded from the calculation of diluted loss per share. Therefore, the weighted average shares outstanding used to calculate both the basic and diluted loss per share was the same. For the year ended December 31, 2021, the effect of dilutive ordinary shares, net of the current year tax charge, is related to Company's outstanding warrants. Share options and convertible loan notes were anti-dilutive for the same year.

12. Property, plant and equipment

	Right-of-use asset (buildings)	**Right-of-use asset (equipment)**	**Leasehold improvements**	**Office equipment**	**IT equipment**	**Total**
Cost of valuation						
At January 1, 2022	**2,903**	**295**	**557**	**173**	**180**	**4,108**
Additions	—	—	—	7	3	10
Disposals	(451)	(300)	—	(16)	(10)	(777)
Currency translation effects	13	5	—	—	—	18
At December 31, 2022	**2,465**	**—**	**557**	**164**	**173**	**3,359**
Depreciation						
At January 1, 2022	**(1,025)**	**(231)**	**(124)**	**(69)**	**(129)**	**(1,578)**
Disposals	451	300	—	16	10	777
Depreciation for the year	(514)	(69)	(95)	(23)	(26)	(727)
At December 31, 2022	**(1,088)**	**—**	**(219)**	**(76)**	**(145)**	**(1,528)**
Net book value						
At January 1, 2022	1,878	64	433	104	51	2,530
At December 31, 2022	**1,377**	**—**	**338**	**88**	**28**	**1,831**

MEREO BIOPHARMA GROUP PLC
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

	Right-of-use asset (buildings)	Right-of-use asset (equipment)	Leasehold improvements	Office equipment	IT equipment	Total
Cost of valuation						
At January 1, 2021	**1,848**	**1,169**	**164**	**71**	**132**	**3,384**
Additions	923	—	393	109	48	1,473
Lease modification	133	30	—	—	—	163
Disposals	—	(868)	—	(7)	—	(875)
Currency translation effects	(1)	(36)	—	—	—	(37)
At December 31, 2021	**2,903**	**295**	**557**	**173**	**180**	**4,108**

Depreciation						
At January 1, 2021	**(531)**	**(1,023)**	**(85)**	**(65)**	**(107)**	**(1,811)**
Disposals	—	868	—	7	—	874
Depreciation for the year	(494)	(76)	(39)	(11)	(22)	(642)
At December 31, 2021	**(1,025)**	**(231)**	**(124)**	**(69)**	**(129)**	**(1,578)**
Net book value						
At January 1, 2021	1,318	146	79	6	25	1,573
At December 31, 2021	**1,878**	**64**	**433**	**104**	**51**	**2,530**

In August 2022, the Company's lease for office space in Redwood City, California expired, and certain equipment was disposed. In June 2021, the Company entered into a new lease agreement for additional office space in London, UK. The Company also extended the lease term of the existing office space, which resulted in the modification of the right-of-use asset.

The Company leases office space and equipment for use in administrative and research and development activities. In the year-ended December 31, 2022, the Company made lease payments of £0.9 million (2021: £0.7 million). The maturity of lease liabilities as of December 31, 2022 are as follows:

	Within 1 year	**Between 1 and 3 years**	**Between 3 and 5 years**	**Over 5 years**	**Total**
	£'000s	**£'000s**	**£'000s**	**£'000s**	**£'000s**
Maturity of lease liabilities	466	1,072	150	—	**1,688**

Further details on the movements within lease liability are included in Note 23.

13. Intangible assets

	Acquired development programs
	£'000s
Cost	
At January 1, 2021	**33,005**
At December 31, 2021	**33,005**
At December 31, 2022	**33,005**
Revisions to estimated value	
At January 1, 2021	**(1,357)**
Revision to estimated value	2,373
Out-license of intangible asset	(9,457)
At December 31, 2021	**(8,441)**
Revision to estimated value	(448)
At December 31, 2022	**(8,889)**
Net book value	
At December 31, 2021	24,564
At December 31, 2022	**24,116**

The Company's strategy is to acquire and develop clinical-stage development programs for the treatment of rare diseases.

On January 25, 2021, the Company's license and collaboration agreement with Ultragenyx for the development and commercialization of setrusumab for OI became effective. Under the terms of the agreement, the Company received an upfront payment of £36.5 million ($50 million). Additionally, the Company will be eligible to receive up to $254 million in future milestones and royalties. The license and collaboration agreement grants Ultragenyx an exclusive license to develop and commercialize setrusumab in the US and rest of the world, excluding Europe where the Company retains commercial rights. As a result, intangible assets with a carrying value of £9.5 million were derecognized and recorded within "Cost of revenue" in the Company's consolidated statement of comprehensive income/(loss). Refer to Note 3 for additional information.

In October 2017, the Company acquired the exclusive license for alvelestat and included the option to acquire certain assets from AstraZeneca AB ("AstraZeneca"). On that date the fair value of alvelestat was measured at £7.2 million, which consisted of upfront cash and equity payments as well as deferred cash and equity consideration. The provision for deferred cash consideration is re-measured to fair value at each balance sheet date and recognized as an increase to, or reduction of, the intangible asset. During the year, the provision for deferred cash consideration has decreased by £0.4 million (2021: increase of £2.4 million) due to changes in estimated timelines and the probability of contractual milestones being achieved. Refer to Note 18 and Note 24 for additional information.

During the year the Company did not revise the value of any other intangible assets. As the intangible assets remain under development, no amortization charge has been recognized (2021: £nil).

14. Impairment testing of acquired development programs not yet available for use

Acquired development programs not yet available for use are assessed annually for impairment. The carrying amount of acquired development programs is as follows:

	December 31,	
	2022	**2021**
	£'000s	**£'000s**
BPS-804/UX143 (setrusumab)	2,159	2,159
MPH-966 (alvelestat)	7,760	8,208
BGS-649 (leflutrozole)	9,886	9,886
BCT-197 (acumapimod)	4,311	4,311
Total	**24,116**	**24,564**

The Company considers the future development costs, the probability of successfully progressing each program to product approval and the likely commercial returns after product approval, among other factors, when reviewing for indicators of impairment. The results of this testing did not indicate any impairment of the acquired products' rights for the year ended December 31, 2022. Management believes that the likelihood of a materially different outcome using different assumptions is remote.

MEREO BIOPHARMA GROUP PLC
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

The acquired development programs are assets which are not used in commercialized products. These assets have not yet begun to be amortized but have been tested for impairment by assessing their value in use. Value in use calculations for each program are utilized to calculate the recoverable amount. The calculations use pre-tax cash flow projections covering the period through product development to commercial sales up to the later of loss of patent protection or market exclusivity, which extend beyond five years from the balance sheet date. Approved products are assumed to be out-licensed such that the Company receives upfront payments, milestone receipts and royalties on commercial sales; therefore, the Company does not incur any costs of commercialization after out-licensing except when such terms are agreed.

Key assumptions for the value in use calculations are described as follows:

- Development costs to obtain regulatory approval – costs are estimated net of any contributions expected from collaborative arrangements with future partners. Management have developed cost estimates based on their previous experience and in conjunction with the expertise of their clinical development partners;
- Launch dates of products – these reflect management's expected date of launch for products based on the timeline of development programs required to obtain regulatory approval. The assumptions are based on management's and clinical development partners' prior experience;
- Probability of successful development – management estimates probabilities of success for each phase of development based on industry averages and knowledge of specific programs;
- Out-licensing signature fees, milestones and royalty rates on sales – management estimates these amounts based on prior experience and access to values from similar transactions in the industry, which are collated and accessible from specialist third-party sources;
- Sales projections – these are based on management's internal projections using external market data and market research commissioned by the Company;
- Profit margins and other operational expenses – these are based on the Company's internal projections of current product manufacturing costings, with input from manufacturing partners where applicable, and estimates of operating costs based on management's prior industry experience;
- Cash flow projections – for all assets, cash flows are assessed over an industry-standard asset life of 20 years; and

- Discount rates – the discount rate is estimated on a pre-tax basis reflecting the estimated cost of capital of the Company and is applied consistently across each of the acquired development programs. The cost of capital was determined to be 15.0% (2021: 12.0%).

Where an out-licensing agreement has been reached with a third party, known and observable inputs replace management assumptions if available.

At this stage of product development, the key sensitivity for all development programs is the probability of successful completion of clinical trials in order to obtain regulatory approval necessary for commercial sales. Therefore, full impairment of a development program is expected should such clinical trials be unsuccessful.

15. Other receivables

	December 31,	
	2022	**2021**
	£'000s	**£'000s**
Lease deposits	293	408
VAT recoverable	362	387
Other	107	624
Total	**762**	**1,419**

16. Cash and short-term deposits

	December 31,	
	2022	**2021**
	£'000s	**£'000s**
Cash	5,230	93,727
Short-term deposits	51,104	569
Total	**56,334**	**94,296**

Short-term deposits are available immediately or within 90 days and earn interest at the respective short-term deposit rates.

17. Trade and other payables

	December 31,	
	2022	**2021**
	£'000s	**£'000s**
Trade payables	2,886	2,285
Social security and other taxes	167	190
Other payables	25	24
Total	**3,078**	**2,499**

Trade and other payables are non-interest bearing and have an average term of one month.

18. Provisions

	December 31,	
	2022	2021
	£'000s	£'000s
Social security contribution on vested share options	9	—
Provision for deferred cash consideration	4,634	4,123
Restructuring	179	—
Total	**4,822**	**4,123**
Current	4,822	2,803
Non-current	—	1,320

	Social security contribution on vested share options	Deferred cash consideration	Restructuring
At January 1, 2021	**109**	**1,525**	**—**
Arising/(released) during the year, net	(109)	—	—
Increase in provision due to the unwinding of the time value of money	—	225	—
Increase in provision due to a change in estimates relating to timelines and probabilities of contractual milestones being achieved (revision to intangible asset, see Note 13)	—	2,373	—
At December 31, 2021	**—**	**4,123**	**—**
Arising/(released) during the year, net	9	—	179
Increase in provision due to the unwinding of the time value of money	—	451	—
Increase in provision due to changes in foreign exchange rates	—	508	—
Decrease in provision due to a change in estimates relating to timeline and probabilities of contractual milestones being achieved (revision to intangible asset, see Note 13)	—	(448)	—
At December 31, 2022	**9**	**4,634**	**179**

The provision for social security contributions on share options is calculated based on the number of vested options outstanding at the reporting date that are expected to be exercised. The provision is based on the estimated taxable gain arising on exercise of the share options, using the best estimate of the market price at the balance sheet date.

The deferred cash consideration is the estimate of the quantifiable but not certain future cash payment obligations due to AstraZeneca for the acquisition of certain assets (see Note 13). This

provision is calculated as the risk-adjusted net present value of future cash payments to be made by the Company. The payments are dependent on reaching certain milestones based on the commencement and outcome of clinical trials. The likelihood of achieving such milestones is reviewed at the balance sheet date and increased or decreased as appropriate.

In October 2022, the Company announced an updated operating plan, including a targeted reduction in the employee base of up to 40% and a significant reduction in other costs. In connection with the implementation of the operating plan, restructuring costs primarily relating to employee severance and other termination benefits of £0.2 million were paid during the year and as of December 31, 2022, the remaining provision is £0.2 million.

19. Private placement

On June 3, 2020, the Company completed a £56 million private placement transaction which comprised of the issuance of 89,144,630 ordinary shares of £0.003 each at a price of £0.174 per share for total proceeds of £15.5 million, and the issue of Tranche 1 convertible loan notes (the "Loan Notes") for total proceeds of £40.5 million. The investors also received conditional warrants to subscribe for an additional 161,048,366 ordinary shares (the "Warrants").

The terms of the Loan Notes and Warrants, and, in particular, their ability to be converted into ordinary shares was conditional on the passing of certain resolutions (the "Resolutions") at a subsequent general meeting of shareholders held on June 30, 2020. At that date, the Resolutions were passed, and the Loan Notes became convertible into ordinary shares.

Loan Notes

The Loan Notes bear interest at a rate of 6% per annum and have an initial maturity date of June 30, 2023. The Loan Notes are convertible into ordinary shares at the discretion of the holder and, if not converted by the initial maturity date, may be extended for an additional seven years, but will cease to bear interest from any extension date. The Loan Notes were initially recognized at their fair value of £38.6 million (debt host instrument in the amount of £26.7 million and the embedded derivative in the amount of £11.9 million, before transaction costs).

Loan Notes in an aggregate principal amount of £40.5 million were issued on June 3, 2020 and became convertible upon the passing of the Resolutions. As a result, on June 30, 2020, Loan Notes in an aggregate principal amount of £21.8 million, together with accrued interest, were automatically converted into 125,061,475 ordinary shares, and Loan Notes in an aggregate principal amount of £18.9 million remained outstanding as of December 31, 2020. See Note 21.

During the year ended December 31, 2022, the Company issued and allotted 40,020,280 ordinary shares (2021: 40,397,976 ordinary shares) at a price of £0.174 per share on conversion of Loan Notes. As of December 31, 2022, Loan Notes in an aggregate principal amount of £6.2 million (2021: £12.4 million) remain outstanding.

Warrants

Participants in the private placement transaction received conditional warrants to subscribe for further ordinary shares in an aggregate number equal to 50 percent of both the ordinary shares purchased and the ordinary shares issuable upon conversion of the Loan Notes. A total of 161,048,366 Warrants were issued. The fair value of the warrants at inception was £4.1 million.

The Warrants have an exercise price of £0.348 per share and are exercisable at any time until their expiry on June 30, 2023. The Warrants can be exercised for cash or on a cashless basis at the discretion of the warrant holder. Certain Warrants outstanding at the expiry date may be converted into Tranche 2 Notes, with an expiry date of up to seven years from conversion, and do not bear interest. See Note 20.

The Loan Notes and the Warrants were recognized as separate financial instruments. Transaction costs directly attributable to the private placement transaction were apportioned across the ordinary shares, Loan Notes and Warrants.

20. Warrant liability

	December 31,	
	2022	2021
	£'000s	£'000s
At January 1	**8,336**	**50,775**
Issued during the year	—	—
Settled during the year	—	(2,400)
Fair value changes during the year	(7,805)	(40,039)
At December 31	**531**	**8,336**

The change in fair value of the warrant liability represents an unrealized gain in the years ended December 31, 2022 and 2021.

Warrants – private placement

As a part of the private placement transaction on June 3, 2020, the participating investors received conditional warrants entitling them to subscribe for an aggregate of 161,048,366 ordinary shares in the Company. The warrants were conditional on certain Resolutions being passed at the Company's general meeting on June 30, 2020. On the passing of the Resolutions, the warrants entitled the investors to subscribe for ordinary shares at an exercise price of £0.348 per warrant and are exercisable until June 30, 2023. The warrants are classified as liabilities as the Company does not have an unconditional right to avoid redeeming the instruments for cash. The fair value of the warrant liability was £0.4 million as of December 31, 2022 (£8.0 million as of December 31, 2021). The change in the fair value of £7.6 million was recognized as a gain in the consolidated statement of comprehensive (loss)/income. During the year-ended December 31, 2022, no warrants were exercised (2021: 15,414,626). Refer to Note 22 for details of the warrant exercises.

Warrants – bank loan

As of December 31, 2022 and 2021, the former lenders of the Company have warrants outstanding to purchase a total of 1,243,908 ordinary shares at an exercise price of £2.95 per share exercisable until August 2027 and a total of 1,243,908 ordinary shares at an exercise price of $0.4144 per share exercisable until October 2028.

At December 31, 2022, the fair value of these warrants were £0.1 million (2021: £0.3 million). There were no warrants exercised during the year ended December 31, 2022 (2021: nil).

Total outstanding warrants

At December 31, 2022, a total of 147,431,351 warrants are outstanding (2021: 147,431,351). The warrants outstanding are equivalent to 24% of the issued ordinary share capital of the Company (2021: 25%).

The following table lists the weighted average inputs to the models used for the fair value of warrants:

	December 31,	
	2022	2021
Expected volatility (%)	95	75
Risk-free interest rate (%)	3.99	0.9
Expected life of warrants (years)	0.5	1.5
Market price of ADS ($)	0.75	1.60
Model used	Black-Scholes	Black-Scholes

MEREO BIOPHARMA GROUP PLC
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

21. Convertible loan notes

	December 31,	
	2022	2021
	£'000s	£'000s
Novartis Loan Note	4,449	3,771
Loan Notes – private placement	6,636	10,613
Total	**11,085**	**14,384**
Current	11,085	—
Non-current	—	14,384

Novartis Loan Note

On February 10, 2020, the Company entered into a convertible equity financing with Novartis Pharma (AG) ("Novartis") under which Novartis purchased a £3.8 million convertible loan note (the "Novartis Loan Note").

The Novartis Loan Note is convertible at the discretion of the holder, at a fixed price of £0.265 per ordinary share and bears an interest rate of 6% per annum with a maturity date of February 10, 2023. In connection with the Novartis Loan Note, the Company issued 1,449,614 warrants which are exercisable until February 2025 at an exercise price of £0.265. Refer to Note 28 for additional information.

Loan Notes – private placement

The initial issuance of Loan Notes in an aggregate principal amount of £40.5 million were issued on June 3, 2020 and formed part of the private placement transaction (see Note 19) were classified as a financial liability on initial recognition. Non-closely related embedded derivatives relating to the conversion feature, term-extension and change of control features were bifurcated and accounted for at FVTPL, with the debt host contract being measured at amortized cost.

The fair value of the embedded derivative liability was £11.9 million on initial recognition and the fair value of the liability component was £24.4 million (net of transaction costs). In 2020, between initial recognition and the passing of the Resolutions (see Note 19), changes in the fair value of the embedded derivative totaling £63.2 million were recognized as an expense in the consolidated statement of comprehensive (loss)/income.

The Loan Notes were not convertible until certain Resolutions were passed at the Company's general meeting on June 30, 2020, following which Loan Notes in an aggregate principal amount of £21.7 million (together with accrued interest) were automatically converted into 125,061,475 ordinary shares. Accordingly, a reduction in interest bearing loans of £13.3 million together with the derecognition of the embedded derivative relating to the conversion feature of £41.6 million was recognized; no gain or loss was recognized on conversion. The remaining portion of the embedded derivative relating to the conversion feature attributable to the Loan Notes outstanding of £33.5 million was reclassified to equity to reflect the effective change in the terms of the feature following the passing of the Resolutions.

The movements in the carrying value of the liability component of the Loan Notes is included in the table below. Refer to Note 22 for details of Loan Notes converted to equity.

	December 31,	
	2022	2021
	£'000s	£'000s
January 1	10,613	12,946
Issued	—	—
Interest charge	1,981	2,974
Converted to equity	(5,958)	(5,307)
December 31	**6,636**	**10,613**

22. Issued capital and reserves

	Ordinary shares	Ordinary share capital	Share premium
	Number	£'000s	£'000s
As at January 1, 2020	**97,959,622**	**294**	**121,684**
Issued on February 11, 2020	14,295,520	43	2,511
Issued on February 20, 2020	12,252,715	37	2,267
Issued on June 4, 2020	89,144,630	267	15,244
Issued on June 30, 2020	125,061,475	375	21,386
Issued on December 23, 2020	239,179	1	—
Transaction costs for issued share capital	—	—	(1,307)
As at December 31, 2020	**338,953,141**	**1,017**	**161,785**
Issued during the year	245,955,098	738	85,909
Transaction costs for issued share capital	—	—	(234)
As at December 31, 2021	**584,908,239**	**1,755**	**247,460**
Issued during the year	40,020,280	120	6,843
As at December 31, 2022	**624,928,519**	**1,875**	**254,303**

Since January 1, 2020, the following alterations to the Company's share capital have been made. For each share issuance, ordinary shares of £0.003 in nominal value in the capital of the Company were issued.

- On February 11, 2020, the Company issued and allotted 11,432,925 ordinary shares at a price of £0.20 per share to Aspire Capital Fund, LLC ("Aspire Capital"). Gross cash received was £2.3 million. Aspire Capital has also committed to subscribe for up to an additional $25 million of ordinary shares exchangeable for ADSs from time to time during a 30-month period at the Company's request. In consideration for this, the Company paid Aspire Capital a commission satisfied through a non-cash transaction wholly by the issue of a further 2,862,595 of the Company's ordinary shares (equivalent to 572,519 ADSs) at a price of £0.08.
- On February 20, 2020, the Company issued and allotted 12,252,715 ordinary shares at a price of £0.19 per share. Gross cash received was £2.3 million;

- On June 4, 2020, the Company issued and allotted 89,144,630 ordinary shares at a price of £0.174 per share to investors. Gross cash received was £15.5 million. The ordinary shares were in substance issued at a discount to the gross cash received. The fair value of the consideration of the ordinary shares was determined to be £13.4 million and therefore the ordinary shares were in substance issued at a discount of £2.1 million, which was recorded as a reduction to other reserves (other reserves represent amounts that relate to changes to the Company's paid up equity and which are not capital reserves) in the consolidated statement of changes in equity. The incremental directly attributable transaction costs in relation to the issue of the ordinary shares were included within share premium;
- On June 30, 2020, the Company issued and allotted 125,061,475 ordinary shares at a price of £0.174 per share to investors on conversion of the Loan Notes. The legal proceeds were £21.8 million;
- On December 23, 2020, 690,205 Warrants (equivalent to 138,041 ADSs) were exercised. This transaction was completed by way of a cashless exercise resulting in 47,835 ADSs being issued at the aggregate nominal value of the ordinary shares underlying the ADSs issued, in place of the exercise price of £0.348 per ordinary share.
- On February 12, 2021, the Company issued and allotted 198,375,000 ordinary shares of the Company with a nominal value of £0.003 at a price of £0.395 per share, equivalent to 39,675,000 ADS at a price of $2.726 per ADS, after underwriting discounts and commissions, resulting in proceeds of £78.4 million. Transaction costs incurred for the issuance of share capital was £0.2 million.
- During the year ended December 31, 2021, 14,954,491 warrants (equivalent to 2,990,898 ADSs) were exercised by way of a cashless exercise resulting in 4,621,147 ordinary shares (924,229 ADSs) being issued at the aggregate nominal value of the ordinary shares underlying the ADSs issued, in place of the exercise price of £0.348 per ordinary share. A further 460,135 warrants (equivalent to 92,027 ADSs) were exercised on a cash basis at the exercise price of £0.348, which resulted in aggregate proceeds of £0.2 million.
- On May 4, 2021, the Company issued and allotted 2,100,840 ordinary shares of £0.003 in nominal value in the capital of the Company at a price of £0.517 per share to Cancer Focus Fund, as part of a non-cash, equity-settled transaction where the Company entered into partnership with Cancer Focus Fund for a Phase 1b/2 study of etigilimab in Clear Cell Ovarian Cancer to be conducted at The University of Texas MD Anderson Cancer Center. The study will be financed by Cancer Focus Fund, in exchange for upfront consideration of $1.5 million (£1.09 million) of the Company's ordinary shares and additional payments based on the achievement of certain milestones. The Company initially recognized a prepayment of £1.09 million with reference to fair value of the ordinary shares granted, of which £0.2 million was subsequently recorded in the consolidated statement of comprehensive income/(loss) during the year ended December 31, 2021.
- During the year ended December 31, 2021, the Company issued and allotted 40,397,976 ordinary shares of £0.003 in nominal value in the capital of the Company at an exercise price of £0.174 per share on non-cash conversion of Loan Notes.
- During the year ended December 31, 2022, the Company issued and allotted 40,020,280 ordinary shares of £0.003 in nominal value in the capital of the Company at an exercise price of £0.174 per share on non-cash conversion of Loan Notes.

Other capital reserves

	Share-based payments	Equity component of convertible loan notes	Other warrants issued	Merger reserve	Other reserves	Total
At January 1, 2020	**18,285**	**—**	**44**	**40,818**	**—**	**59,147**
Share-based payments expense during the year	1,558	—	—	—	—	1,558
Novartis convertible loan note instrument and warrants	—	1,084	—	—	—	1,084
Conversion of Loan Notes	—	—	—	—	33,104	33,104
Reclassification of the embedded derivative	—	33,481	—	—	—	33,481
At December 31, 2020	**19,843**	**34,565**	**44**	**40,818**	**33,104**	**128,374**
Share-based payments expense during the year	3,302	—	—	—	—	3,302
Share options exercised	(119)	—	—	—	—	(119)
Conversion of Loan Notes	—	(1,722)	—	—	—	(1,722)
At December 31, 2021	**23,026**	**32,843**	**44**	**40,818**	**33,104**	**129,835**
Share-based payments expense during the year	3,862	—	—	—	—	3,862
Share options exercised	(82)	—	—	—	—	(82)
Issuance of warrants	—	—	70	—	—	70
Conversion of Loan Notes	—	(1,005)	—	—	—	(1,005)
At December 31, 2022	**26,806**	**31,838**	**114**	**40,818**	**33,104**	**132,680**

Share-based payments

The Company has various share option schemes under which options to subscribe for the Company's shares have been granted to certain executives, non-executive directors ("NEDs") and employees.

The share-based payment reserve is used to recognize (i) the value of equity settled share-based payments provided to employees, including key management personnel, as part of their remuneration and (ii) deferred equity consideration. Refer to Note 26 for further details.

Equity component of convertible loan instrument

The convertible loan notes issued to Novartis are a compound instrument consisting of a liability and an equity component. The value of the equity component (cost of the conversion option) as at December 31, 2022 is £1.08 million (December 31, 2021: £1.08 million).

On June 30, 2020, the Loan Notes in an aggregate principal amount of £21.8 million (together with accrued interest) were automatically converted into 125,061,475 ordinary shares. This resulted in £33.5 million recognized in other reserves in equity as a difference between the share capital and share premium recognized on conversion and the carrying value of the embedded derivative financial liability extinguished (see Note 19).

Other warrants issued

The funding arrangements with The Alpha-1 Project are a compound instrument consisting of a liability and an equity component. In 2022, the Company issued 1,101,683 warrants over ordinary shares and received funding of £0.2 million, of which less than £0.1 million was allocated to the equity component. The total value of the equity component (consideration received for the warrants) as at December 31, 2022 is £0.1 million (2021: less than £ 0.1 million).

Merger reserve

The consideration paid to acquire Mereo BioPharma 5, Inc. was 24,783,320 ordinary shares with an acquisition date fair value of £40.9 million, based on the Company's quoted share price. The nominal value of the issued capital was £0.1 million with the excess, £40.8 million, classified within other capital reserves as a 'Merger reserve'.

Other reserves

On June 30, 2020, the Company issued and allotted 125,061,475 ordinary shares of £0.003 in nominal value in the capital of the Company at a price of £0.174 per share to investors following the partial conversion of the Loan Notes. The legal proceeds were £21.8 million. This resulted in £33.1 million recognized in other reserves as a difference between the carrying value of the financial liability extinguished and the legal proceeds.

Accumulated loss

	Year ended December 31,		
	2022 £'000s	**2021 £'000s**	**2020 £'000s**
Other reserves	7,401	7,401	5,001
Accumulated losses	(331,164)	(296,968)	(309,693)

Other reserves represent a capital reduction undertaken in 2016 which created a reserve of £7.0 million. On June 3, 2020, the Company issued and allotted 89,144,630 ordinary shares to investors. The difference between the gross proceeds, £15.5 million, and the fair value of the consideration of the ordinary shares, £13.4 million, of £2.1 million, was recognized as a reduction to other reserves. During the year ended December 31, 2021, 15,414,626 private placement warrants were exercised, resulting in a £2.4 million reduction in the warrant liability which was recognized as an addition to "Other reserves."

23. Changes in liabilities arising from financing activities

	Lease liability	Novartis Loan Note	Warrant liability	Deferred cash consideration	Loan Notes – private placement	Other	Total
Carrying value at January 1, 2021	**1,794**	**3,196**	**50,775**	**1,525**	**12,946**	**62**	**70,298**
Financing cash flows	(692)	—	—	—	—	—	(692)
Non-cash changes							
Settled during the year	—	—	(2,400)	—	(5,307)	—	(7,707)
Interest expense	230	575	—	206	2,974	18	4,003
Lease addition	910	—	—	—	—	—	910
Lease modification	163	—	—	—	—	—	163
Changes in fair value	—	—	(40,039)	2,373	—	—	(37,666)
Changes in foreign exchange	(29)	—	—	19	—	—	(10)
Carrying value at December 31, 2021	**2,376**	**3,771**	**8,336**	**4,123**	**10,613**	**80**	**29,299**
Financing cash flows	(937)	—	—	—	—	153	(784)
Non-cash changes							
Settled during the year	—	—	—	—	(5,958)	—	(5,958)
Interest expense	209	678	—	451	1,981	19	3,338
Issuance of warrants	—	—	—	—	—	(70)	(70)
Changes in fair value	—	—	(7,805)	(448)	—	—	(8,253)
Changes in foreign exchange	40	—	—	508	—	—	548
Carrying value at December 31, 2022	**1,688**	**4,449**	**531**	**4,634**	**6,636**	**182**	**18,120**

24. Financial and capital risk management and fair value measurement

Capital risk management

The Company's objectives when managing capital are to safeguard the ability to continue as a going concern and ensure that sufficient capital is in place to fund the Company's R&D activities and operations. The Company's principal methods of adjusting the capital available are through issuing new shares, licensing and/or collaboration agreements or arranging suitable debt financing. The Company's share capital and share premium are disclosed in Note 22. The Company's convertible loans are disclosed in Note 21. The Company monitors the availability of capital with regards to its committed and forecasted future expenditure on an ongoing basis.

MEREO BIOPHARMA GROUP PLC
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

The Company has an Employee Benefit Trust which holds ADSs to satisfy exercises of options under the Company's share option schemes (see Note 26).

Financial risk management objectives and policies

The Company seeks to maintain a balance between equity capital and convertible debt to provide sufficient cash resources to execute the business plan. In addition, the Company maintains a balance between cash held on deposit and short-term investments in pound sterling and other currencies to reduce its exposure to foreign exchange fluctuations in respect of its planned expenditure.

Company's principal financial instruments comprise warrants, convertible loan notes and trade payables which arise directly from its operations. The Company has various financial assets, including receivables and cash and short-term deposits.

Interest rate risk

The Company's policy in relation to interest rate risk is to monitor short and medium-term interest rates and to place cash on deposit for periods that optimize the amount of interest earned while maintaining access to sufficient funds to meet the cost of is operating activities and future research and development activities.

The Company's interest payable on convertible loan notes is fixed. Consequently, there is no material exposure to interest rate risk in respect of interest payable.

Credit risk

The Company is dependent on a number of third parties for the delivery of its programs and, where required, pays upfront deposits and fees in advance of the delivery of services. The Company considers all of its material counterparties to be creditworthy and the credit risk for each of its major counterparties to be low, but continues to assess credit risk as part of its management of these third-party relationships. The Company's maximum exposure to credit risk for the components of the balance sheet at December 31, 2022 are the carrying amounts.

Liquidity risk

The Company's policy is to maintain adequate cash reserves at highly rated banks and financial institutions and also seeks to invest in short-term deposits to achieve a competitive rate of return. The Company's liquid resources are invested with regard to the timing of payments to be made in the ordinary course of business, while monitoring its funding requirements through preparation of short-term, mid-term and long-term forecasts.

The table below summarizes the maturity profile of the Company's financial liabilities based on contractual undiscounted payments at December 31, 2022:

	Within 1 year	Between 1 and 3 years	Between 3 and 5 years	Over 5 years	Total
	£'000s	£'000s	£'000s	£'000s	£'000s
Leases	611	1,222	152	—	1,985
Trade and other payables	3,078	—	—	—	3,078
Accruals	4,491	—	—	—	4,491

The Company does not face a significant liquidity risk with regards to its lease liabilities.

The Company may incur potential payments upon achievement of clinical, regulatory and commercial milestones, as applicable, or royalty payments that may be required to be made under

license agreements the Company entered into with various entities pursuant to which the Company has in-licensed certain intellectual property, including license agreements with Novartis and AstraZeneca. Due to the uncertainty of the achievement and timing of the events requiring payment under these agreements, the amounts to be paid are not fixed or determinable at this time and no such amounts are included herein.

Foreign currency and market risk

Foreign currency risk arises from R&D activities, commercial transactions and recognized assets and liabilities in foreign currencies, with the principal currency exposure being fluctuations in pound sterling, U.S. dollars and Euros.

The functional currency of the Company and all subsidiaries is pound sterling, except for Mereo BioPharma 5, Inc. whose functional currency is U.S. dollars. The Company incurs expenditures in foreign currencies and is exposed to the risks of foreign exchange rate movements, with the impact recognized in the consolidated statement of comprehensive income/(loss).

Funding secured in 2021 and 2020 was principally in U.S dollars and, although the Company currently has no revenue from product sales, proceeds received from upfront milestones under its licensing and collaboration agreements are denominated in U.S. dollars, while the majority of operating costs are denominated in pound sterling, U.S. dollars and Euros.

The Company seeks to minimize this exposure by passively maintaining foreign currency cash balances at levels appropriate to meet foreseeable foreign currency expenditures. The Company does not hedge potential future cash flows or income.

The table below shows analysis of the pound sterling equivalent of period-end cash and short-term deposits balances by currency:

	December 31,	
	2022	**2021**
	£'000s	**£'000s**
Pound sterling	52,812	92,104
U.S. dollars	2,484	2,018
Euro	1,029	165
Swiss francs	9	9
Total	**56,334**	**94,296**

The table below shows those transactional exposures that give rise to net currency gains and losses recognized in the consolidated statement of comprehensive income/(loss). Such exposures comprise the net monetary assets and monetary liabilities of the Company that are not denominated in the functional currency of the relevant subsidiary. As at December 31, these exposures were as follows:

	December 31,	
	2022	**2021**
Net foreign currency assets/(liabilities)	£ '000s	£'000s
U.S. dollars	872	920
Euro	768	(142)
Swiss francs	(179)	9
Total	**1,461**	**787**

MEREO BIOPHARMA GROUP PLC
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

The most significant currencies in which the Company transacts, other than pound sterling, are the U.S. dollar and the Euro. The Company also transacts in other currencies as necessary.

The following table illustrates the sensitivity to a 10% weakening or strengthening in the period-end rate in the U.S. dollar and the Euro against pound sterling:

December 31, 2022	**U.S. dollar £'000s**	**Euro £'000s**
Loss before tax	(79)	(70)
Equity	(79)	(70)

December 31, 2021	**U.S. dollar £'000s**	**Euro £'000s**
Profit before tax	(84)	13
Equity	(84)	13

Financial instruments by category

	Fair value through profit or loss December 31,		**Amortized cost December 31,**	
	2022	**2021**	**2022**	**2021**
Financial assets	£'000s	£ '000s	£ '000s	£ '000s
Cash and short-term deposits	—	—	56,334	94,296
Other receivables	—	—	400	1,032
Total financial assets	**—**	**—**	**56,734**	**95,328**
Financial liabilities				
Provisions	4,634	4,123	187	**—**
Convertible loan notes	**—**	**—**	11,086	14,384
Warrant liability	531	8,336	**—**	**—**
Trade and other payables	**—**	**—**	2,911	2,309
Accruals	**—**	**—**	4,491	3,826
Lease liability	**—**	**—**	1,688	2,376
Total financial liabilities	**5,165**	**12,459**	**20,363**	**22,895**

The carrying values of financial assets and financial liabilities recorded at amortized cost in the consolidated financial statements are approximately equal to their fair values.

Fair value hierarchy

Liabilities measured at fair value	**Date of valuation**	**Total £'000s**	**Quoted prices in active markets (Level 1) £'000s**	**Significant observable inputs (Level 2) £'000s**	**Significant unobservable inputs (Level 3) £'000s**
Provision for deferred consideration (Note 18)	December 31, 2022	4,634	—	—	4,634
Warrant liability (Note 20)	December 31, 2022	531	—	129	402

MEREO BIOPHARMA GROUP PLC
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

Liabilities measured at fair value	Date of valuation	Total	Quoted prices in active markets (Level 1)	Significant observable inputs (Level 2)	Significant unobservable inputs (Level 3)
		£'000s	£'000s	£'000s	£'000s
Provision for deferred consideration (Note 18)	December 31, 2021	4,123	—	—	4,123
Warrant liability (Note 20)	December 31, 2021	8,336	—	341	7,995

There were no transfers between Level 1 and Level 2 during the years ended December 31, 2022 and 2021.

The following table presents the changes in Level 3 items for the years ended December 31, 2022 and December 31, 2021.

	Provision for deferred cash consideration	Warrant liability
	£'000s	£'000s
January 1, 2021	**1,525**	**49,930**
Settled during the year	—	(2,400)
Unwinding of the time value of money (recognized as a finance cost)	225	—
Change in estimate relating to probabilities (revision to intangible asset, see Note 13)	2,373	—
Change in fair value	—	(39,535)
December 31, 2021	**4,123**	**7,995**
Unwinding of the time value of money (recognized as a finance cost)	451	—
Change in foreign exchange rates	508	—
Change in estimate relating to probabilities (revision to intangible asset, see Note 13)	(448)	—
Change in fair value	—	(7,593)
December 31, 2022	**4,634**	**402**

The following methods and assumptions were used to estimate the fair values:

- The fair value of the provision for deferred cash consideration is estimated by discounting future cash flows using rates currently available for debt on similar terms and credit risk. In addition to being sensitive to a reasonably possible change in the forecast cash flows or the discount rate, the fair value of the deferred cash consideration is also sensitive to a reasonably possible change in the probability of reaching certain milestones. The valuation requires management to use unobservable inputs in the model, of which the significant unobservable inputs are disclosed in the tables below. The Company regularly assesses a range of reasonably possible alternatives for those significant unobservable inputs and determines their impact on the total fair value.
- At December 31, 2022, the Company estimates the fair value of the contingent consideration liability to be £nil. CVR payments of £0.7 million in 2022 and £0.4 million in 2020 were made relating to the Navi milestones received from OncXerna. The estimated contingent consideration payable is based on a risk adjusted, probability-based scenario. Under this approach the likelihood of future payments being made to the former shareholders of Mereo BioPharma 5, Inc. under the CVR arrangement is considered. The estimate could materially change over time as the development plan and subsequent commercialization of the Navi product progresses.

- The warrant liability is estimated using a Black-Scholes model, taking into account appropriate amendments to inputs in respect of volatility, remaining expected life of the warrants and rates of interest at each reporting date.

The significant unobservable inputs used in the fair value measurements categorized within Level 3 of the fair value hierarchy, together with a quantitative sensitivity analysis as at December 31, 2022 and 2021 are as follows:

	Valuation technique	Significant unobservable inputs	Input range (weighted average)	Sensitivity of the input to fair value
Provision for deferred cash consideration	Discounted cash flow	WACC	2022: 15%	1% increase/decrease would result in a decrease/increase in fair value by £25,000
		WACC	2021: 12%	1% increase/decrease would result in a decrease/increase in fair value by £31,000
		Probability of success	2022: 40.6%-81.2%	10% increase/decrease would result in an increase/decrease in fair value by £0.6 million
		Probability of success	2021: 40.6% - 81.2%	10% increase/decrease would result in an increase/decrease in fair value by £0.5 million
Contingent consideration liability	Discounted cash flow	Ongoing uncertainty in the clinical development of the Navi product		Total potential payments future payments relating to the contingent consideration liability on a gross, undiscounted basis are approximately $80 million.
		Regulatory approval and commercialization risks		Sensitivity of the input to fair value is primarily driven by uncertainty in the clinical development of the Navi product. Future potential payments under the CVR arrangement are contingent on i) future development milestones and ii) future sales of the Navi product, following regulatory approval and commercialization. In January 2020, the Company entered into the license agreement as detailed in Note 13. Although pursuant to the license agreement the Company is entitled to additional payments of up to $302 million, there continues to be significant uncertainty in respect of any milestone and royalty payments under the license agreement.
Warrant liability related to the private placement	Black-Scholes model	Expected volatility	2022: 95.5%	Volatility was estimated by reference to the 0.4 year historical volatility of the historical share price of the Company, matching the maturity of the instrument. If the volatility is decreased to 91.8% based on 3-month historical volatility, the carrying value of the warrants as of December 31, 2022 would decrease to £0.3 million.

Expected volatility	2021: 75.1%	Volatility was estimated by reference to the 1.4 years historical volatility of the historical share price of the Company, matching the maturity of the instrument. If the volatility is decreased to 67.4% based on 1-year historical volatility, the carrying value of the warrants as of December 31, 2021 would decrease to £6.7 million.

MEREO BIOPHARMA GROUP PLC
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

25. Commitments and contingencies

Each of Mereo BioPharma 1 Limited, Mereo BioPharma 2 Limited and Mereo BioPharma 3 Limited (together, the "Subsidiaries") issued to Novartis loan notes (which were assigned by Novartis to the Company in exchange for ordinary shares pursuant to the Subscription Agreement) and each of the Subsidiaries agreed to make future payments to Novartis comprising amounts equal to ascending specified percentages of tiered annual worldwide net sales (beginning at high single digits and reaching into double digits at higher sales) by such Subsidiary of products that include the assets acquired. The levels of ascending percentages of tiered annual worldwide net sales are the same for each Subsidiary under the respective Purchase Agreements.

Each Subsidiary further agreed that in the event it transfers, licenses, assigns or leases all or substantially all of its assets, it will pay Novartis a percentage of the proceeds of such transaction. The Company will retain the majority of the proceeds from such a transaction. Such percentage is the same for each Subsidiary under the respective Purchase Agreements. The payment of a percentage of proceeds is not payable with respect to any transaction involving equity interests of Mereo BioPharma Group plc, a merger or consolidation of Mereo BioPharma Group plc, or a sale of any assets of Mereo BioPharma Group plc.

In October 2017, the Company's wholly owned subsidiary Mereo BioPharma 4 Limited entered into an exclusive license and option agreement ("the License Agreement"), to obtain from AstraZeneca an exclusive worldwide, sub-licensable license under AstraZeneca's intellectual property rights relating to alvelestat, with an option to acquire such intellectual property rights following commencement of a pivotal trial and payment of related milestone payments ("the Option"), together with the acquisition of certain related assets. Upon entering into the License Agreement, the Company made a payment of $3.0 million and issued 490,798 ordinary shares to AstraZeneca, for an aggregate upfront payment equal to $5.0 million. In connection with certain development and regulatory milestones, the Company has agreed to make payments of up to $115.5 million in the aggregate and issue additional ordinary shares to AstraZeneca for licensed products containing alvelestat. In addition, the Company has agreed to make payments to AstraZeneca based on specified commercial milestones of the product. The Company has also agreed to pay a specified percentage of sub-licensing revenue to AstraZeneca and to make royalty payments to AstraZeneca equal to ascending specified percentages of tiered annual worldwide net sales by the Company of licensed products (subject to certain reductions), ranging from the high single digits to low double digits. Royalties will be payable on a licensed-product-by-licensed-product and country-by-country basis until the later of ten years after the first commercial sale of such licensed product in such country and expiration of the last patent covering such licensed product in such country that would be sufficient to prevent generic entry. The Company has agreed to use commercially reasonable efforts to develop and commercialize at least one licensed product.

The License Agreement will expire on the expiry of the last-to-expire royalty term with respect to all licensed products. Upon the expiration of the royalty term for a licensed product in a particular country, the licenses to the Company for such product in such country will become fully paid and irrevocable. Prior to exercise of the Option, if at all, the Company may terminate the License Agreement upon prior written notice. Either party may terminate the agreement upon prior written notice for the other party's material breach that remains uncured for a specified period of time or insolvency.

The Company enters into contracts in the normal course of business with contract research organizations ("CROs"), contract manufacturing organizations ("CMOs") and other third parties to assist in the performance of research and development activities and other services and products for operating purposes. The contracts with CROs generally provide for termination on notice, and therefore, are cancellable contracts and not included herein. The Company has manufacturing commitments with CMOs of £0.9 million as of December 31, 2022.

26. Share-based payments

The charge for share-based payments arises across the following schemes:

	Year ended December 31,		
	2022	**2021**	**2020**
	£'000s	**£'000s**	**£'000s**
2019 Equity Incentive Plan	3,149	2,860	922
2019 NED Equity Incentive Plan	713	499	167
2015 Plan	—	—	3
Mereo BioPharma Group plc Share Option Plan	—	68	376
Long Term Incentive Plan	—	(125)	90
Total	**3,862**	**3,302**	**1,558**

2019 Equity Incentive Plan ("EIP") and 2019 Non-Executive Director Equity Incentive Plan ("NED EIP")

The 2019 EIP and 2019 NED EIP were adopted on April 4, 2019, and subsequently amended on February 3, 2020 and January 15, 2021. The 2019 EIP provides for the grant of market value options over ADSs (each ADS is represented by 5 ordinary shares) to executive directors and employees. The 2019 NED EIP provides for the grant of market value options over ADSs to non-executive directors.

During the years ended December 31, 2022, 2021 and 2020, market value options were granted to executive directors and employees under the 2019 EIP. Subject to the executive director or employees continued employment, one-fourth of each such market value option grant shall vest on the first anniversary of the grant date and the remainder shall vest in equal monthly installments over the three-year period following the first anniversary. No performance conditions apply to such market value options.

During the years ended December 31, 2022, 2021 and 2020, market value options were granted to non-executive directors ("NEDs") under the 2019 NED EIP. Subject to the NEDs holding their current office (or being otherwise employed) through each applicable vesting date, such awards shall vest in equal monthly installments over a one-year period following the grant date. No performance conditions apply to such market value options.

The fair value of share options granted were estimated at the date of grant using a Black-Scholes pricing model, taking into account the terms and conditions upon which the share options were granted. The fair value calculation does not include any allowance for dividends as the Company has no available profits for distribution. The exercise price of the share options will be equal to the market price of the underlying shares on the date of grant. The contractual term of the share options is 10 years.

During the year ended December 31, 2022, deferred restricted stock units ("Deferred RSUs") under the 2019 NED EIP were granted to NEDs who elected to receive Deferred RSUs over ADSs in lieu of annual cash compensation for the period commencing February 1, 2022. Subject to the continued service of the NEDs, the Deferred RSUs vest in substantially equal monthly installments over the year. Payment of Deferred RSUs in ADSs will generally be made 180 days following separation of service.

The number of Deferred RSUs to be granted were determined by dividing the estimated amount of the annual cash compensation by the average closing trading price of the Company's ADSs over the most recent 30 trading days as of the grant date.

MEREO BIOPHARMA GROUP PLC
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

The following table illustrates the number and weighted average exercise prices (WAEP) of, and movements in, options for the 2019 EIP and 2019 NED EIP and the number of Deferred RSUs for the 2019 NED EIP during the year-ended December 31, 2022:

	2019 EIP		2019 NED EIP		
	Options over ADS Number	WAEP $	Deferred RSUs Number	Options over ADS Number	WAEP $
Outstanding at January 1, 2022	3,943,702	2.88	—	421,791	2.90
Granted during the year	4,126,400	1.38	386,144	535,488	1.22
Cancelled during the year	(1,164,197)	1.83	(42,104)	(42,192)	1.01
Forfeited during the year	(48,044)	3.97	—	—	
Exercised during the year	—	—	—	—	
Outstanding at December 31, 2022	**6,857,861**	**2.15**	**344,040**	**915,087**	**2.00**
Exercisable at December 31, 2022	2,082,027	2.95	—	832,584	2.09

The following table illustrates the number and weighted average exercise prices (WAEP) of, and movements in, options for the 2019 EIP and 2019 NED EIP during the year-ended December 31, 2021:

	2019 EIP		2019 NED EIP	
	Options over ADS Number	WAEP $	Options over ADS Number	WAEP $
Outstanding at January 1, 2021	1,567,873	2.94	149,416	3.06
Granted during the year	2,696,960	2.83	296,000	2.81
Cancelled during the year	(253,277)	2.66	(23,625)	2.72
Forfeited during the year	(28,521)	5.37	—	—
Exercised during the year	(39,333)	2.11	—	—
Outstanding at December 31, 2021	**3,943,702**	**2.88**	**421,791**	**2.90**
Exercisable at December 31, 2021	727,698	3.16	386,623	2.91

The weighted average remaining contractual life for the share options outstanding as at December 31, 2022 for the 2019 EIP was 8.4 years (2021: 8.7 years) and for the 2019 NED EIP was 8.5 years (2021: 8.6 years).

The weighted average fair value of options granted during the year was $1.20 per ADS (2021: $2.50 per ADS). Options outstanding at the end of the year had an exercise price of between $0.51 and $5.40 per ADS. The weighted average fair value of Deferred RSUs over ADSs granted during the year was $0.99 per ADS.

The 2015 Plan

Under the Mereo BioPharma Group Limited Share Option Plan (the “2015 Plan”), the Company, at its discretion, granted share options to acquire ordinary shares to employees, including executive management and NEDs. Share options vest over four years for executive management and employees and over three years for NEDs. No share options were granted during the year under the 2015 Plan and no further share option grants are envisaged.

	2022		2021	
	Options Number	WAEP £	Options Number	WAEP £
Outstanding at January 1	8,297,694	1.31	8,923,600	1.32
Forfeited during the year	(423,164)	1.55	(625,906)	1.29
Outstanding at December 31	**7,874,530**	**1.46**	**8,297,694**	**1.31**
Exercisable at December 31	7,874,530	1.46	8,297,694	1.31

The weighted average remaining contractual life for the share options outstanding as at December 31, 2022 was 2.6 years (2021: 3.6 years). Options outstanding at the end of the year had an exercise price of between £1.43 and £2.44 per ordinary share.

The Mereo Share Option Plan

The Mereo Share Option Plan ("Share Option Plan") provides for the grant of options to acquire ordinary shares to employees, executive directors and executive officers. Options may be granted to all eligible employees on commencement of employment and may be granted on a periodic basis after that. Under the Share Option Plan, the Board of Directors may determine if the vesting of an option will be subject to the satisfaction of a performance condition. Following the introduction of the EIP and NED EIP, no further share option grants under the Share Option Plan are envisaged.

The following table illustrates the number and weighted average exercise prices (WAEP) of, and movements in, options for the Option Plan during the year:

	2022		2021	
	Options Number	**WAEP £**	**Options Number**	**WAEP £**
Outstanding at January 1	1,323,965	3.04	1,411,395	3.14
Forfeited during the year	(770,805)	3.32	(87,430)	3.11
Outstanding at December 31	**553,160**	**3.49**	**1,323,965**	**3.04**
Exercisable at December 31	553,160	3.49	1,323,965	3.04

The weighted average remaining contractual life for the share options outstanding as at December 31, 2022 was 4.8 years (2021: 5.6 years). Options outstanding at the end of the year had an exercise price of between £3.05 and £3.59 per ordinary share.

Long Term Incentive Plan

Under the Company's Long Term Incentive Plan (LTIP), initiated in 2016, the Company, at its discretion, may grant nil-cost options to acquire shares to employees. Under the LTIP rules, vesting of 75% of the options issued to employees is subject to a share price performance condition (the "Share Price Element") and vesting of 25% of the options is subject to achievement of strategic operational targets (the "Strategic Element"). Share options vest over a maximum of five years, dependent upon achievement of these targets.

The fair value of the LTIP Share Price Element is estimated at the date of grant using a Monte Carlo pricing model, taking into account the terms and conditions upon which the share options were granted. The fair value of the LTIP Strategic Element is estimated at the date of grant using a Black- Scholes pricing model, taking into account the terms and conditions upon which the share options were granted, and the expense recorded is based upon the expected level of achievement of non-market based performance measures (strategic targets).

The fair value calculations do not include any allowance for dividends as the Company has no available profits for distribution. The contractual term of the LTIP options is five years.

	2022 Number	2021 Number
Outstanding at January 1	—	482,748
Lapsed during the year	—	(482,748)
Outstanding at December 31	—	—
Exercisable at December 31	—	—

MEREO BIOPHARMA GROUP PLC
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

All LTIP options lapsed during the year ended December 31, 2021. No LTIP options were granted during the years ended December 31, 2021 and 2022 and no further grants are envisaged.

Deferred Bonus Share Plan

Under the previous terms of the Company's Deferred Bonus Share Plan (DBSP), 30% of the annual bonus for 2017 for the senior management team was payable in deferred shares, which are governed by the DBSP plan rules. At the date of grant of the awards, the monetary bonus amount was divided by the closing share price to give the number of shares issued to the employee under the DBSP. The number of shares is fixed and not subject to adjustment between the issue date and vesting date. Under the DBSP, awards vest after three years from the date of the award.

There are no further performance conditions attached to the award, nor any service conditions (including no requirement for continued employment once the awards have been made).

Since the awards are issued at nil cost, they will be satisfied by the issue of ADSs from the Employee Benefit Trust.

The outstanding number of options as at December 31, 2021 was 100,817 all of which were exercisable and had a weighted average life of 0.1 years. During the year ended December 31, 2022, 22,592 options lapsed (2021: 62,183) and 78,225 options were exercised (2021: nil). There are no options outstanding as at December 31, 2022.

For the 2018 and 2019 financial years, under the Deferred Bonus Plan ("2019 DBP"), 100% of the annual bonus was paid in cash, of which 30% of amounts granted to the senior management team (after deduction of income tax and the relevant employee's national insurance contributions) was required to be utilized to acquire shares in the Company in the open market within 12 months of the grant of the award. No further grants under the DBSP are envisaged.

Deferred equity consideration

In October 2017, the Company's wholly owned subsidiary Mereo BioPharma 4 Limited entered into an exclusive license and option agreement (the "License Agreement") to obtain from AstraZeneca an exclusive worldwide, sub-licensable license under AstraZeneca's intellectual property rights relating to MPH-966, with an option to acquire such intellectual property rights following commencement of a pivotal trial and payment of related milestone payments (the "Option"), together with the acquisition of certain related assets.

Under the agreement with AstraZeneca, the Company may issue up to 1,349,693 ordinary shares which are dependent on achieving certain milestones.

Weighted average inputs

The following table includes the weighted average inputs to the models used for the fair value of share options granted during the year ended December 31, 2022:

	2019 EIP	2019 NED EIP
Expected volatility (%)	96	96
Risk-free interest rate (%)	1.83	1.96
Expected life of share options (years)	10	10
Market price of ADSs ($)	1.38	1.22
Model used	Black-scholes	Black-scholes

During the year ended December 31, 2022, no grants of share options were issued under any other scheme.

The following table includes the weighted average inputs to the models used for the fair value of share options granted during the year ended December 31, 2021:

	2019 EIP	2019 NED EIP
Expected volatility (%)	97	98
Risk-free interest rate (%)	1.15	1.09
Expected life of share options (years)	10	10
Market price of ADSs ($)	2.83	2.81
Model used	Black-scholes	Black-scholes

During the year ended December 31, 2021, no grants were issued under any other scheme.

The expected volatility inputs for the years ended December 31, 2022 and 2021 reflect the assumption that the historical volatility over a period similar to the life of the options is indicative of future trends.

27. Related party disclosures

Compensation of key management personnel of the Company

The remuneration of key management personnel of the Company is set out below in aggregate:

	Year ended December 31,		
	2022	2021	2020
	£'000s	£'000s	£'000s
Short-term benefits	3,699	4,018	4,479
Post-employment benefits	158	173	144
Share-based payment charge	3,043	2,559	875
Total	**6,900**	**6,750**	**5,498**

The amounts disclosed in the table above are the amounts recognized as an expense during the reporting period related to key management personnel. In 2022, key management personnel of the Company consisted of the executive director (the Chief Executive Officer), non-executive directors, and other members of senior executive management (the Chief Financial Officer, the General Counsel, the Chief Portfolio Management and Pipeline Strategy, Chief Business Officer, Chief Scientific Officer, the Chief Patient Access and Commercial Planning, the Senior Vice President Clinical Development, and Senior Vice President and Therapeutic Head).

Employee Benefit Trust

In 2016 the Company set up an Employee Benefit Trust ("EBT"). The EBT holds ADS's to satisfy the exercise of options under the Company's share-based incentive schemes (see Note 26).

No funding was loaned to the EBT by the Company during the year ended December 31, 2022 or 2021. During the years ended December 31, 2022 and 2021, no ordinary shares were purchased by the EBT. A total of 15,645 ADSs held by the EBT were used in the year-ended December 31, 2022 to satisfy the exercise of options under the Company's share-based incentive schemes (2021: 31,205). As of December 31, 2022, the EBT holds 200,606 ADSs (2021: 216,251) along with £17,741 in cash (2021: £17,866).

28. Events after the reporting period

On February 10, 2023, the Company amended the Novartis Loan Note, extending the maturity date to February 10, 2025. Pursuant to the amendment and a new warrant instrument, interest accrued to the amendment date was paid in cash and warrants to purchase 2,000,000 ordinary shares at an exercise price of £0.150 per ordinary share were issued and are exercisable until February 10, 2028.

DESCRIPTION OF THE REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934

The following is a description of the ordinary shares, par value £0.003 per share, of Mereo BioPharma Group plc (the "Company," "we" or "us") which are represented by American Depositary Shares ("ADSs") with each ADS representing five of our ordinary shares registered under Section 12 of the Securities Exchange Act of 1934, as amended (the " Exchange Act"). This description also summarizes relevant provisions of English law. The following summary does not purport to be complete and is subject to, and is qualified in its entirety by reference to, the applicable provisions of English law and the Company's articles of association, a copy of which is filed as Exhibit 1.1 to the Annual Report on Form 20–F of the Company for the fiscal year ended December 3l, 2022. We encourage you to read the articles and the applicable provisions of English law for additional information.

General

We were incorporated as a private limited company with the legal name Mereo BioPharma Group Limited under the laws of England and Wales on March 10, 2015 with the company number 09481161. On June 3, 2016, we re-registered as a public limited company with the legal name Mereo BioPharma Group plc. Our principal executive offices are located at 4th Floor, One Cavendish Place, London, WIG 0QF, United Kingdom. The principal legislation under which we operate and our ordinary shares are issued is the U.K. Companies Act 2006.

Ordinary Shares

The following summarizes the rights of holders of our ordinary shares:

- each holder of our ordinary shares is entitled to one vote per ordinary share at a meeting of shareholders (provided that certain shareholders each have their votes limited to 19.5% of the total voting share capital and any votes which would have otherwise been exercisable by them shall be deemed to be held and exercisable by the other shareholders, other than those and certain other shareholders, on a pro rata basis);

- the holders of the ordinary shares shall be entitled to receive notice of, attend, speak, and vote at our general meetings; and
- holders of our ordinary shares are entitled to receive such dividends as are recommended by our directors and declared by our shareholders.

Registered Shares

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

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

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

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

- the name of any person, without sufficient cause, is entered in or omitted from our register of members; or
- a default is made or unnecessary delay takes place in entering on the register the fact of any person having ceased to be a member or on which we have a lien, provided that such refusal does not prevent dealings in the shares taking place on an open and proper basis.

Pre-emptive Rights

English law generally provides shareholders with pre-emptive rights when new shares are issued for cash; however, it is possible for the articles of association, or shareholders by special resolution, to exclude pre-emptive rights. Such an exclusion of pre-emptive rights may be for a maximum period of up to five years from the date of adoption of the articles of association, if the exclusion is contained in the articles of association, or from the date of the shareholder resolution, if the exclusion is by shareholder resolution. In either case, this exclusion would need to be renewed by our shareholders upon its expiration (i.e., at least every five years).

Articles of Association

The following is a description of our Articles as at the date hereof.

Shares and Rights Attaching to Them

Objects

The objects of our company are unrestricted.

Share Rights

Subject to any special rights attaching to shares already in issue, our shares may be issued with or have attached to them any rights or restrictions as we may resolve by ordinary resolution of the shareholders or, failing such determination, as the board may determine.

Voting Rights

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

- on a show of hands, every shareholder who (being an individual) is present in person and (being a corporation) is present by a duly authorized representative shall have one vote;

- on a show of hands, each proxy present in person has one vote for and one vote against a resolution if the proxy has been duly appointed by more than one shareholder and the proxy has been instructed by one or more of those shareholders to vote for the resolution and by one or more other of those shareholders to vote against it;
- on a show of hands, each proxy present in person has one vote for and one vote against a resolution if the proxy has been duly appointed by more than one shareholder entitled to vote on the resolution and either: (1) the proxy has been instructed by one or more of those shareholders to vote for the resolution and has been given any discretion by one or more other of those shareholders to vote and the proxy exercises that discretion to vote against it; or (2) the proxy has been instructed by one or more of those shareholders to vote against the resolution and has been given any discretion by one or more other of those shareholders to vote and the proxy exercises that discretion to vote for it; or
- on a poll every shareholder who is present in person or by proxy shall have one vote for each share of which he or she is the holder, provided that certain shareholders each have their votes limited to 19.5% of the total voting share capital and any votes which would have otherwise been exercisable by them shall be deemed to be held and exercisable by the other shareholders, other than those and certain other shareholders, on a pro rata basis.

At any general meeting a resolution put to the vote of the meeting shall be decided on a show of hands unless a poll is demanded. Subject to the provisions of the U.K. Companies Act 2006, a poll may be demanded by:

- the chairman of the meeting; the directors;
- two or more persons having the right to vote on the resolution; or
- a person or persons representing not less than 10% of the total voting rights of all shareholders having the right to vote on the resolution.

Restrictions on Voting

No shareholder shall (unless the Directors otherwise determine) be entitled to vote at any general meeting in respect of any share held by him or her unless all sums payable by him or her in respect of that share have been paid.

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

Dividends

We may, subject to the provisions of the U.K. Companies Act 2006 and our Articles, by ordinary resolution of shareholders declare dividends out of profits available for distribution in accordance with the respective rights of shareholders but no such dividend shall exceed the amount recommended by the directors. The board may from time to time pay shareholders such interim dividends as appear to the board to be justified by our financial position but, if at any time, our share capital is divided into different classes the board may not pay such interim dividends in respect of those shares which confer on the holders thereof deferred or non-preferential rights with regard to dividends if, at the time of payment, any preferential dividend is in arrears.

Subject to any special rights attaching to or the terms of issue of any share, all dividends shall be declared and paid according to the amounts paid up on the shares and shall be apportioned and paid pro rata according to the amounts paid up on the shares during any part or parts of the period in respect of which the dividend is paid.

No dividend or other moneys payable by us on or in respect of any share shall bear interest against us unless otherwise provided by the rights attached to the share or the provisions of another agreement between the shareholder and us. Any dividend unclaimed after a period of 12 years from the date such dividend became due for payment shall be forfeited and cease to remain owing.

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

Any general meeting declaring a dividend may by ordinary resolution of shareholders, upon the recommendation of the board, direct payment or satisfaction of such dividend wholly or in part by the distribution of non-cash assets of equivalent value, including shares or other securities in any company.

The directors may, if authorized by an ordinary resolution of shareholders, offer any holders of ordinary shares the right to elect to receive in lieu of a dividend, or part of a dividend, an allotment of ordinary shares credited as fully paid up.

Change of Control

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

Distributions on Winding Up

If we are in liquidation, the liquidator may, if authorized by a special resolution of shareholders and any other authority required at law, divide among shareholders (excluding us to the extent we are a shareholder by virtue only of holding treasury shares) in specie or in kind the whole or any part of our assets (whether or not the assets consist of property of one kind or consist of properties of different kinds and the liquidator may for such purpose set such value as the liquidator deems fair upon any one or more class or classes of property and may determine how such division shall be carried out as between the shareholder s or different classes of shareholders), or vest the whole or any part of such assets in trustees upon such trusts for the benefit of the shareholders as the liquidator determines (and our liquidation may be closed and we may be dissolved), but no shareholder shall be compelled to accept any shares or other assets upon which there is any liability.

Variation of Rights

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

Alteration to Share Capital

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

Preemption Rights

In certain circumstances, our shareholders may have statutory preemption rights under the U.K. Companies Act 2006 in respect of the allotment of new shares as described in "—Pre-emptive Rights".

Transfer of Shares

Any shareholder holding shares in certificated form may transfer all or any of his or her shares by an instrument of transfer in any usual form or any other form approved by the board. Any written instrument of transfer shall be signed by or on behalf of the transferor and (in the case of a partly paid share) the transferee.

ln the case of uncertificated shares, the directors may take such action as they consider appropriate to achieve a transfer. The Uncertificated Securities Regulations 2001 permit shares to be issued and held in uncertificated form and transferred by means of a computer based system.

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

- which is not a fully paid share;
- where the transfer is not lodged at our registered office or such other place as the directors have appointed;
- where the transfer is not accompanied by the share certificate to which it relates, or such other evidence as the board may reasonably require to show the transferor's right to make the transfer, or evidence of the right of someone other than the transferor to make the transfer on the transferor's behalf;
- where the transfer is in respect of more than one class of share; and
- where the number of joint holders to whom the share is to be transferred exceeds four.

If the board declines to register a transfer, it must return to the transferee the instrument of transfer together with notice of the refusal, unless the board suspects that the proposed transfer may be fraudulent.

Shareholder Meetings

Annual General Meetings

In accordance with the U.K. Companies Act 2006, we are required in each year to hold an annual general meeting in addition to any other general meetings in that year and to specify the meeting as such in the notice convening it. The annual general meeting shall be convened whenever and wherever the board sees fit, subject to the requirements of the U.K. Companies Act 2006.

Notice of General Meetings

Under the U.K. Companies Act 2006, 21 clear days' notice must be given for an annual general meeting and any resolutions to be proposed at that meeting. At least 14 clear days' notice is required for any other general meeting.

Subject to the notice requirements of the U.K. Companies Act 2006, a general meeting of our shareholders may be called by the Board whenever and at such times and places as it shall determine. A general meeting may also be convened by the Board on the requisition of two or more shareholders who hold at least 5% of our paid-up capital carrying voting rights at a general meeting.

Quorum of General Meetings

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

Class Meetings

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

Directors

Number of Directors

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

Appointment of Directors

Subject to the provisions of the Articles, we may, by ordinary resolution of the shareholders or a decision of the directors, elect any person to be a director, either to fill a casual vacancy or as an addition to the existing board, provided the total number of directors does not exceed the maximum number fixed by or in accordance with the Articles. However, any person that is not a director retiring from the existing board must be recommended by the board or the person must have confirmed in writing to us their willingness to be elected as a director not later than seven days before the general meeting at which the relevant resolution is proposed.

Any director appointed by the board will hold office only until the next following annual general meeting at which they must retire. In addition, all directors must retire at the third annual general meeting following the annual general meeting at which such director was elected or last re-elected. Such directors are eligible for re-election at the annual general meeting at which they retire.

The shareholders may, at the meeting at which a director retires, fill the vacated office by electing a person and in default the retiring director shall, if willing to continue to act, be deemed to have been re-elected, unless at such meeting it is expressly resolved not to fill such vacated office or unless a resolution for the re-election of such director shall have been put to the meeting and lost.

Other U.K. Law Considerations

Mandatory Purchases and Acquisitions

Pursuant to Sections 979 to 991 of the U.K. Companies Act 2006, where a takeover offer has been made for us and the offeror has acquired or unconditionally contracted to acquire not less than 90% in value of the shares to which the offer relates and not less than 90% of the voting rights carried by those shares, the offeror may give notice to the holder of any shares to which the offer relates which the offeror has not acquired or unconditionally contracted to acquire that he or she wishes to acquire, and is entitled to so acquire, those shares on the same terms as the general offer. The offeror would do so by sending a notice to the outstanding minority shareholders telling them that it will compulsorily acquire their shares. Such notice must be sent within three months of the last day on which the offer can be accepted in the prescribed manner. The compulsory acquisition of the minority shareholders' shares can be completed at the end of six weeks from the date the notice has been given, subject to the minority shareholders failing to successfully lodge an application to the court to prevent such compulsory acquisition any time prior to the end of those six weeks following which the offeror can execute a transfer of the outstanding shares in its favor and pay the consideration to us, which would hold the consideration on trust for the outstanding minority shareholders. The consideration offered to the outstanding minority shareholders whose shares are compulsorily acquired under the U.K. Companies Act 2006 must, in general, be the same as the consideration that was available under the takeover offer.

Sell Out

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

Disclosure of Interest in Shares

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

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

- in respect of the default shares, the relevant shareholder shall not be entitled to vote (either in person or by proxy) at any general meeting or to exercise any other right conferred by a shareholding in relation to general meetings;
- where the default shares represent at least 0.25% of their class, (a) any dividend or other money payable in respect of the default shares shall be retained by us without liability to pay interest and/or (b) no transfers by the relevant shareholder of any default shares may be registered (unless the shareholder himself is not in default and the shareholder provides a certificate, in a form satisfactory to the directors, to the effect that after due and careful enquiry the shareholder is satisfied that none of the shares to be transferred are default shares); and
- any shares held by the relevant shareholder in uncertificated form shall be converted into certificated form and that shareholder shall not after that be entitled to convert all or any shares held by him or her into uncertificated form (except with the authority of the directors) unless the shareholder himself is not in default and the shares which the shareholder wishes to convert are part only of the shareholder's holding and the shareholder provides a certificate, in a form satisfactory to the directors, to the effect that after due and careful enquiry the shareholder is satisfied that none of the shares to be converted into uncertificated form are default shares.

Purchase of Own Shares

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

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

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

The Nasdaq Global Market is not a "recognised investment exchange" on which we may make market purchases.

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

Distributions and Dividends

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

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

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

City Code on Takeovers and Mergers

Following the AIM Delisting, if at the time of a takeover offer the U.K. Panel on Takeovers and Mergers (the "Takeover Panel") determines that we have our place of central management and control in the United Kingdom, we would be subject to the U.K. City Code on Takeovers and Mergers (the "City Code"), which is issued and administered by the Takeover Panel. The City Code provides a framework within which takeovers of companies subject to it are conducted. In particular, the City Code contains certain rules in respect of mandatory offers. Under Rule 9 of the City Code, if a person:

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

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

In November 2020, the Takeover Panel confirmed that, based on our current circumstances, following AIM Delisting we are not subject to the City Code. As a result, our shareholders are not entitled to the benefit of the takeover offer protections provided under the City Code. We believe that this position is unlikely to change at any time in the near future but, in accordance with good practice, we will review the situation on a regular basis and consult with the Takeover Panel if there is any change in our circumstances, which may have a bearing on whether the Takeover Panel would determine our place of central management and control to be in the United Kingdom.

Exchange Controls

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

DESCRIPTION OF AMERICAN DEPOSITARY SHARES

American Depositary Shares

Citibank, N.A. ("Citibank") acts as the depositary for the ADSs. Citibank's depositary offices are located at 388 Greenwich Street, New York, New York 10013. ADSs represent ownership interests in securities that are on deposit with the depositary. ADSs may be represented by certificates that are commonly known as American Depositary Receipts ("ADRs"). The depositary typically appoints a custodian to safekeep the securities on deposit. In this case, the custodian is Citibank, N.A., London Branch, located at 25 Canada Square, Canary Wharf, London, El4 5LB, United Kingdom.

We have appointed Citibank as depositary pursuant to a deposit agreement. A copy of the form of the deposit agreement is on file with the SEC under cover of a registration statement on Form F-6. A copy of the deposit agreement is available from the SEC's website (www.sec.gov). Please refer to registration number 333-249338 when retrieving such copy.

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

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

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

In addition, applicable laws and regulations may require you to satisfy reporting requirements and obtain regulatory approvals in certain circumstances. You are solely responsible for complying with such reporting requirements and obtaining such approvals. Neither the depositary, the custodian, us or any of their or our respective agents or affiliates shall be required to take any actions whatsoever on your behalf to satisfy such reporting requirements or obtain such regulatory approvals under applicable laws and regulations.

The manner in which you own the ADSs (e.g., in a brokerage account vs. as registered holder, or as holder of certificated vs. uncertificated ADSs) may affect your rights and obligations, and the manner in which, and extent to which, the depositary's services are made available to you. As an owner of ADSs, we will not treat you as one of our shareholders and you will not have direct shareholder rights. The depositary will hold on your behalf the shareholder rights attached to the ordinary shares underlying your ADSs. As an owner of ADSs you will be able to exercise the shareholders rights for the ordinary shares represented by your ADSs through the depositary only to the extent contemplated in the deposit agreement. To exercise any shareholder rights not contemplated in the deposit agreement you will, as an ADS owner, need to arrange for the cancellation of your ADSs and become a direct shareholder.

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

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

Dividends and Other Distributions

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

Distributions of Cash

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

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

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

Distributions of Shares

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

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

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

Distributions of Rights

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

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

The depositary will *not* distribute the rights to a Holder if:

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

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

Elective Distributions

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

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

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

Other Distributions

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

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

The distribution will be made net of fees, expenses, taxes, and governmental charges payable by holders under the terms of the deposit agreement.

In order to pay such taxes and governmental charges, the depositary may sell all or a portion of the property received.

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

- we do not request that the property be distributed to such Holder or if we request that the property not be distributed to such Holder; or
- we do not deliver satisfactory documents to the depositary; or
- the depositary determines that all or a portion of the distribution to such Holder is not reasonably practicable. The proceeds of such a sale will be distributed to holders as in the case of a cash distribution.

Redemption

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

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

Changes Affecting Ordinary Shares

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

If any such change were to occur, such Holder's ADSs would, to the extent permitted by law and the deposit agreement, represent the right to receive the property received or exchanged in respect of the ordinary shares held on deposit. The depositary may in such circumstances deliver new ADSs to a Holder, amend the deposit agreement, the ADRs and the applicable registration statement(s) on Form F-6, call for the exchange of such Holder's existing ADSs for new ADSs and take any other actions that are appropriate to reflect as to the ADSs the change affecting the Shares. If the depositary may not lawfully distribute such property to a Holder, the depositary may sell such property and distribute the net proceeds to such Holder as in the case of a cash distribution.

Issuance of ADSs upon Deposit of Ordinary Shares

The depositary may create ADSs on a Holder's behalf if such Holder or such Holder's broker deposit ordinary shares with the custodian. The depositary will deliver these ADSs to the person a Holder indicates only after such Holder pays any applicable issuance fees and any charges and taxes payable for the transfer of the ordinary shares to the custodian. A Holder's ability to deposit ordinary shares and receive ADSs may be limited by the legal considerations in the United States and England and Wales applicable at the time of deposit.

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

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

- the ordinary shares are duly authorized, validly allotted and issued, fully paid, not subject to any call for the payment of further capital, and legally obtained;
- all pre-emptive (and similar) rights, if any, with respect to such ordinary shares have been validly waived, disapplied or exercised; such Holder is duly authorized to deposit the ordinary shares;
- the ordinary shares presented for deposit are free and clear of any lien, encumbrance, security interest, charge, mortgage, or adverse claim, and are not, and the ADSs issuable upon such deposit will not be, "Restricted Securities" (as defined in the deposit agreement); and

- the ordinary shares presented for deposit have not been stripped of any rights or entitlements.

If any of the representations or warranties is incorrect in any way, we and the depositary may, at such Holder's cost and expense, take any and all actions necessary to correct the consequences of the misrepresentation.

Transfer, Combination and Split Up of ADRs

ADR holders will be entitled to transfer, combine, or split up such Holder's ADRs and the ADSs evidenced thereby. For transfers of ADRs, a Holder will have to surrender the ADRs to be transferred to the depositary and also must:

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

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

Withdrawal of Ordinary Shares Upon Cancellation of ADSs

A Holder will be entitled to present such Holder's ADSs to the depositary for cancellation and then receive the corresponding number of underlying ordinary shares at the custodian's offices. A Holder's ability to withdraw the ordinary shares held in respect of the ADSs may be limited by the legal considerations in the United States and England and Wales applicable at the time of withdrawal. In order to withdraw the ordinary shares represented by a Holder's ADSs, such Holder will be required to pay to the depositary the fees for cancellation of ADSs and any charges and taxes payable upon the transfer of the ordinary shares.

A Holder assumes the risk for delivery of all funds and securities upon withdrawal. Once canceled, the ADSs will not have any rights under the deposit agreement.

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

A Holder will have the right to withdraw the securities represented by such Holder's ADSs at any time except for:

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

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

Voting Rights

A Holder generally has the right under the deposit agreement to instruct the depositary to exercise the voting rights for the ordinary shares represented by such Holder's ADSs. The voting rights of holders of ordinary shares are described in "Description of Share Capital and Articles of Association-Articles of Association" in this Annual Report.

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

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

- *in the event of voting by show of hands*, the depositary will vote (or cause the custodian to vote) all ordinary held on deposit at that time in accordance with the voting instructions received from a majority of holders of ADSs who provide timely voting instructions.
- *in the event of voting by poll*, the depositary will vote (or cause the custodian to vote) the ordinary shares held on deposit in accordance with the voting instructions received from the holders of ADSs. The depositary will give a discretionary proxy to a person designated by us to vote any ordinary shares held on deposit for which voting instructions were not received from the holders of ADSs, unless we inform the depositary that (a) we do not wish such proxy to be given, (b) substantial opposition exists, or (c) the rights of holders of ADSs may be adversely affected.

Securities for which no voting instructions have been received will not be voted (except as otherwise contemplated in the Deposit Agreement).

Please note that the ability of the depositary to carry out voting instructions may be limited by practical and legal limitations and the terms of the securities on deposit. We cannot assure a Holder that such Holder will receive voting materials in time to enable such Holder to return voting instructions to the depositary in a timely manner.

Fees and Charges

ADS holders will be required to pay the following fees under the terms of the deposit agreement:

Service	Fee
Issuance of ADSs (e.g., an issuance of ADS upon a deposit of ordinary shares or upon a change in the ADS(s)-to-ordinary shares ratio), excluding ADS issuances as a result of distributions of ordinary Shares	Up to $5.00 per 100 ADSs (or fraction thereof) issued
Cancellation of ADSs (e.g., a cancellation of ADSs for delivery of deposited property or upon a change in the ADS(s)-to-ordinary shares ratio)	Up to $5.00 per 100 ADSs (or fraction thereof) cancelled
Distribution of cash dividends or other cash distributions (e.g., upon a sale of rights and other entitlements)	Up to $5.00 per 100 ADSs (or fraction thereof) held
Distribution of ADSs pursuant to (i) stock dividends or other free stock distributions, or (ii) exercise of rights to purchase additional ADSs	Up to $5.00 per 100 ADSs (or fraction thereof) held
Distribution of securities other than ADSs or rights to purchase additional ADSs (e.g., upon a spin-off)	Up to $5.00 per 100 ADSs (or fraction thereof) held
ADS Services	Up to $5.00 per 100 ADSs (or fraction thereof) held on the applicable record date (s) established by the depositary
Registration of ADS Transfers (e.g., upon a registration of the transfer of registered ownership of ADSs, upon a transfer of ADSs into DTC and vice versa, or for any other reason)	Up to $5.00 per 100 ADSs (or fraction thereof) transferred
Conversion of ADSs of one series for ADSs of another series (e.g., upon conversion of Partial Entitlement ADSs for Full Entitlement ADSs, or upon conversion of Restricted ADSs (each as defined in the Deposit Agreement) into freely transferable ADSs, and vice versa)	Up to $5.00 per 100 ADSs (or fraction thereof) converted

ADS holders will also be responsible to pay certain charges such as:

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

ADS fees and charges payable upon (i) the issuance of ADSs, and (ii) the cancellation of ADSs are charged to the person to whom the ADSs are issued (in the case of ADS issuances) and to the person whose ADSs are cancelled (in the case of ADS cancellations). In the case of ADSs issued by the depositary into DTC, the ADS issuance and cancellation fees and charges may be deducted from distributions made through DTC, and may be charged to the DTC participant(s) receiving the ADSs being issued or the DTC participant(s) holding the ADSs being cancelled, as the case may be, on behalf of the beneficial owner(s) and will be charged by the DTC participant(s) to the account of the applicable beneficial owner(s) in accordance with the procedures and practices of the DTC participants as in effect at the time. ADS fees and charges in respect of distributions and the ADS service fee are charged to the holders as of the applicable ADS record date. In the case of distributions of cash, the amount of the applicable ADS fees and charges is deducted from the funds being distributed. In the case of (i) distributions other than cash and (ii) the ADS service fee, holders as of the ADS record date will be invoiced for the amount of the ADS fees and charges and such ADS fees and charges may be deducted from distributions made to holders of ADSs. For ADSs held through DTC, the ADS fees and charges for distributions other than cash and the ADS service fee may be deducted from distributions made through DTC, and may be charged to the DTC participants in accordance with the procedures and practices prescribed by DTC and the DTC participants in turn charge the amount of such ADS fees and charges to the beneficial owners for whom they hold ADSs. In the case of (i) registration of ADS transfers, the ADS transfer fee will be payable by the holders of ADSs whose ADSs are being transferred or by the person to whom the ADSs are transferred, and (ii) conversion of ADSs of one series for ADSs of another series, the ADS conversion fee will be payable by the holder whose ADSs are converted or by the person to whom the converted ADSs are delivered.

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

Amendments and Termination

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

A Holder will be bound by the modifications to the deposit agreement if a Holder continues to hold such Holder's ADSs after the modifications to the deposit agreement become effective. The deposit agreement cannot be amended to prevent a Holder from withdrawing the ordinary shares represented by such Holder's ADSs (except as permitted by law).

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

Termination

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

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

Books of Depositary

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

The depositary will maintain in New York facilities to record and process the issuance, cancellation, combination, split-up, and transfer of ADSs.

These facilities may be closed from time to time, to the extent not prohibited by law.

Transmission of Notices, Reports and Proxy Soliciting Material

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

Limitations on Obligations and Liabilities

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

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

- We and the depositary may rely without any liability upon any written notice, request or other document believed to be genuine and to have been signed or presented by the proper parties.
- We and the depositary also disclaim liability for any consequential or punitive damages for any breach of the terms of the deposit agreement.
- No disclaimer of any Securities Act liability is intended by any provision of the deposit agreement.
- Nothing in the deposit agreement gives rise to a partnership or joint venture, or establishes a fiduciary relationship, among Mereo, the depositary and Holders.
- Nothing in the deposit agreement precludes Citibank (or its affiliates) from engaging in transactions in which parties adverse to Mereo or the ADS owners have interests, and nothing in the deposit agreement obligates Citibank to disclose those transactions, or any information obtained in the course of those transactions, to Mereo or to the ADS owners, or to account for any payment received as part of those transactions.

As the above limitations relate to our obligations and the depositary's obligations to you under the deposit agreement, we believe that, as a matter of construction of the clause, such limitations would likely to continue to apply to ADS holders who withdraw the ordinary shares from the ADS facility with respect to obligations or liabilities incurred under the deposit agreement before the cancellation of the ADSs and the withdrawal of the ordinary shares, and such limitations would most likely not apply to ADS holders who withdraw the ordinary shares from the ADS facility with respect to obligations or liabilities incurred after the cancellation of the ADSs and the withdrawal of the ordinary shares and not under the deposit agreement.

In any event, you will not be deemed, by agreeing to the terms of the deposit agreement, to have waived our or the depositary's compliance with U.S. federal securities laws and the rules and regulations promulgated thereunder. In fact, you cannot waive our or the depositary's compliance with U.S. federal securities laws and the rules and regulations promulgated thereunder.

Taxes

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

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

Foreign Currency Conversion

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

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

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

Governing Law/Waiver of Jury Trial

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

As an owner of ADSs, you irrevocably agree that any legal action arising out of the Deposit Agreement, the ADSs or the ADRs, involving the Company or the Depositary, may only be instituted in a state or federal court in the city of New York.

AS A PARTY TO THE DEPOSIT AGREEMENT, HOLDERS IRREVOCABLY WAIVE, TO THE FULLEST EXTENT PERMITTED BY APPLICABLE LAW, ANY AND ALL RIGHT TO TRIAL BY JURY IN ANY LEGAL PROCEEDING AGAINST US AND/OR THE DEPOSITARY ARISING OUT OF, OR RELATING TO, THE DEPOSIT AGREEMENT, ANY ADR AND ANY TRANSACTIONS CONTEMPLATED IN THE DEPOSIT AGREEMENT (WHETHER BASED ON CONTRACT, TORT, COMMON LAW OR OTHERWISE).

PRIVATE AND CONFIDENTIAL

[*name*]
[*address*]

[*date*]

Dear [*name*],

Restated Letter of Appointment

The Board of Directors (**Board**) of Mereo BioPharma Group plc (**Company**) is pleased to confirm your appointment as an independent non-executive [director][chairman] effective as of [*date*] (**Effective Date**). Your restated terms pursuant to this letter will become effective on the Effective Date.

This letter sets out the main terms of your appointment from the Effective Date. By accepting this appointment, you agree that this letter is a contract for services and is not a contract of employment and you confirm that you are not subject to any restrictions which prevent you from holding office as a director of the Company.

1. FEES AND EXPENSES

1.1 You shall be paid an annual fee of £[ ] gross, which shall be paid in equal instalments monthly in arrears through the payroll after deduction of any taxes and other amounts that are required by law. This fee covers all duties but does not include fees for service on any Board committee and any Boards of the Company's subsidiaries which will be notified to you separately in writing.

1.2 The Company shall reimburse you for all reasonable and properly documented expenses that you incur in performing the duties of your office including travel and sundry expenses, in accordance with the Company's expense reimbursement policies.

1.3 On termination of your appointment, you shall only be entitled to such fees as may have accrued to the date of termination, together with reimbursement in the normal way of any expenses properly incurred before that date.

2. ROLE AND DUTIES

2.1 The Board as a whole is collectively responsible for the success of the Company. Subject to and without limitation on the Company's articles of incorporation, bylaws and any charter or similar authorisation to the Board or any committee of the Board, the Board's role is to seek to:

(a) promote the long-term sustainable success of the Company, generating value for shareholders and contributing to wider society;

(b) act with integrity;

(c) ensure that the necessary resources are in place for the Company to meet its objectives, and measure performance against them;

(d) establish a framework of prudent and effective controls, which enable risk to be assessed and managed; and

(e) ensure that policies and practices are consistent with the Company's values and support its long-term sustainable success.

2.2 As a non-executive director you shall have the same general legal responsibilities to the Company as any other director. You are expected to perform your duties (whether statutory, fiduciary or common law) faithfully, diligently and to a standard commensurate with the functions of your role and your knowledge, skills and experience.

2.3 You shall exercise your powers in your role as a non-executive director having regard to relevant obligations under prevailing law and regulation, including the Companies Act 2006 and, where applicable, the Market Abuse Regulation (596/2014/EU), the rules of the Securities and Exchange Commission, the Nasdaq Stock Market and Delaware General Corporation Law.

2.4 You shall have particular regard to the general duties of directors in Part 10 of the Companies Act 2006, including the duty to promote the success of the Company under which all directors must act in the way they consider, in good faith, would be most likely to promote the success of the Company for the benefit of its members as a whole. In doing so, as a director, you must have regard (among other matters) to:

(a) the likely consequences of any decision in the long term;

(b) the interests of the Company's employees;

(c) the need to foster the Company's business relationships with suppliers, customers and others;

(d) the impact of the Company's operations on the community and the environment;

(e) the desirability of the Company maintaining a reputation for high standards of business conduct; and

(f) the need to act fairly as between the members of the Company.

2.5 If and when applicable, you shall have particular regard to the Nasdaq's Listed Company Rules and the Delaware General Corporation Law provisions applicable to the board of directors and committees thereof and their respective members and advisers.

[ ] [In addition to the general legal responsibilities to the Company as any other director, in your role as chairman, you should seek to fulfil the following list of responsibilities:

(a) chair the Board and general meetings of the Company and relevant committees of the Board and relevant Board and general meetings of any subsidiaries of the Company;

(b) in consultation with the Chief Executive, set the Board's agenda (primarily focused on strategy, performance, value creation and accountability) and strive to ensure that issues relevant to these areas are reserved for board decision and adequate time is available for discussion of all agenda items, in particular strategic issues;

(c) create the conditions for overall board and individual director effectiveness, s etting clear expectations concerning the style and tone of Board discussions;

(d) ensure that the Board determines the nature and extent of the significant risks that the Company is willing to embrace in implementing its strategy;

(e) ensure that the Board has effective decision-making processes and applies sufficient challenge to major proposals;

(f) ensure that all directors are aware of their responsibilities and are able to discharge their statutory duties;

(g) ensure that Board committees are properly structured with appropriate terms of reference and that committee membership is periodically refreshed;

(h) encourage all Board members to engage in Board and committee meetings by drawing on their skills, experience and knowledge;

(i) ensure that sufficient time is allowed at the board for committees to report on the nature and content of discussion, on recommendations, and on actions to be taken;

(j) hold meetings with the non-executive directors without the executives present to facilitate a full and frank airing of views;

(k) develop productive working relationships with all executive directors and the chief executive to gain a detailed understanding of the business;

(l) demonstrate ethical leadership and promote the highest standards of integrity, probity and corporate governance throughout the Company and particularly at Board level;

(m) ensure that the Board receives accurate, timely and clear information;

(n) demonstrate objective judgement and facilitate constructive board relations and the effective contribution of all non-executive directors;

(o) ensure that the new directors participate in a full, formal and tailored induction programme;

(p) ensure that the performance of the Board, its committees and individual directors is evaluated at least once a year, select an effective approach and act on the results of such evaluation; and

(q) periodically review, with the company secretary, whether the Board and Company's governance processes are fit for purpose and consider any improvements and initiatives that could strengthen the governance.]

2.6 In your role as a non-executive director, it is expected that you shall also be required to fulfil the following list of responsibilities, in the course of your good faith performance of services to the Company and in the exercise of your reasonable business judgment:

(a) provide constructive challenge, strategic guidance, offer specialist advice hold management to account and help develop proposals on strategy;

(b) monitor the performance of senior management in meeting agreed goals and objectives and monitor the reporting of performance;

(c) satisfy yourself on the integrity of financial information and that financial controls and systems of risk management are robust and defensible;

(d) be responsible for determining appropriate levels of remuneration of executive directors and have a prime role in appointing and, where necessary, removing senior management and in succession planning;

(e) insist on receiving high-quality information sufficiently in advance of Board meetings and seek clarification or amplification if you consider the information provided is inadequate or lacks clarity;

(f) make sufficient time available to discharge your responsibilities effectively;

(g) exercise relevant powers under, and abide by, the Articles;

(h) disclose the nature and extent of any direct or indirect interest you may have in any matter being considered at a Board or committee meeting and, except as permitted under the Articles you will not vote on any resolution of the Board, or of one of its committees, on any matter where you have any direct or indirect interest;

(i) immediately report your own wrongdoing or the wrongdoing or proposed wrongdoing of any employee or other director of the Company of which you become aware to the Chair of the Audit Committee;

(j) exercise your powers as a director in accordance with the Company's policies and procedures and the Bribery Act 2010; and

(k) not do anything that would cause you to be disqualified from acting as a director.

2.7 Unless the Board specifically authorises you to do so, you shall not enter into any legal or other commitment or contract on behalf of or with the Company.

2.8 You shall be entitled to request all relevant information about the Company's affairs as is reasonably necessary to enable you to discharge your duties.

2.9 If you are required to register yourself or your personal service company with HM Revenue and Customs as a "Trust or Company Service Provider" under the Money Laundering, Terrorist Financing and Transfer of Funds (Information on the Payer) Regulations 2017, you will be responsible for effecting such registration and for compliance with other requirements of the Money Laundering, Terrorist Financing and Transfer of Funds (Information on the Payer) Regulations 2017 and applicable legislation.

2.10 Notwithstanding anything to the contrary in this Article 2, you acknowledge and agree that in your capacity as director, you will have such duties, authorities and responsibilities and other obligations as provided under the Company's articles of incorporation and bylaws and charter documents, in each case, as in effect from time to time, and you will act in compliance with the applicable rules and regulations promulgated by the SEC and Nasdaq.

2.11 You acknowledge and agree that in your capacity as director, you are acting solely as an independent contractor and not as an employee, legal representative or agent of the Company.

3. CONFIDENTIALITY

3.1 You acknowledge that all information acquired during your appointment is confidential to the Company and should not be released, communicated or disclosed to third parties or used for any reason other than in the interests of the Company, either during your appointment or following termination (by whatever means), without prior clearance from the Board (or a committee thereof). This restriction shall cease to apply to any confidential information which may (other than by reason of your breach) become available to the public generally.

3.2 You acknowledge the need to hold and retain Company information (in whatever format you may receive it) under appropriately secure conditions.

3.3 Nothing in this paragraph 3 shall prevent you from disclosing information which you are entitled to disclose under the Public Interest Disclosure Act 1998, provided that the disclosure is made in accordance with the provisions of that Act and you have complied with the Company's policy from time to time in force regarding such disclosures.

3.4 Nothing in this Agreement shall be construed to prohibit you from reporting or disclosing information or reporting possible violations of federal or state law or regulations to any governmental agency or self-regulatory organisation with oversight responsibility for the Company, or making other disclosures that are protected under whistleblower or other provisions of any applicable federal or state law or regulations (it being understood that prior authorisation of the Company is not required to make any such reports or disclosures, and you are not required to notify the Company that you have made such reports or disclosures).

4. TIME COMMITMENT

4.1 You will be expected to devote such time as is necessary for the proper performance of your duties. This will include attendance at Board meetings, Board committee meetings, the AGM, meetings with the other non-executive directors, meetings with shareholders, meetings forming part of the Board evaluation process and updating. In addition, you will be required to consider all relevant papers before each meeting.

4.2 The nature of the role makes it impossible to be specific about the maximum time commitment. You may be required to devote additional time to the Company in respect of preparation time and ad hoc matters which may arise, and particularly when the Company is undergoing a period of increased activity. At certain times it may be necessary to convene additional Board, committee or shareholder meetings.

4.3 The overall time commitment stated in paragraph 4.1 will increase if you become a committee member or chair, or if you are given additional responsibilities, such as being appointed as non-executive director on the boards of any of the Company's subsidiaries. Details of the expected increase in time commitment will be covered in any relevant communication confirming the additional responsibility.

4.4 By accepting this appointment, you confirm that, taking into account all of your other commitments, you are able to allocate sufficient time to the Company to discharge your responsibilities effectively. You should obtain the agreement of the Chairman and the Nomination Committee before accepting additional commitments that might affect the time you are able to devote to your role as a non-executive director of the Company.

5. APPOINTMENT

5.1 Subject to the provisions of this letter, including but not limited to clauses 5.2 and 5.4 below, your appointment shall be for a term of three years commencing on the Effective Date until the conclusion of the Company's annual general meeting (**AGM**) occurring approximately three years from that date, unless terminated earlier by either party giving to the other three months' prior written notice.

5.2 Your appointment is subject to the Company's articles of association, as amended from time to time (**Articles**). Nothing in this letter shall be taken to exclude or vary the terms of the Articles as they apply to you as a director of the Company. Your appointment is subject to confirmation by the shareholders at the next AGM, and at any subsequent AGM as required by the Articles or as the Board resolves.

5.3 Continuation of your appointment is contingent on your continued satisfactory performance and any relevant statutory provisions relating to removal of a director. If the shareholders do not re-elect you as a director, or you are retired from office under the Articles, your appointment shall terminate automatically, with immediate effect and without compensation , other than earned but unpaid fees and unreimbursed business expense reasonably incurred, and except as otherwise provided in any equity compensation plan or award.

5.4 Any term renewal is subject to Board review and AGM re-election. Notwithstanding any mutual expectation, there is no right to re-nomination by the Board, either annually or after any three-year period.

5.5 You may be required to serve on one or more Board committees. You will be provided with the relevant terms of reference on your appointment to such a committee. You may be required to serve as a non-executive director on the board of any of the Company's subsidiaries and will be provided with the relevant terms of reference on your appointment to such board(s). Except as otherwise determined by the Board or an authorised Board committee, you will not receive any additional compensation for service on any such Board committee or any subsidiary board.

5.6 Notwithstanding paragraph 5.1 to paragraph 5.5, the Company may terminate your appointment with immediate effect if you have:

(a) committed a material breach of your obligations under this letter;

(b) committed any serious or repeated breach or non-observance of your obligations to the Company (which include an obligation not to breach your statutory, fiduciary or common-law duties);

(c) been guilty of any fraud or dishonesty or acted in any manner which, in the Company's opinion, brings or is likely to bring you or the Company into disrepute or is materially adverse to the Company's interests;

(d) been convicted of an arrestable criminal offence other than a road traffic offence for which a fine or non-custodial penalty is imposed;

(e) been declared bankrupt or have made an arrangement with or for the benefit of your creditors, or if you have a county court administration order made against you under the County Court Act 1984;

(f) been disqualified from acting as a director; or

(g) not complied with the Company's anti-corruption and bribery policy and procedures.

5.7 On termination of your appointment, you shall, at the Company's request, resign from your office as non-executive director of the Company and any offices you hold in any of the Company's group companies.

5.8 If matters arise which cause you concern about your role, you should discuss these matters with the Chief Executive and Chairman (who may determine that discussion with the Board (or a committee thereof) is appropriate). If you have any concerns which cannot be resolved, and you choose to resign for that, or any other, reason, you should provide an appropriate written statement to the Chief Executive for circulation to the Board.

6. INDEPENDENT PROFESSIONAL ADVICE

In some circumstances you may consider that you need professional advice in the furtherance of your duties as a non-executive director and it may be appropriate for you to seek advice from independent advisers at the Company's expense. A copy of the Board's agreed procedure under which directors may obtain such independent advice is available from the Company's General Counsel. The Company shall reimburse the reasonable cost of expenditure incurred by you in accordance with its policy. For the avoidance of doubt, nothing in this paragraph 6 shall be construed to limit any right of the Board or any committee thereof, under any charter document or rule of any stock exchange or regulatory authority or otherwise, to retain and/or receive the advice of outside compensation consultants, legal counsel and other advisers or limit any obligation of the Company to provide appropriate funds for the compensation of any such outside advisers.

7. OUTSIDE INTERESTS

7.1 You have already disclosed to the Board the significant commitments you have outside your role in the Company. You must inform the Chief Executive or the Nomination Committee in advance of any changes to these commitments. In certain circumstances, you may have to seek the Board's agreement before accepting further commitments which either might give rise to a conflict of interest or a conflict with any of your duties to the Company, or which might impact on the time that you are able to devote to your role at the Company.

7.2 It is accepted and acknowledged that you have business interests other than those of the Company and have declared any conflicts that are apparent at present. If you become aware of any further potential or actual conflicts of interest, these should be disclosed to the Chairman, the Chief Executive and the Nomination Committee as soon as you become aware of them and again you may have to seek the agreement of the Board.

8. INSIDE INFORMATION AND DEALING IN THE COMPANY'S SHARES

8.1 Your attention is drawn to the requirements under both law and regulation as to the disclosure of inside information, in particular to the Market Abuse Regulation (596/2014/EU), section 52 of the Criminal Justice Act 1993 on insider dealing, as well as section 10(b) and section 16(b) of the US Exchange Act and SEC Rule 10b-5. You should avoid making any statements or taking any other action that might risk a breach of these requirements. If in doubt, please contact the Chief Executive or General Counsel.

8.2 During your period of appointment you are required to comply with any applicable regulations or laws in relation to dealing in the Company's publicly traded or quoted securities including, section 10(b) and section 16(b) of the US Exchange Act and SEC Rule 10b-5, the Sarbanes-Oxley Act and any other code or policy as the Company may adopt from time to time which sets out the terms for dealings by directors in the Company's securities. A copy of the current share dealing code adopted by the Company will be provided to you separately.

9. REVIEW PROCESS

The performance of individual directors and the whole Board and its committees is evaluated annually. If, in the interim, there are any matters which cause you concern about your role you should discuss them with the Chief Executive or the Nomination Committee as soon as you can.

10. INSURANCE AND INDEMNITY

10.1 The Company has directors' and officers' liability insurance and it intends to maintain such cover for the full term of your appointment at a level customary for companies in the pharmaceutical industry of a similar size and stage of development. A copy of the policy document is available from the Company's General Counsel.

10.2 The Company shall grant you a deed of indemnity against certain liabilities that may be incurred as a result of your office to the extent permitted by section 234 of the Companies Act 2006 and Delaware General Corporation Law.

11. CHANGES TO PERSONAL DETAILS

You shall advise the General Counsel promptly of any change in your address or other personal contact details.

12. RETURN OF PROPERTY

On termination of your appointment with the Company however arising, or at any time at the Board's request, you shall immediately return to the Company all documents, records, papers or other property belonging to the Company or any company in the Company's group which may be in your possession or under your control, and which relate in any way to the Company's or a group company's business affairs and you shall not retain any copies thereof.

13. MORAL RIGHTS

You hereby irrevocably waive any moral rights in all works prepared by you, in the provision of your services to the Company, to which you are now or may at any future time be entitled under Chapter IV of the Copyright Designs and Patents Act 1988 or any similar provisions of law in any jurisdiction, including (but without limitation) the right to be identified, the right of integrity and the right against false attribution, and agree not to institute, support, maintain or permit any action or claim to the effect that any treatment, exploitation or use of such works or other materials, infringes your moral rights.

14. DATA PROTECTION

14.1 The Company will hold, collect and otherwise process certain personal data as set out in the Company's privacy notice, which is available on the intranet or the Company's Human Resources department. All personal data will be treated in accordance with applicable data protection laws and regulations.

15. THIRD PARTY RIGHTS

No one other than you and the Company shall have any rights to enforce the terms of this letter.

16. ENTIRE AGREEMENT

16.1 This letter and any document referred to in it constitutes the entire terms and conditions of your appointment and supersedes and extinguishes all previous agreements, promises, assurances, warranties, representations and understandings between you and the Company, whether written or oral, relating to its subject matter.

16.2 You agree that you shall have no remedies in respect of any representation, , assurance or warranty (whether made innocently or negligently) that is not set out in this letter and you shall not have any claim for innocent or negligent misrepresentation based on any statement in this letter.

17. VARIATION

No variation of this letter shall be effective unless it is in writing and signed by you and the Company (or respective authorised representatives).

18. GOVERNING LAW AND JURISDICTION

Your appointment with the Company and any dispute or claim arising out of or in connection with it or its subject matter or formation (including non-contractual disputes or claims) shall be governed by and construed in accordance with the law of England and Wales and you and the Company irrevocably agree that the courts of England and Wales shall have exclusive jurisdiction to settle any dispute or claim that arises out of or in connection with this appointment or its subject matter or formation (including non-contractual disputes or claims).

19. TAXES

19.1 Fees payable pursuant to this Appointment may be subject to deductions for UK income tax and National Insurance contributions as required by law. You are responsible for the payment of all federal, state or local taxes payable in any other jurisdictions.

19.2 This letter agreement is intended to comply with or be exempt from Section 409A of the Internal Revenue Code of 1986, as amended (**Code**) or an exception thereunder and shall be interpreted, construed and administered in accordance therewith. Notwithstanding the foregoing, the Company makes no representations that the payments or benefits provided under this letter comply with or are exempt from Code Section 409A and in no event shall the Company be liable for all or any portion of any taxes, penalties, interest or other expenses that may be incurred by the you as a result of this letter failing to comply with or be exempt from Code Section 409A. To the extent that any reimbursements are subject to Code Section 409A, any such reimbursement payment due to you shall be paid to you in all events on or before the last day of your taxable year following the taxable year in which the related expense was incurred. The reimbursements are not subject to liquidation or exchange for another benefit and the amount of such benefits and reimbursements that you receive in one taxable year shall not affect the amount of such benefits or reimbursements that you receive in any other taxable year.

Please indicate your acceptance of these terms by signing and returning to the attached copy of this letter to Dr. Denise Scots-Knight, Chief Executive, Mereo BioPharma Group plc.

Yours sincerely

_____

For and on behalf of Mereo BioPharma Group plc

I agree to the above terms of my appointment as a non-executive director of Mereo BioPharma Group plc as set out in this letter.

Signed on **by**

_____

[*name*]

Exhibit 4.46

DEED OF CONSENT AND AMENDMENT TO NOTE INSTRUMENT

THIS DEED is dated February 2023

BETWEEN:

(1) **MEREO BIOPHARMA GROUP PLC**, a public limited company incorporated in England and Wales with company number 04206001 whose registered office is at 4th Floor, One Cavendish Place, London, England W1G 0QF (the "**Company**"); and

(2) **NOVARTIS PHARMA AG**, a company incorporated and registered in Switzerland whose registetered office is at Postfach, 4002 Basel Switzerland ("**Novartis**").

WHEREAS

(A) The Company adopted a convertible loan note instrument on 10 February 2020, as subsequently amended on 24 November 2020, a copy of which is appended hereto as Appendix 1 (the "**Note Instrument**") constituting certain loan notes convertible into Ordinary Shares in the capital of the Company (the "**Notes**").

(B) Pursuant to the Note Instrument the principal amount outstanding under the Notes (and any accrued and unpaid interest thereon) will become due and payable in full on 10 February 2023 (the "**Effective Date**").

(C) The Company and Novartis have agreed, with effect from the Effective Date, to extend the Maturity Date of the Notes to 10 February 2025 (the "**Maturity Date Extension**") in consideration for:

(i) the issue by the Company to Novartis of 2,000,000 warrants to subscribe for ordinary shares of £0.003 each in the capital of the Company (the "**2023 Warrants**"), on the terms and subject to the conditions set out in the warrant instrument attached hereto at Appendix 2 (the "**2023 Warrant Instrument**");

(ii) the payment by the Company to Novartis of a cash amount of £691,466.22, such amount being equal to the accrued and unpaid interest on the Notes up to and including 10 February 2023 (the "**Accrued Interest Sum**"); and

(ii) the amendment of certain additional terms of the Note Instrument (together with the Maturity Date Extension, the "**Note Amendment**").

(D) The parties are entering into this Deed to document the Note Amendment and the arrangements for issuance of the 2023 Warrants and payment of the Accrued Interest Sum.

IT IS AGREED AS FOLLOWS:

1. INTERPRETATION

Terms defined in the Note Instrument shall have the same meanings as given therein when used in this Deed unless otherwise defined herein.

2. AMENDMENT CONSENT AND AGREEMENT TO ISSUE 2023 WARRANTS

2.1 Amendment

2.1.1 The current definition of "*Interest Rate*" at clause 1.1 of the Note Instrument shall, as of the Effective Date, be deleted in its entirety and replaced with the following wording

Interest Rate	*(i) from the date of this instrument to and including 10 February 2023, a rate of 6% per annum; and* *(ii) from 11 February 2023 to the Maturity Date, a rate of 9% per annum*

2.1.2 The current definition of "*Maturity Date*" at clause 1.1 of the Note Instrument, shall, as of the Effective Date, be deleted in its entirety and replaced with the following wording:

Maturity Date	*10 February 2025*

2.1.3 The current paragraph 1 (*Interest*) at Schedule 2 to the Note Instrument shall, as of the Effective Date, be deleted in its entirety and replaced with the following wording:

1.1 Interest shall be payable on any outstanding Notes (so far as not converted under Schedule 3) at the applicable Interest Rate.

1.2 Any interest due under paragraph 1.1 of this Schedule 2 shall be payable in immediately available funds on the Maturity Date, unless the Noteholder elects to convert the accrued interest to Ordinary Shares in accordance with Part 2 of Schedule 3 (or such interest has otherwise been satisfied, whether by payment in cash or otherwise in a manner agreed between the Noteholder and the Company).

1.3 Interest, if payable, shall accrue daily at the applicable Interest Rate and shall be calculated on the basis of a 365-day year and the actual number of days elapsed from and including 11 February 2023 to the Redemption Date.

1.4 If the Company fails to pay redemption monies when due, interest shall continue to accrue on the unpaid amount at the applicable Interest Rate.

2.1.1 The current paragraph 4 (*Redemption*) at Schedule 2 to the Note Instrument shall, as of the Effective Date, be deleted in its entirety and replaced with the following wording:

4.1 The Notes then in issue (so far as not converted under Schedule 3) shall, to the extent not previously converted, be redeemed at the principal amount together with interest on the Notes outstanding at the applicable Interest Rate on the Maturity Date (to the extent such interest has not already been satisfied, whether by payment in cash or otherwise).

4.2 Within five Business Days of the Redemption Date, the Company shall repay to the Noteholder the principal amount of the Notes so redeemed, together with interest on such Notes outstanding at the Interest Rate (to the extent such interest has not already been satisfied, whether by payment in cash or otherwise).

2.2 Consent, 2023 Warrants and Accrued Interest Sum

2.2.1 By their execution of this Deed Novartis hereby grant consent to the Note Amendment and the provisions of this Deed (including the transactions contemplated herein) and in consideration for such consent, the Company undertakes that it shall:

(a) issue the 2023 Warrants to Novartis on the Effective Date in accordance with the terms of the 2023 Warrant Instrument, and deliver a duly executed copy of the 2023 Warrant Instrument to Novartis within 3 Business Days of such date; and

(b) pay the Accrued Interest Sum to the following bank account:

Name: Novartis Pharma AG

Bank: HSBC Bank plc

Address: 8 Canada Square, Canary Wharf, London E14 5HQ

Account: 21343610

Sort Code: 40-02-50

BIC: MIDLGB22

or such other bank account as is notified by Novartis to the Company in writing, within 3 Business Days of the Effective Date.

3. ADDITIONAL AGREEMENTS

3.1 Any Ordinary Shares to be issued by the Company to Novartis or any permitted transferee under the 2023 Warrants shall be issued in accordance with Regulation S under the Securities Act or another exemption from the registration requirements of the Securities Act.

3.2 Each 2023 Warrant shall bear a legend stating that the warrant and the securities to be issued upon its exercise have not been registered under the Securities Act and that the warrant may not be exercised by or on behalf of any U.S. person unless registered under the Securities Act or an exemption from such registration is available

3.3 Each person exercising a 2023 Warrant is required to give:

(i) a written certification that it is not a U.S. person and the warrant is not being exercised on behalf of a U.S. person; or

(ii) a written opinion of counsel to the effect that the warrant and the securities delivered upon exercise thereof have been registered under the Securities Act or are exempt from registration thereunder.

3.4 The 2023 Warrants may not be exercised within the United States, and the Ordinary Shares issuable upon exercise thereof may not be delivered within the United States unless registered under the Securities Act or an exemption from such registration is available.

3.5 Notwithstanding the terms of the any of the Note Instrument and the 2023 Warrant Instrument, the Company and Novartis shall promptly take all action reasonably advisable to enable all Underlying Securities to be deposited with the Depositary outside of any segregated ADS facility as may be imposed pursuant to Rule 144 of the Securities Act of 1933. For the avoidance of doubt, such actions shall include (i) the execution of any issuance and delivery instruction in a form substantially similar to that included in Schedule 3 of the 2023 Warrant Instrument and (ii) if the Depositary requires any opinion of counsel regarding the free tradability of the Underlying Securities, an opinion of external counsel of the Company in a form satisfactory to the Depositary. Novartis understands and agrees that Ordinary Shares issued upon exercise of 2023 Warrants will become eligible for deposit into the unrestricted ADS following the end of the Regulation S distribution compliance period of forty (40) days from the date of issuance. All expenses incurred in connection with the foregoing actions, including any opinion of counsel, shall be borne by the Company.

3.6 The Company covenants that by 31 December 2024, it shall cause to be registered on Form F-3 or Form S-3 and the related prospectus supplement all but not less than all of the securities issuable to Novartis or any permitted transferee under the 2023 Warrants and, to the extent such registration is no longer valid: (i) the Notes and (ii) the 1,449,614 warrants to subscribe for ordinary shares of 0.003 each in the capital of the Company (the "**2020 Warrants**") issued to Novartis pursuant to the Warrant Instrument of by the Company dated 10 February 2020 (the "**2020 Warrant Instrument**",

and all such securities referenced above, together the "**Underlying Securities**") to be offered on a delayed or continuous basis pursuant to Rule 415 of the Securities Act. All expenses incurred in connection with the registration of the Underlying Securities on Form F-3 or Form S-3, including all registration, filing, and qualification fees, printers' and accounting fees, and fees and disbursements of counsel for the Company, shall be borne by the Company.

4. MISCELLANEOUS

4.1 This Deed shall be governed by and construed in accordance with English law and the parties submit to the exclusive jurisdiction of the English courts.

4.2 Any amounts payable by any party pursuant to this Deed and/or the Notes shall be paid free and clear of all withholdings or deductions, save as may be required by law.

4.3 This Deed may be executed in counterparts which together shall constitute one document.

Appendix 1

Note Instrument

Appendix 2

2023 Warrant Instrument

IN WITNESS WHEREOF this agreement has been executed as a deed and delivered by the parties on the date first above written.

Executed and delivered as a **DEED** by **MEREO BIOPHARMA GROUP PLC** acting by

_____ _____ *Director*
a Director

_____ _____ *Director/Company Secretary*
Director/Company Secretary

Executed and delivered as a **DEED** by **NOVARTIS PHARMA AG** acting by

_____ _____ *Authorised Signatory*
Authorised Signatory

_____ _____ *Authorised Signatory*
Authorised Signatory

Exhibit 4.47

DATED 2023

MEREO BIOPHARMA GROUP PLC

WARRANT INSTRUMENT
relating to the issue of warrants entitling the holders to
subscribe for Warrant Shares in the capital of
MEREO BIOPHARMA GROUP PLC

CONTENTS

1	DEFINITIONS AND INTERPRETATION	2
2	CONSTITUTION AND FORM OF WARRANTS	6
3	NUMBER OF WARRANT SHARES	6
4	CERTIFICATES	6
5	TIMING FOR EXERCISE OF SUBSCRIPTION RIGHTS	7
6	EXERCISE OF SUBSCRIPTION RIGHTS	7
7	COMPLETION	8
8	TRANSFER OF WARRANTS	9
9	MODIFICATION AND CESSATION OF RIGHTS	9
10	INFORMATION AND RIGHTS OF WARRANTHOLDER(S)	10
11	RESTRICTIONS ON AND UNDERTAKINGS OF THE COMPANY	10
12	WARRANTIES	11
13	NOTICES	11
14	COSTS AND EXPENSES	
15	CONTRACTS (RIGHTS OF THIRD PARTIES) ACT 1999	11
16	FURTHER ASSURANCE	11
17	SEVERABILITY	11
18	GOVERNING LAW	11
SCHEDULE 1 FORM OF WARRANT CERTIFICATE		13
SCHEDULE 2 CONDITIONS		17

THIS WARRANT INSTRUMENT is made on 2023

BY:

(1) **MEREO BIOPHARMA GROUP PLC,** a public limited company incorporated in England and Wales with company number 04206001 whose registered office is at 4th Floor, One, Cavendish Place, London, England, W1G 0QF ("**Company**").

BACKGROUND:

(A) The Company, by resolution of its directors, has agreed to issue 2023 Warrants to subscribe for Warrant Shares in the capital of the Company on the terms set out in this instrument.

(B) Either all of the registered holders of shares in the Company have irrevocably waived all pre-emption rights conferred on them (whether by the Companies Act, the Articles or otherwise) or such pre-emption rights have been validly disapplied in relation to the number of 2023 Warrants and shares in the Company issued pursuant to this instrument.

(C) This instrument has been executed by the Company as a deed in favour of the Warrantholder.

IT IS AGREED:

1 **DEFINITIONS AND INTERPRETATION**

1.1 In this instrument the following words and expressions shall (unless the context requires otherwise) have the following meanings:

2023 Warrants	the warrants of the Company constituted by this instrument and all rights conferred by it (including the Subscription Rights);
ADS	means American Depositary Shares representing interests in the Ordinary Shares pursuant to a sponsored American Depositary Receipt facility with the Depositary;
ADS Exchange Ratio	means the ratio applicable to the exchange of Ordinary Shares for ADSs from time to time, which, as at the date of this instrument, is a ratio of 5 Ordinary Shares for each ADS;
AIM	the AIM market operated by the London Stock Exchange;
Articles	the articles of association of the Company for the time being;
Auditors	the Company's auditors;

Business Day	a day (which for these purposes ends at 5.30 pm) on which banks are open for commercial business in the City of London and New York City other than a Saturday or Sunday;
Companies Act	the Companies Act 2006;
Competitor	means any entity (other than a reputable financial institution) whose business directly competes with the business carried out by a Group Company;
Conditions	the terms and conditions set out in Schedule 2 (subject to any alterations made in accordance with the provisions of this instrument);
Consent	the consent in writing of the Warrantholder(s) for the time being holding outstanding 2023 Warrants subject to outstanding Subscription Rights;
Depositary	means the Depositary engaged by the Company for the issuance and transfer of ADSs;
Directors	the board of directors of the Company (and/or, where relevant, a Group Company) for the time being;
Effective Date	has the meaning given in the Note Amendment Deed;
Exercise Date	the date of delivery to the registered office of the Company of the items specified in clause 6.2 (and the date of such delivery shall be the date on which such items are received at the Company's registered office);
Final Date	5 years from the Effective Date;
Issuance and Delivery Instruction	means an issuance and delivery instruction in such form as notified from the Company to the Warrantholder from time to time, the current form of which is attached hereto at Schedule 3;
Issue Date	the Effective Date;
London Stock Exchange	London Stock Exchange plc;
Group	(i) the Company and its subsidiaries (if any), (ii) any holding company of the Company, and (iii) any subsidiaries of such holding companies from time to time and **Group Company** means any member of the Group;
Notice of Subscription	the notice addressed to the Company by a Warrantholder exercising its Subscription Rights in the form, or substantially in the form, set out in the schedule to the Warrant Certificate;

Note Amendment Deed	a deed of consent and amendment between the Company and the Warrantholder dated on or about the date hereof;
Ordinary Shares	ordinary shares in the capital of the Company and having the rights and privileges set out in the Articles;
Permitted Transferee	are: (a) a nominee of the Warrantholder; (b) a subsidiary of the Warrantholder; (c) a holding company of the Warrantholder; and (d) any subsidiaries of such holding companies from time to time.
Recognised Investment Exchange	a recognised investment exchange or overseas investment exchange (within the meaning thereof given for the purposes of section 285 of the Financial Services and Markets Act 2000, and shall include, without limitation, AIM or NASDAQ);
Register	the register of persons for the time being entitled to the benefit of the 2023 Warrants to be maintained pursuant to the Conditions;
Registrars	the registrars of the Company for the time being;
Subscription Price	the implied price of one Ordinary Share (which shall be determined by dividing (x) being the volume weighted average price of one ADS on the trading day immediately prior to the Issue Date by (y) being the number of Ordinary Shares currently represented by a single ADS in accordance with the ADS Exchange Ratio, as converted into pounds sterling by the Company applying the relevant U.S. dollar to GBP sterling exchange rate using the closing rate published by Bloomberg at 9:00 P.M., London time, the day prior to the Issue Date;
Subscription Rights	the rights of the Warrantholder(s) to subscribe for Warrant Shares under clause 6;
Warrant Certificate	a certificate evidencing a Warrantholder’s entitlement to 2023 Warrants in the form set out in Schedule 1;

Warrant Shares	Ordinary Shares to be issued pursuant to the terms of the 2023 Warrants;
Warrantholder	in relation to a 2023 Warrant, the person whose name appears in the Register as the holder of the 2023 Warrant.

1.2 In this instrument, unless the context otherwise requires:

1.2.1 words and expressions defined in the Companies Act or the Articles shall have the same meanings in this instrument (unless otherwise expressly defined in this instrument);

1.2.2 headings are used for convenience only and shall be ignored in interpreting this instrument;

1.2.3 reference to a clause or schedule is a reference to a clause of, or schedule to, this instrument;

1.2.4 reference to (or to any specific provision of) this instrument or any other document or instrument shall be construed as a reference to this instrument, that provision or that document or instrument as in force for the time being and as amended from time to time in accordance with its terms and the prior sanction of a Consent (where consent is required by the terms of this instrument as a condition to such amendment being made);

1.2.5 reference to any gender includes all genders, references to the singular includes the plural (and vice versa) and reference to persons includes bodies corporate, unincorporated associations and partnerships (whether or not any of the same have a separate legal personality);

1.2.6 reference to a statutory provision includes reference to:

(a) the statute or statutory provision as modified or re-enacted from time to time; and

(b) any subordinate legislation made under the statutory provision (as modified or re-enacted as set out in clause 1.2.6(a) above);

1.2.7 any words following the terms ‘including’, ‘include’, ‘in particular’, ‘for example’ or any other similar expression shall be construed as illustrative and shall not limit the sense of the words, description, phrase or term preceding those words; and

1.2.8 references to statutory obligations include obligations arising under articles of the Treaty establishing the European Community, and regulations, directives and decisions of the European Union as well as United Kingdom Acts of Parliament and subordinate legislation.

1.3 Unless otherwise specifically provided, where any notice, resolution or document is required by this instrument to be signed by any person, the reproduction of the signature of such person by fax or email shall suffice, provided that confirmation by first class letter is despatched by close of business on the next following Business Day, in which case the effective notice, resolution or document shall be that sent by fax or email (served in accordance with paragraphs 11 and 12 of Schedule 2), not the confirmatory letter.

1.4 This instrument incorporates the schedules to it.

2 CONSTITUTION AND FORM OF WARRANTS

2.1 This instrument constitutes the 2023 Warrants, which in aggregate give the Warrantholder(s) the right, upon the terms and subject to the conditions set out in this instrument, to subscribe in cash at a price per share equal to the Subscription Price for such number of Warrant Shares as is set out in clause 3.

2.2 Each Warrantholder shall be entitled to subscribe in cash at the Subscription Price for that number of Warrant Shares in respect of which it is entitled to be recorded as the holder in the Register on the terms set out in this instrument.

2.3 The 2023 Warrants shall be in registered form.

2.4 The 2023 Warrants are issued subject to the Articles and otherwise on the terms of this instrument (including the Conditions).

2.5 The Company agrees with the Warrantholder(s) and, in consideration of being issued a Warrant Certificate, each Warrantholder agrees with the Company that the Articles (insofar as they relate to the Warrants) and the terms of this instrument shall be binding upon the Company and each Warrantholder and all persons claiming through or under either of them.

2.6 No application will be made for the 2023 Warrants to be listed or dealt on any Recognised Investment Exchange (as that term is defined in the Financial Services and Markets Act 2000 (as amended)).

3 NUMBER OF WARRANT SHARES

The number of Warrant Shares over which 2023 Warrants will be issued is 2,000,000.

4 CERTIFICATES

4.1 The Company shall issue to each Warrantholder a Warrant Certificate in respect of that number of 2023 Warrants to which it is entitled as soon as reasonably practicable following a Warrantholder becoming entitled to such 2023 Warrants in accordance with clause 3.

4.2 If a Warrant Certificate is mutilated, defaced, lost, stolen or destroyed, the Company will replace it on such terms as to evidence and indemnity as the Company may reasonably require and subject to the Warrantholder who is seeking the replacement paying the Company’s reasonable costs (if any) in connection with the issue of the replacement.

4.3 Mutilated or defaced Warrant Certificates must be surrendered before replacements will be issued.

5 TIMING FOR EXERCISE OF SUBSCRIPTION RIGHTS

5.1 The Subscription Rights may be exercised at any time from the date of this instrument until 17:00 GMT on the Final Date and shall be exercised in accordance with clause 6.

5.2 A failure by any Warrantholder to exercise its Subscription Rights ahead of such time on the Final Date shall mean that such Warrantholder's outstanding 2023 Warrants shall immediately lapse and be cancelled and such Warrantholder shall have no further rights under this instrument.

6 EXERCISE OF SUBSCRIPTION RIGHTS

6.1 The Subscription Rights may be exercised in whole or in part at any time.

6.2 In order to exercise its Subscription Rights validly, a Warrantholder must deliver the following items to the registered office of the Company:

6.2.1 the Warrant Certificate for the 2023 Warrants in respect of which the Subscription Rights are being exercised, together with the Notice of Subscription duly completed;

6.2.2 the name and address of the Warrantholder to which the Warrant Shares arising on an exercise of Subscription Rights are to be issued (or, if such shares are to be delivered as ADSs, the name and address of the custodian (or its nominee) of the Depositary; and

6.2.3 if and to the extent that the Ordinary Shares issued are to be delivered as ADSs, a completed Issuance and Delivery Instruction in the form set out at Schedule 3 hereto (as such form may be amended from time to time by notice to the Warrantholder) duly completed and executed by the Warrantholder.

6.3

6.3.1 The Subscription Price for each of the Warrant Shares shall be made by electronic wire transfer of immediately available funds to such account as is notified by the Company within 3 Business Days of the relevant Notice of Subscription delivered pursuant to clause 6.2.1 and no Warrant Shares shall be issued to the Warrantholder (or, in the case of Ordinary Shares to be delivered as ADSs, issued to the custodian (or its nominee) of the Depositary) until the aggregate Subscription Price has been satisfied.

6.3.2 In the event of any failure by a Warrantholder to deliver a duly completed Issuance and Delivery Instruction within 3 Business Days of delivering its Notice of Subscription, the Company shall disregard the Warrantholder's request for delivery of the relevant Ordinary Shares as ADSs and shall issue the number of Ordinary Shares specified in the Notice of Subscription to the Warrantholder in accordance with clause 7.

6.4 In the event that a Warrantholder requires Ordinary Shares arising on exercise of the 2023 Warrants to be delivered as ADSs, the entitlement of such Warrantholder to ADSs shall be calculated using the ADS Exchange Ratio. No fractional ADSs will be issued, and any fractional entitlements to an ADS shall be issued to the relevant Warrantholder in the form of Ordinary Shares in accordance with clauses 6 and 7 of this instrument, rounded down to the nearest whole share.

7 COMPLETION

7.1 Following a valid exercise of Subscription Rights by a Warrantholder, the Company shall in accordance with clause 7.3:

7.1.1 allot and issue credited as fully paid the Warrant Shares to which the Warrantholder is entitled by exercising the Subscription Rights (the "**Allotted Shares**") to:

(a) the Warrantholder (or to its nominee or trustee as notified to the Company in the Notice of Subscription); or

(b) in the event that the Warrantholder has required pursuant to clause 6.2 that Ordinary Shares to be issued from the Exercise of Subscription Rights are to be delivered as ADSs and delivered a duly completed Issuance and Delivery Instruction, and there is an effective registration statement covering the Ordinary Shares to be issued on such exercise, issue to, deposit with (and otherwise register in the name of) the custodian of the Depositary (or its nominee), and following such issuance and deposit the Company will direct the Depositary to issue an amount of ADSs via DTC (with such ADSs being eligible for listing on Nasdaq) in accordance with the corresponding Issuance and Delivery Instruction;

7.1.2 immediately following allotment and issue in accordance with clause 7.1.1, enter, or procure that the Company's Registrars enter (i) the Warrantholder's name (or its nominee's or trustee's name) or (ii) in the case of any Ordinary Shares to be delivered as ADSs, the name of the custodian (or its nominee) of the Depositary in the register of members of the Company as the holder of the Allotted Shares; and

7.1.3 immediately following entry into the register of members in accordance with clause 7.1.2, send to the person identified by the Warrantholder pursuant to clause 7.1.1 free of charge, share certificate(s) in respect of the Allotted Shares (other than any Allotted Shares delivered as ADSs, in respect of which no share certificate shall be issued to the custodian of the Depositary.

7.2 The obligations of the Company under clause 7.1 shall be fulfilled:

7.2.1 where the Allotted Shares are to be delivered as Ordinary Shares, within ten (10) days after the Notice of Subscription is lodged at the registered office of the Company; or

7.2.2 where the Allotted Shares are to be delivered as ADSs, within thirty (30) days after the Notice of Subscription is lodged at the registered office of the Company or as soon as reasonably practicable thereafter.

7.3 The Allotted Shares shall:

7.3.1 be allotted and issued fully paid;

7.3.2 rank pari passu with the Ordinary Shares of the Company then in issue;

7.3.3 rank for any dividend or other distribution which has previously been announced or declared if the date by which the holder of Warrant Shares must be registered to participate in such dividend or other distribution is after the Exercise Date pursuant to which the Subscription Rights have been exercised; and

7.3.4 be free from all claims, liens, charges, encumbrances, equities and third party rights.

7.4 If following allotment of shares pursuant to the exercise of some of the Subscription Rights, some Subscription Rights remain, the Company shall issue a Warrant Certificate to the Warrantholder within 15 Business Days for the balance of the Warrantholder's Subscription Rights.

8 TRANSFER OF 2023 WARRANTS

8.1 Subject to clause 8.2, the 2023 Warrants may be transferred in whole by any Warrantholder to any person, provided that the Company has given its prior written consent to such transfer.

8.2 A Warrantholder has the right, with prior written notice, but without the consent of the Company, to transfer the 2023 Warrants in whole to a Permitted Transferee, subject to compliance with the provisions of Schedule 2 hereto.

8.3 Notwithstanding any other provisions of this instrument, no transfer shall be made to any person which is a Competitor of the Company or any other Group Company.

8.4 The provisions of Schedule 2 to this instrument shall regulate any transfer of a Warrant.

9 MODIFICATION AND CESSATION OF RIGHTS

9.1 This instrument may be modified only with the prior sanction of Consent.

9.2 This instrument ceases to have effect on the earlier of:

9.2.1 the date upon which all Subscription Rights have been exercised in full; and

9.2.2 the Final Date.

10 **INFORMATION AND RIGHTS OF WARRANTHOLDER(S)**

10.1 The Company shall:

10.1.1 at the request of the Warrantholder, send to each Warrantholder a copy of its annual reports and audited accounts together with all documents required by law to be annexed to that report at the same time they are provided to the holders of the Ordinary Shares;

10.1.2 at the request of the Warrantholder, send to each Warrantholder copies of any statements, notices or circulars sent to the holders of the Ordinary Shares; and

10.1.3 give to each Warrantholder written notice of its intention to declare or pay a dividend or other distribution on the Ordinary Shares no later than the date on which notice of the general meeting approving such dividend or distribution is sent to the holders of the Ordinary Shares.

10.2 The Warrantholder(s) may attend all general meetings of members of the Company and meetings of the holders of Ordinary Shares but may not vote at those meetings by virtue of or in respect of their holdings of 2023 Warrants.

10.3 Each Warrantholder shall keep confidential any information received by it in its capacity as a Warrantholder which is of a confidential nature except:

10.3.1 as required by law or any applicable regulations;

10.3.2 to the extent the information is in the public domain through no default of the Warrantholder; and

10.3.3 each Warrantholder will be entitled to divulge such information to any other Warrantholder and any proposed transferee of 2023 Warrants on the same terms as to confidentiality.

11 **RESTRICTIONS ON AND UNDERTAKINGS OF THE COMPANY**

11.1 For so long as the 2023 Warrants are outstanding, the Company will:

11.1.1 to the extent that the Company has a limit on its authorised share capital, keep available for issue and free from pre-emptive rights, out of its authorised but unissued share capital, such number of Warrant Shares as will enable the Subscription Rights of the Warrantholder(s) to be satisfied in full;

11.1.2 ensure that the Directors have all necessary authorisations and disapplications of pre-emption (including under the Companies Act) to allot such number of Warrant Shares as will enable the Subscription Rights of the Warrantholder(s) to be satisfied in full at any time;

11.1.3 notify the Warrantholder before cancelling the admission to trading of the Ordinary Shares on any Recognised Investment Exchange on which the Ordinary Shares are traded from time to time;

11.1.4 not make any issue, grant or distribution or take any other action the effect of which would be that on exercise of any of the Subscription Rights it would be required to issue Warrant Shares at a discount to their nominal value.

12 WARRANTIES

12.1 The Company warrants to the Warrantholder(s) that:

12.1.1 it has the power to execute and to perform its obligations under this instrument;

12.1.2 it has taken all action necessary to authorise the execution of, and the performance of its obligations under this instrument;

12.1.3 all Warrant Shares which may be issued upon the exercise of the rights represented by the 2023 Warrants will be, upon issuance, be duly authorised, validly issued and fully paid and free of any liens and encumbrances

13 NOTICES

Any notice to the Warrantholder(s) required for the purposes of any provision of this instrument shall be given in accordance with the provisions of paragraphs 10 to 13 (inclusive) of Schedule 2.

14 CONTRACTS (RIGHTS OF THIRD PARTIES) ACT 1999

A person who is not a party to this instrument shall have no rights under the Contracts (Rights of Third Parties) Act 1999 to enforce any term of this instrument. This clause does not affect any right or remedy of any person which exists or is available otherwise than pursuant to that Act.

15 FURTHER ASSURANCE

The Company shall, at its own cost and expense, execute all such deeds and documents and do all such acts and things as may reasonably be required in order to give effect to this instrument, including vesting on issue the full legal and beneficial title to the Warrant Shares in the Warrantholder.

16 SEVERABILITY

Each of the provisions of this instrument is distinct and severable from the others and if at any time one or more of such provisions is or becomes valid, unlawful or unenforceable (whether wholly or to any extent), the validity, lawfulness and enforceability of the remaining provisions (or the same provision to any other extent) of this instrument shall not in any way be affected or impaired.

17 GOVERNING LAW

The provisions of this instrument and the Conditions and any dispute or claim arising out of or in connection with them (including any dispute or claim relating to non-contractual obligations) shall be subject to and governed by English law and the Company and the Warrantholder(s) submit to the exclusive jurisdiction of the English Courts in relation to any such dispute or claim.

The Company intends this instrument to be a deed poll and accordingly it or its duly authorised representatives execute and deliver it as such.

SCHEDULE 1
Form Of Warrant Certificate

MEREO BIOPHARMA GROUP PLC ("COMPANY")
A company registered in England and Wales
under Company number 04206001

WARRANT CERTIFICATE

This certificate is issued pursuant to the warrant instrument issued by the Company on _____ 2023 ("**Warrant Instrument**"). Words and expressions used in this certificate which are defined in the Warrant Instrument have the meanings given to them in the Warrant Instrument.

Certificate number:	[●]
Date of issue:	_____ 2023
Name and address of Warrantholder:	[●]

Number of Warrant Shares for which the Warrantholder may subscribe: [●].

This is to certify that the Warrantholder named above is the registered holder of the right to subscribe in cash for Warrant Shares at the subscription price set out above subject to the Articles and otherwise on the terms and conditions set out in the Warrant Instrument (a copy of which is available for inspection at the registered office of the Company).

This Warrant and the ordinary shares of the Company to be issued upon its exercise have not been registered under the Securities Act of 1933, as amended (the "Securities Act"). This Warrant may not be exercised by or on behalf of any U.S. person unless registered under the Securities Act or an exemption from such registration is available.

By exercising this Warrant the Warrantholder hereby certifies that:

(A) It is not a U.S. person and the Warrant is not being exercised on behalf of a U.S. person; or

(B) Is providing a written opinion of counsel to the effect that the Warrant and the ordinary shares of the Company delivered upon exercise thereof have been registered under the Securities Act or are exempt from registration thereunder.

Executed as a **DEED**, but not delivered until the date specified on this instrument, by

MEREO BIOPHARMA GROUP PLC
acting by

_____
Director

_____
Director/Company Secretary

_____*Director*

_____*Director/Company Secretary*

Schedule to the Warrant Certificate

Notice of Subscription

To: The Directors

MEREO BIOPHARMA GROUP PLC ("Company")

This notice is issued pursuant to the warrant instrument issued by the Company on ("**Warrant Instrument**"). Words and expressions used in this notice which are defined in the Warrant Instrument have the meanings given to them in the Warrant Instrument.

We hereby irrevocably elect to exercise [*number*] 2023 Warrants issued to us by the Company pursuant to the Warrant Instrument and purchase thereunder (and surrender herewith the relevant warrant certificate) as follows:

(1)

(A) Warrant Shares to be issued to the Warrantholder (or its nominee or trustee) as Ordinary Shares pursuant to the Warrant Instrument;

(B) Warrant Shares to be issued to the custodian of the Depositary for delivery to the Warrantholder as ADSs pursuant to the Warrant Instrument.

(2) We hereby confirm that we will procure payment in the sum of £[*amount*] being the aggregate Subscription Price for such Warrant Shares.

We direct the Company:

[*use for a request under option (1)(A) above*] to issue [*number*] of Ordinary Shares to be issued pursuant to this exercise in the following numbers to the following proposed allottees, each of which is either a Warrantholder, a nominee or trustee of a Warrantholder or a transferee of one of those persons approved in accordance with clause 8.1 of the Warrant Instrument]

Number/percent age of shares	**Name of proposed allottee**	**Address of proposed allottee**
1		

[*AND/OR*] *use for a request under option (1)(B) above*] to issue, allot, and deposit [*number*] of Ordinary Shares to be issued pursuant to this exercise to the custodian (or its nominee) of the Depositary and that following such issuance and deposit, to direct the Depositary to issue an amount of ADSs via DTC in accordance with the Issuance and Delivery Instruction corresponding to this Notice of Subscription.

The Warrantholder represents and warrants that this Notice of Subscription has been duly signed and constitutes a valid and binding act to exercise the said 2023 Warrants.

Place and date:

Name of Warrantholder:

_____

By:

Title:

The above exercise is acknowledged and accepted.

Place and date:

MEREO BIOPHARMA GROUP PLC

_____

By:

Title:

SCHEDULE 2
Conditions

1 An accurate Register will be kept and maintained at all times by the Company at its registered office and there shall be entered in the Register:

1.1 the names and addresses of the persons for the time being entitled to be registered as the holders of the 2023 Warrants;

1.2 the number of 2023 Warrants held for the time being by every registered holder; and

1.3 the date on which the name of every registered holder is entered in the Register in respect of the 2023 Warrants in its name.

2 Any change in the name or address of any Warrantholder shall promptly be notified to the Company which shall cause the Register to be altered accordingly. The Warrantholders or any of them and any person authorised by any Warrantholder shall be at liberty at all reasonable times during office hours to inspect the Register and to take copies of or extracts from it or any part of it.

3 The Company shall be entitled to treat each Warrantholder as the absolute owner of a 2023 Warrant and accordingly shall not, except as ordered by a court of competent jurisdiction or as required by law, be bound to recognise any equitable or other claim to or interest in a 2023 Warrant on the part of any other person, whether or not it shall have express or other notice of such a claim.

4 Each Warrantholder will be recognised by the Company as entitled to the 2023 Warrants free from any equity, set-off or cross-claim on the part of the Company against the original or any intermediate holder of the 2023 Warrants.

5 Each transfer of a 2023 Warrant shall be made by an instrument of transfer in the usual or common form or in any other form which may be approved for the time being by the Directors.

6 The instrument of transfer of a 2023 Warrant shall be executed by or on behalf of the transferor but need not be executed by or on behalf of the transferee. The transferor shall be deemed to remain the holder of the 2023 Warrant until the name of the transferee is entered in the Register in respect of the 2023 Warrant being transferred.

7 The Directors may decline to recognise any instrument of transfer of a 2023 Warrant unless the instrument is deposited at the registered office of the Company accompanied by the Warrant Certificate for the 2023 Warrant to which it relates, and such other evidence as the Directors may reasonably require to show the right of the transferor to make the transfer. The Directors may waive production of any Warrant Certificate upon production to them of satisfactory evidence of the loss or destruction of the Warrant Certificate together with such indemnity as they may require.

8 No fee shall be charged for any registration of a transfer of a 2023 Warrant or for the registration of any other documents which in the opinion of the Directors require registration.

9 The registration of a transfer shall be conclusive evidence of the approval by the Directors of such a transfer.

10 Each Warrantholder shall register with the Company an address to which notices can be sent. If any Warrantholder fails to register an address with the Company, notice may be given to that Warrantholder by sending it by any of the methods referred to in paragraph 11 of this Schedule 2 to that Warrantholder's last known place of business or residence or, if none, by exhibiting it for three days at the registered office for the time being of the Company.

11 Notices and other communications to Warrantholders may be given by personal delivery, prepaid letter by first class post or, subject to clause 1.3 of this instrument, fax or email. In proving service of any notice or other communication sent by post, it shall be sufficient to prove that the envelope containing the notice or other communication was properly addressed and stamped and was deposited in a post box or at the post office.

12 A notice or other communication given pursuant to the provisions of paragraph 11 of this Schedule 2 shall be deemed to have been served:

12.1 at the time of delivery, if delivered personally to the registered address; and

12.2 on the second Business Day following its posting, if sent by prepaid letter by first class post to an address in the United Kingdom.

13 All notices and other communications with respect to 2023 Warrants standing in the names of joint registered holders shall be given to whichever of such persons is named first in the Register and such notice so given shall be sufficient notice to all the registered holders of such 2023 Warrants.

14 Any person who, whether by operation of law, transfer or other means whatsoever, shall become entitled to any 2023 Warrant, shall be bound by every notice in respect of such 2023 Warrant which, prior to its name and address being entered on the Register, shall have been duly given to the person from which it derives its title to such Warrant.

15 When a given number of days' notice or notice extending over any other period is required to be given, the day of service shall be included but the day upon which such notice will expire shall not be included in such number of days or other period. The signature to any notice to be given by the Company may be written or printed.

Schedule 3

ADS Issuance and Delivery Instruction

[DATE]
Citibank, N.A., as Depositary
388 Greenwich Street
New York, New York 10013
Attn.: Mr. Brian M. Teitelbaum (brian.m.teitelbaum@citi.com)
With a copy simultaneously delivered to:
Citibank, N.A., London Branch
25 Canada Square
Canary Wharf
London E14 5LB, England
Attn.: UK Custody Settlements
Custody Team (uksettlements@citi.com)

Re: Issuance and Delivery Instruction - Mereo BioPharma Group plc (CUSIP No.: 589492107) – Deposit & Hold

Dear Sirs:

Reference is made to the Deposit Agreement, dated as of April 23, 2018, as amended and supplemented from time to time (the "Deposit Agreement"), by and among Mereo BioPharma Group plc, a public limited company incorporated under the laws of England and Wales and its successors (the "Company"), Citibank, N.A., a national banking association organized and existing under the laws of the United States of America, as Depositary (the "Depositary"), and all Holders and Beneficial Owners of American Depositary Shares (the "ADSs") issued thereunder. All capitalized terms used, but not otherwise defined herein, shall have the meaning assigned thereto in the Deposit Agreement.

In accordance with the terms and subject to the limitations set forth in the Deposit Agreement, promptly following the Depositary's receipt of confirmation from the Custodian that the Custodian has received a deposit of the number of Shares specified below made by the Company for the benefit of the undersigned holder thereof (the "Holder" and together with the Company, the "Undersigned"), the Undersigned hereby jointly instruct the Depositary, and the Depositary hereby agrees:

(i) to promptly accept for deposit the number of Shares and issue the number of ADSs as specified below:

Number of Shares deposited: _____ Shares

Number of ADSs (CUSIP No.: 589492107; each ADS representing five (5) Shares to be issued: _____ ADSs

and (ii) to promptly deliver such Program ADSs, as follows:

Name of DTC Participant to which the ADSs are to be delivered:

_____

DTC Participant Account No.: _____

Account No. for recipient of ADSs at DTC

Participant (f/b/o/ information):

_____

Name on whose behalf the above number of ADSs are to be issued and delivered:

_____

Contact person at DTC Participant: _____

Daytime telephone number of contact person at DTC: _____

The Company hereby confirms and certifies that (A) the above Shares represented by ADSs may be resold without registration under the Securities Act of 1933, as amended (the "Securities Act") pursuant to an exemption from the registration requirements of the Securities Act, or (B) a registration statement (the "Registration Statement") has been filed with the U.S. Securities and Exchange Commission (the "Commission") to register the resale of the above Shares represented by ADSs and is effective under the Securities Act and no stop order suspending the effectiveness of the Registration Statement has been issued and no proceedings for such purpose have been instituted or are pending or, to the best knowledge of the Company, are contemplated or threatened by the Commission, and such ADSs will be freely transferable following the issuance thereof by the Depositary, and there are no legal restrictions on subsequent transfers of the ADSs to be issued hereunder under the laws of England and Wales or the United States.

The Holder hereby represents and covenants to, and for the benefit of, the Depositary and Citibank, N.A. - London Branch (the "Custodian"), that (i) the Holder is not an "affiliate" of the Company as that term is defined in Rule 144 promulgated by the Commission under the Securities Act and has not been an affiliate at any time during the 90 days immediately preceding the date hereof, and (ii) all stamp duty taxes, including, without limitation, the U.K. Stamp Duty Reserve Tax ("SDRT"), will be paid in full and on a timely basis to the extent such taxes are payable in respect of the deposit of the Shares and the issuance and delivery of the ADSs as contemplated herein.

Each of the Holder and, to the extent it is not unlawful for the Company to do so under the applicable laws of England and Wales, the Company agrees to indemnify the Depositary and the Custodian for, and to hold the Depositary and the Custodian harmless against, all losses, liabilities, taxes, charges, penalties or expenses (including reasonable legal fees and disbursements), incurred by the Depositary and/or by the Custodian or to which the Depositary and/or the Custodian may become subject to and arising directly or indirectly from the failure by any person to pay (or discharge) any applicable stamp duty taxes, including, without limitation, SDRT, or any other similar duty or tax in connection with the deposit of the Shares and the issuance and delivery of the ADSs as contemplated herein, save to the extent that such losses, liabilities, taxes, charges, penalties or expenses are due to the negligence or bad faith of the Custodian or the Depositary.

[HOLDER]	MEREO BIOPHARMA GROUP PLC
By: _____	By: _____
Name:	Name:
Title:	Title:

SIGNATURE PAGE

Executed as a **DEED**, but not delivered until the date specified on this instrument, by

MEREO BIOPHARMA GROUP PLC
acting by

_____ _____*Director*
Director

_____ _____*Director/Company Secretary*
Director/Company Secretary

Exhibit 8.1

Subsidiaries of Mereo BioPharma Group plc

Legal Name of Subsidiary	Jurisdiction of Organization
Mereo BioPharma 1 Limited	United Kingdom
Mereo BioPharma 2 Limited	United Kingdom
Mereo BioPharma 3 Limited	United Kingdom
Mereo BioPharma 4 Limited	United Kingdom
Mereo BioPharma Ireland Limited	Ireland
Mereo US Holdings Inc.	Delaware
Mereo BioPharma 5, Inc.	Delaware
NAVI Subsidiary, Inc.	Delaware

Exhibit 12.1

Certification by the Chief Executive Officer
Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

I, Denise Scots-Knight, certify that:

1. I have reviewed this annual report on Form 20-F of Mereo BioPharma Group plc (the "Company");

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)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) 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 and risk 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: March 28, 2023

/s/ Denise Scots-Knight, Ph.D.
Name: Denise Scots-Knight, Ph.D.
Title: Chief Executive Officer

Exhibit 12.2

Certification by the Chief Financial Officer
Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

I, Christine Fox, certify that:

1. I have reviewed this annual report on Form 20-F of Mereo BioPharma Group plc (the "Company");

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)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) 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 and risk 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: March 28, 2023

/s/ Christine Fox
Name: Christine Fox
Title: Chief Financial Officer

Exhibit 13.1

Certification by the Chief Executive Officer
Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

In connection with the annual report of Mereo BioPharma Group plc (the "Company") on Form 20-F for the year ended December 31, 2022 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Denise Scots-Knight, Chief Executive Officer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to my knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

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

Date: March 28, 2023

By: /s/ Denise Scots-Knight, Ph.D.
Name: Denise Scots-Knight, Ph.D.
Title: Chief Executive Officer

Exhibit 13.2

Certification by the Chief Financial Officer
Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

In connection with the annual report of Mereo BioPharma Group plc (the "Company") on Form 20-F for the year ended December 31, 2022 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Christine Fox, Chief Financial Officer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to my knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

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

Date: March 28, 2023

By: /s/ Christine Fox
Name: Christine Fox
Title: Chief Financial Officer

Exhibit 15.1

Consent of Independent Registered Public Accounting Firm

Mereo BioPharma Group plc
London, United Kingdom

We hereby consent to the incorporation by reference in the Registration Statements on Form F-3 (No. 333-239708 and No. 333-258495) and Form S-8 (No. 333-231636 and No. 333-236498 and No. 333-252147 and No. 333-262151 and No. 333-269388) of Mereo BioPharma Group plc of our report dated March 28, 2023, relating to the consolidated financial statements which appears in this Annual Report on Form 20-F.

/s/ BDO LLP

Reading, United Kingdom

March 28, 2023

Exhibit 15.2

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement on Form S-8 (No. 333-269388) pertaining to both the Mereo BioPharma Group plc 2019 Equity Incentive Plan, as amended, and the Mereo BioPharma Group plc 2019 Non-Employee Equity Incentive Plan, as amended;

(2) Registration Statement on Form S-8 (No. 333-231636) pertaining to both the Mereo BioPharma Group plc 2019 Equity Incentive Plan and the Mereo BioPharma Group plc 2019 Non-Employee Equity Incentive Plan;

(3) Registration Statement on Form S-8 (No. 333-236498) pertaining to both the Mereo BioPharma Group plc 2019 Equity Incentive Plan and the Mereo BioPharma Group plc 2019 Non-Employee Equity Incentive Plan;

(4) Registration Statement on Form S-8 (No. 333-252147) pertaining to i) Mereo BioPharma Group plc 2019 Equity Incentive Plan, as amended; ii) Mereo BioPharma Group plc 2019 Non-Employee Equity Incentive Plan, as amended, iii) Mereo BioPharma Group plc Share Option Scheme 2016, as amended; iv) Mereo BioPharma Group plc Deferred Bonus Share Plan 2016, as amended; v) Mereo BioPharma Group plc Long Term Incentive Plan 2016, as amended and vi) Mereo BioPharma Group Share Option Scheme 2015, as amended;

(5) Registration Statement on Form S-8 (No. 333-262151) pertaining to both the Mereo BioPharma Group plc 2019 Equity Incentive Plan, as amended, and the Mereo BioPharma Group plc 2019 Non-Employee Equity Incentive Plan, as amended; and

(6) Registration Statements on Form F-3 (No. 333-239708 and No. 333-258495) of Mereo BioPharma Group plc and in the related Prospectuses;

of our report dated March 31, 2021, with respect to the consolidated financial statements of Mereo BioPharma Group plc included in this Annual Report (Form 20-F) for the year ended December 31, 2022.

/s/ Ernst & Young LLP
Reading, United Kingdom
March 28, 2023