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 001-39487

Silence Therapeutics plc

(EXACT NAME OF REGISTRANT AS SPECIFIED IN ITS CHARTER)

Not Applicable
(Translation of Registrant's Name into English)

United Kingdom
(Jurisdiction of incorporation or organization)

72 Hammersmith Road
London W14 8TH
United Kingdom
(Address of principal executive offices)

Craig Tooman
Chief Executive Officer
Silence Therapeutics plc
72 Hammersmith Road
London W14 8TH
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(Name, Telephone, E-mail and/or Facsimile number and Address of Company Contact Person)

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

Title of each class	Trading symbol(s)	Name of each exchange on which registered
American Depositary Shares, each representing 3 ordinary shares, nominal value £0.05 per share	SLN	The Nasdaq Stock Market LLC

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

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

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

Ordinary shares, nominal value £0.05 per share: 107,808,471 as of December 31, 2022

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

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

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

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

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

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

If an emerging growth company that prepares its financial statements in accordance with U.S. GAAP, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards 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

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GENERAL INFORMATION

Unless otherwise indicated or the context otherwise requires, all references in this report to the terms “Silence,” “Silence Therapeutics,” “Silence Therapeutics plc,” “the company,” “we,” “us” and “our” refer to Silence Therapeutics plc together with its subsidiaries. In this Annual Report, the U.S. Securities and Exchange Commission is referred to as the “SEC”, the Securities Act of 1933, as amended, is referred to as the “Securities Act” and the Securities Exchange Act of 1934, as amended, is referred to as the “Exchange Act.”

PRESENTATION OF FINANCIAL AND OTHER DATA

We maintain our books and records in pounds sterling and report under International Financial Reporting Standards, or IFRS, as issued by the International Accounting Standards Board, or IASB. None of the financial statements included in this report were prepared in accordance with generally accepted accounting principles in the United States. All references in this report to “$” are to U.S. dollars and all references to “£” are to pounds sterling. Except with respect to U.S. dollar amounts presented as contractual terms or otherwise indicated, all amounts presented in this report in U.S. dollars have been translated from pounds sterling solely for convenience at an assumed exchange rate of $1.21 per £1.00, based on the noon buying rate of the Federal Reserve Bank of New York on December 31, 2022. We make no representation that any pounds sterling or U.S. dollar amounts referred to in this Annual Report could have been, or could be, converted into U.S. dollars or pounds sterling, as the case may be, at any particular rate, or at all. These translations should not be considered representations that any such amounts have been, could have been or could be converted from pounds sterling into U.S. dollars at that or any other exchange rate as of that or any other date.

We have made rounding adjustments to some of the figures included in this Annual Report. Accordingly, numerical figures shown as totals in some tables may not be an arithmetic aggregation of the figures that preceded them. Additionally, numerical figures under £100,000 have been rounded to the nearest thousand in this Annual Report.

All references to “shares” or “ordinary shares” in this Annual Report refer to ordinary shares of Silence Therapeutics plc with a nominal value of £0.05 per share. All references to ADSs refer to American Depositary Shares, each representing three ordinary shares of Silence Therapeutics plc, which are denominated in U.S. dollars and listed on Nasdaq.

TRADEMARKS, TRADENAMES AND SERVICE MARKS

This Annual Report includes trademarks, tradenames and service marks, certain of which belong to us and others that are the property of other organizations. Solely for convenience, trademarks, tradenames and service marks referred to in this report appear without the ®, ™ and SM symbols, but the absence of those symbols is not intended to indicate, in any way, that we will not assert our rights or that the applicable owner will not assert its rights to these trademarks, tradenames and service marks to the fullest extent under applicable law. We do not intend our use or display of other parties’ trademarks, trade names or service marks to imply, and such use or display should not be construed to imply, a relationship with, or endorsement or sponsorship of us by, these other parties.

CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report contains forward-looking statements that involve substantial risks and uncertainties. In some cases, you can identify forward-looking statements by the words “may,” “might,” “will,” “could,” “would,” “should,” “expect,” “intend,” “plan,” “objective,” “anticipate,” “believe,” “estimate,” “predict,” “potential,” “continue” and “ongoing,” or the negative of these terms, or other comparable terminology intended to identify statements about the future. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. The forward-looking statements and opinions contained in this Annual Report are based upon information available to us as of the date of this Annual Report and, while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. Forward-looking statements include statements about:

- the development of our product candidates, including statements regarding the timing of initiation, completion and the outcome of preclinical studies or clinical trials and related preparatory work, the period during which the results of the trials will become available and our research and development programs;
- our ability to obtain and maintain regulatory approval of our product candidates in the indications for which we plan to develop them, and any related restrictions, limitations or warnings in the label of an approved drug or therapy;
- our plans to collaborate, or statements regarding the ongoing collaborations, with third parties;
- our plans to research, develop, manufacture and commercialize our product candidates;
- the timing of our regulatory filings for our product candidates;
- the size and growth potential of the markets for our product candidates;
- our ability to raise additional capital;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our expectations regarding our ability to obtain and maintain intellectual property protection;
- our ability to attract and retain qualified employees and key personnel;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- our estimates regarding future revenue, expenses and needs for additional financing;
- our belief that our existing cash, cash equivalents and U.S. Treasury Bills will be sufficient to fund our operating expenses and capital expenditure requirements through the first quarter of 2024; and
- regulatory developments in the United States, United Kingdom, European Union, or EU, and other jurisdictions.

You should refer to the section of this Annual Report titled “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. Forward-looking statements speak only as of the date they are made, and we do not undertake any obligation to update them in light of new information or future developments or to release publicly any revisions to these statements in order to reflect later events or circumstances or to reflect the occurrence of unanticipated events.

You should read this Annual Report and the documents that we reference in this Annual Report and have filed as exhibits to the Annual Report completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of our forward-looking statements by these cautionary statements.

PART I

ITEM 1: IDENTITY OF DIRECTORS, SENIOR MANAGEMENT AND ADVISORS

Not applicable.

ITEM 2: OFFER STATISTICS AND EXPECTED TIMETABLE

Not applicable.

ITEM 3: KEY INFORMATION

A. [Reserved.]

B. Capitalization and Indebtedness.

Not applicable.

C. Reasons for the Offer and Use of Proceeds.

Not applicable.

D. Risk Factors.

Investing in American Depositary Shares representing our ordinary shares, or ADSs, involves a high degree of risk. You should carefully consider the following risk factors and all other information contained in this Annual Report, including our consolidated financial statements and the related notes, before investing in the ADSs. The risks and uncertainties described below are those significant risk factors, currently known and specific to us, that we believe are relevant to an investment in the ADSs. If any of these risks materialize, our business, results of operations or financial condition could suffer, the price of the ADSs could decline and you could lose part or all of your investment. Additional risks and uncertainties not currently known to us or that we now deem immaterial may also harm us and adversely affect your investment in the ADSs.

Risks Associated with Our Business

Our business is subject to a number of risks of which you should be aware before making an investment decision. You should carefully consider all of the information set forth in this report and, in particular, should evaluate the specific factors set forth in the section titled “Risk Factors” before deciding whether to invest in our ADSs. Among these important risks are, but not limited to, the following:

- Our need for substantial additional financial resources to continue as a going concern, continue ongoing development of our product candidates and pursue our business objectives; if we are unable to obtain these additional resources when needed, we may be forced to delay or discontinue our planned operations, including clinical testing of our product candidates.

- The approach we are taking to discover and develop drugs is novel and we may not be successful in our efforts to identify or discover potential drug product candidates to bring into clinical trials.

- If clinical trials of our product candidates fail to commence or, once commenced, fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities, or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

- We have a history of net losses and we anticipate that we will continue to incur significant losses for the foreseeable future.

- We will need additional capital, which may not be available on acceptable terms, or at all.

- We face competition from other companies that are working to develop novel drugs and technology platforms using technologies similar to ours. If these companies compete with us for limited manufacturing supplies, or for animals critical for preclinical testing, or otherwise develop drugs more rapidly than we do, or their technologies, including delivery technologies, are more effective, our ability to successfully commercialize drugs may be adversely affected.

- We rely on third parties to conduct some aspects of our manufacturing, research and development activities, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of manufacturing, research or clinical testing.

- If we are unable to obtain or protect intellectual property rights related to our current or future product candidates, we may not be able to compete effectively in any or all markets.

- An active trading market for our ADSs may not develop and you may not be able to resell your ADSs at or above the price you pay for them, if at all.

- We qualify as a foreign private issuer and, as a result, we will not be subject to U.S. proxy rules and will be subject to Exchange Act reporting obligations that, to some extent, are more lenient and less frequent than those of a U.S. domestic public company.

- If equity research analysts do not publish research or reports, or publish unfavorable research or reports, about us, our business or our market, the price and trading volume of our ADSs could decline.

- If we are a passive foreign investment company, there could be adverse U.S. federal income tax consequences to U.S. Holders.

- The withdrawal of the United Kingdom from the European Union, commonly referred to as “Brexit,” may adversely impact our ability to obtain regulatory approvals of our product candidates in the European Union, result in restrictions or imposition of taxes and duties for importing our product candidates into the European Union, may require additional licenses and procedural steps and may require us to incur additional expenses in order to develop, manufacture and commercialize our product candidates in the European Union.

- The Ukraine/Russia War could adversely affect our operations, including increases in the prices of the supplies used in our business, supply chain interruptions and increased cybersecurity risks.

- Inflation may adversely affect our operations, including increases in the prices of goods and services required for our operations.

Implications of Being an Emerging Growth Company and a Foreign Private Issuer

Emerging Growth Company

We are an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. As such, we may take advantage of certain exemptions from various reporting requirements that are applicable to other publicly traded entities that are not emerging growth companies. These exemptions include:

- not being required to comply with the auditor attestation requirements of Section 404(b) of the Sarbanes-Oxley Act of 2002;

- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board, or PCAOB, regarding mandatory audit firm rotation or a supplement to the auditor’s report

providing additional information about the audit and the financial statements (*i.e.*, an auditor discussion and analysis);

- not being required to submit certain executive compensation matters to shareholder advisory votes, such as "say-on-pay," "say-on-frequency," and "say-on-golden parachutes"; and

- not being required to disclose certain executive compensation related items such as the correlation between executive compensation and performance and comparisons of the chief executive officer's compensation to median employee compensation.

We will remain an emerging growth company until the earliest of: (1) the last day of the first fiscal year in which our annual gross revenues exceed $1.235 billion; (2) the last day of 2025; (3) the date that we become a "large accelerated filer" as defined in Rule 12b-2 under the Exchange Act, which would occur on the last day of any fiscal year that the aggregate worldwide market value of our common equity held by non-affiliates exceeds $700 million as of the last business day of our most recently completed second fiscal quarter; or (4) the date on which we have issued more than $1.0 billion in non-convertible debt securities during any three-year period.

Foreign Private Issuer

We report under the Exchange Act as a non-U.S. company with foreign private issuer status. Even after we no longer qualify as an emerging growth company, as long as we qualify as a foreign private issuer under the Exchange Act, we will be exempt from certain provisions of the Exchange Act that are applicable to U.S. domestic public companies, including:

- the sections of the Exchange Act regulating the solicitation of proxies, consents or authorizations in respect of a security registered under the Exchange Act;

- the sections of the Exchange Act requiring insiders to file public reports of their stock ownership and trading activities and liability for insiders who profit from trades made in a short period of time; and

- the rules under the Exchange Act requiring the filing with the SEC of quarterly reports on Form 10-Q containing unaudited financial and other specific information, and current reports on Form 8-K upon the occurrence of specified significant events.

Foreign private issuers are also exempt from certain more stringent executive compensation disclosure rules. Thus, even if we no longer qualify as an emerging growth company, but remain a foreign private issuer, we will continue to be exempt from the more stringent compensation disclosures required of companies that are neither an emerging growth company nor a foreign private issuer.

Risks Related to Our Financial Condition and Need for Additional Capital

We have a history of net losses and we anticipate that we will continue to incur significant losses for the foreseeable future.

We are a clinical-stage biopharmaceutical company. As of the date hereof, our operations have been primarily limited to developing our siRNA product platform, undertaking basic research around siRNA targets, conducting preclinical and clinical studies and out-licensing some of our intellectual property rights. We have not yet obtained marketing approval for any product candidates and may not for the foreseeable future, if ever. Consequently, any predictions about our future success or viability, or any evaluation of our business and prospects, may not be accurate.

We have incurred net losses in each year since our inception. Our net losses were £40.5 million for the year ended December 31, 2022, £39.4 million for the year ended December 31, 2021, and £32.5 million for the year ended December 31, 2020. As of December 31, 2022, we had an accumulated loss of £263.3 million. Our losses have resulted from costs incurred to research and development, including our preclinical and clinical development activities.

We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future, although these losses may fluctuate significantly between periods. We anticipate that our expenses will increase substantially as we continue the research, preclinical and clinical development of our product candidates, both independently and under our collaboration agreements with third parties. We would also incur additional expenses in connection with seeking marketing approvals for any product candidates that successfully complete clinical trials, if any, and establishing a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval. We will also need to maintain, expand and protect our intellectual property portfolio, hire additional personnel, and create additional infrastructure to support our operations and our product development efforts. We expect that all of these additional expenses will cause our total expenses to substantially exceed our revenue over the near term, resulting in continuing operating losses and increasing accumulated deficits.

We have never generated any revenue from product sales and may never be profitable.

Our ability to generate revenue and achieve profitability depends on our ability, alone or with collaboration partners, to successfully complete the development of, obtain the necessary regulatory approvals for and commercialize our product candidates. We do not anticipate generating revenues from sales of products for the foreseeable future, if ever. Our ability to generate future revenues from product sales will depend heavily on our success in:

- identifying and validating therapeutic targets;
- completing our research and preclinical development of product candidates;
- initiating and completing clinical trials for product candidates;
- seeking, obtaining and maintaining marketing approvals for product candidates that successfully complete clinical trials;
- establishing and maintaining supply and manufacturing relationships with third parties, or establishing our own manufacturing capability;
- launching and commercializing product candidates for which we obtain marketing approval, either with a collaborator or, if launched independently, successfully establishing a sales force, marketing and distribution infrastructure;
- maintaining, expanding and protecting our intellectual property portfolio; and
- attracting, hiring and retaining qualified personnel.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to predict the timing or amount of increased expenses and when we will be able to achieve or maintain profitability, if ever. In addition, our expenses could increase if we were required by the U.S. Food and Drug Administration, or FDA, the European Medicines Agency, or EMA, the U.K. Medicines and Healthcare products Regulatory Agency, or MHRA, or other regulatory agencies to perform studies and trials in addition to those that we currently anticipate.

Even if one or more of our product candidates is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product on our own. Even if we were able to generate revenues from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations.

We will require additional financial resources to continue as a going concern and to continue ongoing development of our product candidates and pursue our business objectives; if we are unable to obtain these additional resources when needed or on acceptable terms, we may be forced to delay or discontinue our planned operations, including clinical testing of our product candidates.

We have used substantial funds to develop our RNAi technologies and will require substantial funds to conduct further research and development, including preclinical testing and clinical trials of our product candidates, and to manufacture, market and sell any of our products that may be approved for commercial sale. Because the length of time or activities associated with successful development of our product candidates may be greater than we anticipate, we are unable to estimate the actual funds we will require to develop and commercialize them. As of December 31, 2022, our accumulated losses since inception were £263.3 million. We expect our operating expenditures and net losses to increase significantly in connection with our ongoing clinical trials and our internal research and development capabilities.

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is expensive. We expect our research and development expenses to substantially increase in connection with our ongoing activities, particularly as we advance our product candidates towards or through clinical trials. We will need additional capital to fund our operations and such funding may not be available to us on acceptable terms, or at all. We may need additional capital or to otherwise obtain funding through additional strategic collaborations if we choose to initiate clinical trials for product candidates other than those which are funded by our collaboration partners. In any event, we will require additional capital to obtain regulatory approval for, and to commercialize, future product candidates.

For the foreseeable future, we expect to rely primarily on additional non-dilutive collaboration arrangements, as well as equity and/or debt financings, to fund our operations. Raising additional capital through the sale of securities could cause significant dilution to our shareholders. Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. Our ability to raise additional funds will depend, in part, on the success of our preclinical studies and clinical trials and other product development activities, regulatory events, our ability to identify and enter into licensing or other strategic arrangements, and other events or conditions that may affect our value or prospects, as well as factors related to financial, economic and market conditions, many of which are beyond our control. There can be no assurances that sufficient funds will be available to us when required or on acceptable terms, if at all. If we are unable to raise additional capital when required or on acceptable terms, we may be required to:

- significantly delay, scale back or discontinue the development or commercialization of any future product candidates;
- seek strategic alliances for research and development programs at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available;
- dispose of technology assets, or relinquish or license on unfavorable terms, our rights to technologies or any future product candidates that we otherwise would seek to develop or commercialize; and
- file for bankruptcy or cease operations altogether.

Any of these events would have a material adverse effect on our business, operating results and prospects and could significantly impair the value of your investment in our ADSs.

The Company has incurred recurring losses since inception, including net losses of £40.5 million for the year ended December 31, 2022. As of December 31, 2022, the Company had accumulated losses of £263.3 million and cash outflows from operating activities for the year ended 31 December 2022 of £45.5 million. The Company expects to incur 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.

To-date, the Company has funded its operations through upfront payments and milestones from collaboration agreements, equity offerings and proceeds from private placements, as well as management of expenses and other financing options to support its continued operations. During 2021, the Company received $40.0 million (£30.8 million) of the upfront payments in respect of the AstraZeneca collaboration, $45 million from a private placement of ADSs (approximately $42.0 million / £30.8 million, net of expenses) and approximately $16.0 million (£10.7 million)

of the upfront payment, (net of taxes withheld, based on the exchange rate at the payment date), related to the Hansoh Pharmaceutical Group Company Limited or Hansoh, collaboration executed on October 14, 2021. In August 2022 the Company raised additional funds through a registered direct offering with aggregate gross proceeds of $56.5 million (approximately £46.4 million) before deducting $4.1 million (approximately £3.3 million) in underwriting discounts, commissions and estimated offering expenses. As of December 31, 2022, the Company had cash and cash equivalents and U.S Treasury Bills of £71.1 million ($86.0 million).

The Company has the responsibility to evaluate whether conditions and/or events raise material uncertainty about its ability to meet its future financial obligations as they become due within one year after the date that the financial statements are issued. The forecast for evaluating the going concern basis of the Company includes continued investment in our technology platform and product pipeline. The forecast does not include collaboration milestones which have not been fully achieved or other assumptions for potential future non-dilutive or dilutive funding sources. Based on this evaluation, the Company believes that its current cash and cash equivalents are only sufficient to fund its operating expenses through the first quarter of 2024. This indicates that a material uncertainty exists that may cast significant doubt (or raise substantial doubt as contemplated by Public Company Accounting Oversight Board ("PCAOB") standards) on the Company's ability to continue as a going concern and therefore the Company may be unable to realize assets and discharge liabilities in the normal course of business.

The Company will need to raise additional funding to fund its operation expenses and capital expenditure requirements in relation to its clinical development activities. The Company may seek additional funding through public or private financings, debt financing or collaboration agreements. Specifically, the Company may receive future milestone payments of up to $14 million from existing collaboration agreements in the next 12 months which will extend the ability to fund operations beyond the first quarter of 2024. However, these future milestone payments are dependent on achievement of certain development or regulatory objectives that may not occur. The Company has an authorized open market sale agreement and can potentially raise funds through the sale of ADSs. However, there is no assurance that we will be successful in obtaining sufficient funding on terms acceptable to us, or if at all. The inability to obtain future funding could impact; the Company's financial condition and ability to pursue its business strategies, including being required to delay, reduce or eliminate some of its research and development programs, or being unable to continue operations or unable to continue as a going concern.

These consolidated financial statements have been prepared assuming that the Company will continue as a going concern which contemplates the continuity of operations, realization of assets and the satisfaction of liabilities in the ordinary course of business and do not include adjustments that would result if the Company were unable to continue as a going concern.

The forecast of cash resources is forward-looking information that involves risks and uncertainties, and our actual cash requirements may vary materially from our current expectations for a number of other factors that may include, but are not limited to, changes in the focus and direction of our development programs, slower and/or faster than expected progress of our research and development efforts, changes in governmental regulation, competitive and technical advances, rising costs associated with the development of our product candidates, our ability to secure partnering arrangements, and costs of filing, prosecuting, defending and enforcing our intellectual property rights. Global political and economic events, including the COVID-19 pandemic and increased inflation, have already resulted in a significant disruption of global financial markets. If the disruption persists and deepens, we could experience an inability to access additional capital or make the terms of any available financing less attractive, which could in the future negatively affect our operations. If we exhaust our capital reserves more quickly than anticipated, regardless of the reason, and we are unable to obtain additional financing on terms acceptable to us or at all, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Raising additional capital may cause dilution to our holders, including holders of our ADSs, restrict our operations or require us to relinquish rights to our technologies or product candidates.

We expect that additional capital will be needed in the future to continue our planned operations, including expanded research and development activities and potential commercialization efforts. Until such time, if ever, as we

can generate substantial product revenues, we expect to finance our cash needs through any or a combination of securities offerings, debt financings, license and collaboration agreements and research grants and tax credits.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, including in any at-the-market offering through our open market sale agreement, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a shareholder. Debt financing and preferred equity financing, if available, could result in fixed payment obligations, and we may be required to accept terms that restrict our ability to incur additional indebtedness, force us to maintain specified liquidity or other ratios or restrict our ability to pay dividends or make acquisitions. If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may be required to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. In addition, we could also be required to seek funds through arrangements with collaborators or others at an earlier stage than otherwise would be desirable.

If we raise funds through research grants or take advantage of research and development tax credits, we may be subject to certain requirements, which may limit our ability to use the funds or require us to share information from our research and development. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to a third party to develop and market product candidates that we would otherwise prefer to develop and market ourselves. Raising additional capital through any of these or other means could adversely affect our business and the holdings or rights of our shareholders, and may cause the market price of our ADSs to decline.

Risks Related to the Discovery, Development, Regulatory Approval and Potential Commercialization of Our Product Candidates

The approach we are taking to discover and develop drugs is novel and may never lead to marketable products.

We have concentrated our therapeutic product research and development efforts on siRNA technology, and our future success depends on the successful development of this technology and products based on our siRNA product platform. Although the FDA has approved five siRNA treatments for marketing in the United States since 2018, no assurance can be given that the FDA will approve any other siRNA treatments such as ours.

The scientific discoveries that form the basis for our efforts to discover and develop product candidates based on siRNA technology are relatively new. The scientific evidence to support the feasibility of developing product candidates based on these discoveries is both preliminary and limited. If we do not successfully develop and commercialize product candidates based upon our technological approach, we may not become profitable and the value of our ordinary shares may decline.

Further, our focus solely on siRNA technology for developing drugs as opposed to multiple, more proven technologies for drug development increases the risks associated with the ownership of our ordinary shares. If we are not successful in developing any product candidates using siRNA technology, we may be required to change the scope and direction of our product development activities. In that case, we may not be able to identify and successfully implement an alternative product development strategy.

We may not be successful in our efforts to identify or discover potential product candidates.

The success of our business depends primarily upon our ability to identify, develop and commercialize siRNA therapeutics. Our research programs may show initial promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for a number of reasons, including:

- our research methodology or that of any strategic collaborator may be unsuccessful in identifying potential product candidates that are successful in clinical development;
- potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval;

- our current or future strategic collaborators may change their development profiles for potential product candidates or abandon a therapeutic area; or

- new competitive developments in the evolving field of RNAi, including gene therapy or gene editing, may render our product candidates obsolete or noncompetitive.

If any of these events occur, we may be forced to abandon our development efforts for a program or programs, which would have a material adverse effect on our business and could potentially cause us to cease operations. Research programs to identify new product candidates require substantial technical, financial and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful.

We may not be successful in our efforts to increase our pipeline, including by pursuing additional indications for our current product candidates, identifying additional indications for our proprietary platform technology or in-licensing or acquiring additional product candidates for other indications.

We may not be able to develop or identify product candidates that are safe, tolerable and effective. Even if we are successful in continuing to build our pipeline, the potential product candidates that we identify, in-license or acquire may not be suitable for clinical development, including as a result of being shown to have harmful side effects or other characteristics that indicate that they are unlikely to be products that will receive marketing approval and achieve market acceptance.

Preclinical studies and clinical trials of our product candidates may not be successful. If we are unable to generate successful results from these studies and trials, or experience significant delays in doing so, our business may be materially harmed.

We have invested a significant portion of our efforts and financial resources in the identification and development of siRNA-based product candidates. Our ability to generate product revenues, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of our product candidates.

The success of our product candidates will depend on several factors, including, *inter alia*, the following:

1. successfully designing preclinical studies which may be predictive of clinical outcomes;

2. successfully conducting and completing clinical trials;

3. obtaining and maintaining marketing approvals from applicable regulatory authorities;

4. obtaining and maintaining patent or trade secret protection for future product candidates;

5. establishing and maintaining supply and manufacturing relationships with third parties or establishing our own manufacturing capability; and

6. successfully commercializing our products, if and when approved, whether alone or in collaboration with others.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully complete the development of, or commercialize, our product candidates, which would materially harm our business.

If clinical trials of our product candidates fail to commence or, once commenced fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities, or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

In clinical development, the risk of failure for product candidates is high. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive regulatory approval. We are the sponsor of Investigational Medicinal Product Dossiers in multiple jurisdictions and must achieve and maintain compliance with the requirements of various regulatory authorities. Before obtaining marketing approval from regulatory authorities for the sale of product candidates, we or a strategic collaborator must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidates in humans. As of the date hereof, we have three product candidates in clinical development, and our other product candidates are preclinical. Clinical trials are expensive, difficult to design and implement, can take many years to complete and are uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. Moreover, clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in clinical trials have nonetheless failed to obtain marketing approval for their products.

Events which may result in a delay or unsuccessful completion of clinical development include, among other things:

- delays in reaching an agreement with the FDA, EMA, MHRA or other regulatory authorities on final trial design;
- imposition of a clinical hold on our clinical trial operations or trial sites by the FDA or other regulatory authorities;
- delays in reaching agreement on acceptable terms with prospective CROs and clinical trial sites;
- inability to adhere to clinical trial requirements directly or with third parties such as CROs;
- delays in obtaining required Institutional Review Board, or IRB, approval at each clinical trial site;
- delays in recruiting suitable patients to participate in a trial;
- delays in the testing, validation, manufacturing and delivery of the product candidates to the clinical sites;
- delays in having patients complete participation in a trial or return for post-treatment follow-up;
- delays caused by patients dropping out of a trial due to protocol procedures or requirements, product side effects or disease progression;
- clinical sites dropping out of a trial to the detriment of enrollment;
- time required to add new clinical sites;
- negative outcomes, including deficiencies in good clinical practices, or GCP, in routine inspections by regulatory authorities in the countries where our clinical trials are being conducted;
- investigator fraud, including data fabrication by clinical trial personnel;
- delays by our contract manufacturers to produce and deliver sufficient supply of clinical trial materials; or
- delays in delivering sufficient supply of clinical trial materials to clinical sites and challenges in patient recruitment, including due to the COVID-19 pandemic, as well as challenges regarding global clinical trial supply shipments, importation and customs clearances.

If we or our current or future strategic collaborators are required to conduct additional clinical trials or other testing of any product candidates beyond those that are currently contemplated, are unable to successfully complete clinical trials of any such product candidates or other testing, or if the results of these trials or tests are not positive or are only moderately positive, or if there are safety concerns, we and they may:

- be delayed in obtaining marketing approval for our future product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as originally intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to additional post-marketing testing requirements; or
- have the product removed from the market after obtaining marketing approval.

Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. In addition, our product development costs will also increase if we experience delays in testing or marketing approvals. We do not know whether any clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, which would impair our ability to successfully commercialize our product candidates and may harm our business and results of operations. Any inability to successfully complete clinical development, whether independently or with a strategic collaborator, could result in additional costs to us or impair our ability to generate revenues from product sales, regulatory and commercialization milestone payments and royalties.

Conducting successful clinical trials requires the enrollment of large numbers of patients, and suitable patients may be difficult to identify and recruit.

Patient enrollment in clinical trials and completion of patient participation and follow-up depends on many factors, including the size of the patient population; the nature of the trial protocol; the attractiveness of, or the discomforts and risks associated with, the treatments received by enrolled subjects; the availability of appropriate clinical trial investigators; support staff; the number of ongoing clinical trials in the same indication that compete for the same patients; proximity of patients to clinical sites and ability to comply with the eligibility and exclusion criteria for participation in the clinical trial and patient compliance. For example, patients may be discouraged from enrolling in our clinical trials if the trial protocol requires them to undergo extensive post-treatment procedures or follow-up to assess the safety and effectiveness of our products or if they determine that the treatments received under the trial protocols are not attractive or involve unacceptable risks or discomforts. Patients may also not participate in our clinical trials if they choose to participate in contemporaneous clinical trials of competitive products.

We rely on third parties to conduct some aspects of our manufacturing, research and development activities, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of research or clinical testing, or may terminate our agreements.

We do not expect to independently conduct all aspects of our manufacturing and drug discovery activities, research or preclinical and clinical studies of product candidates. We currently rely and expect to continue to rely on third parties to conduct some aspects of our drug development studies and chemical syntheses. Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it would delay our product development activities. Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our studies in accordance with regulatory requirements or our stated study plans and protocols, we will not be able to complete, or may be delayed in completing, the necessary preclinical studies to enable us to progress viable product candidates for

investigational new drug, or IND, submissions and will not be able to, or may be delayed in our efforts to, successfully develop and commercialize such product candidates.

Although our research and development services can only be performed by us or at our discretion, we rely on third party clinical investigators, CROs, clinical data management organizations, medical institutions and consultants to design, conduct, supervise and monitor preclinical studies and clinical trials in relation to our product candidates. Because we rely on third parties and do not have the ability to conduct clinical trials independently, we have less control over the timing, quality and other aspects of clinical trials than we would if we conducted them on our own. These investigators, CROs and consultants are not our employees and we have limited control over the amount of time and resources that they dedicate to our programs. These third parties may have contractual relationships with other entities, some of which may be our competitors, which may draw time and resources from our programs. If we cannot contract with acceptable third parties on commercially reasonable terms, or at all, or if these third parties do not carry out their contractual duties, satisfy legal and regulatory requirements for the conduct of clinical trials or meet expected deadlines, our clinical development program could be delayed or otherwise adversely affected. In all events, we are responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. The FDA and comparable foreign regulatory agencies require us to comply with GCP for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible, accurate and complete and that the rights, integrity and confidentiality of trial participants are protected. We rely, for example, on third parties for aspects of quality control which are especially important in monitoring compliance with GCP requirements and avoiding any investigator fraud or misconduct in clinical research, such as practices including adherence to an investigational plan; accurate recordkeeping; drug accountability; obtaining completed informed consent forms; timely reporting of any adverse drug reactions; notifying appropriate IRBs and Ethics Committees of progress reports and any significant changes; and obtaining documented IRB approvals. Our reliance on third parties that we do not control does not relieve us of these responsibilities and requirements. The third parties with which we contract might not be diligent, careful or timely in conducting our clinical trials, as a result of which we could experience one or more lapses in quality controls or other aspects of clinical trial management, and the clinical trials could be delayed or unsuccessful. Any such event could have a material adverse effect on our business, financial condition, results of operations and prospects.

Our dependence on collaborators for capabilities and funding means that our business could be adversely affected if any collaborator materially amends or terminates its collaboration agreement with us or fails to perform its obligations under that agreement. Our current or future collaborations, if any, may not be scientifically or commercially successful. Disputes may arise in the future with respect to the ownership of rights to technology or products developed with collaborators, which could have an adverse effect on our ability to develop and commercialize any affected product candidate. Our current collaborations allow, and we expect that any future collaborations will allow, either party to terminate the collaboration for a material breach by the other party. In addition, our collaborators may have additional termination rights for convenience with respect to the collaboration or a particular program under the collaboration, under certain circumstances. For example, our collaboration agreement with Mallinckrodt plc, or Mallinckrodt, for an exclusive worldwide license for SLN501 (SLN500 program candidate) and additional complement-target products, our collaboration agreement with AstraZeneca PLC, or AstraZeneca, to discover, develop and commercialize siRNA therapeutics for the treatment of cardiovascular, renal, metabolic and respiratory diseases, and our collaboration agreement with Hansoh Pharmaceutical Group Company Limited, or Hansoh, to develop siRNAs for three undisclosed targets, may be terminated by Mallinckrodt, AstraZeneca and Hansoh, respectively, at any time upon prior written notice to us. If we were to lose a collaborator, we would have to attract a new collaborator or develop expanded R&D, sales, distribution and marketing capabilities internally, which would require us to invest significant amounts of financial and management resources.

We rely on third-party manufacturers to produce our preclinical, clinical product candidates and certain starting material components, and we intend to rely on third parties to produce future clinical supplies of product candidates that we advance into clinical trials and commercial supplies of any approved product candidates.

Reliance on third-party manufacturers entails risks, including risks that we would not be subject to if we manufactured the product candidates ourselves, including:

- the inability to meet any product specifications and quality requirements consistently;

- a delay or inability to procure or expand sufficient manufacturing capacity;
- manufacturing and product quality issues related to scale-up of manufacturing;
- costs and validation of new equipment and facilities required for scale-up;
- a failure to comply with applicable government regulations;
- the inability to negotiate manufacturing or supply agreements with third parties under commercially reasonable terms or at all;
- termination or non-renewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us;
- the reliance on a limited number of sources, such that if we were unable to secure a sufficient supply of these product components, we will be unable to manufacture and sell future product candidates in a timely fashion, in sufficient quantities or under acceptable terms; and
- the losses incurred by us if our insurance coverage is insufficient to cover any loss, contamination or damage of chemical materials, product components or products made by any of our CMOs, once the materials or products have been shipped to us and the risk of loss has been transferred to us.

We face risks inherent in relying on contract manufacturing organizations, or CMOs, as any disruption, such as a fire, natural hazards, pandemic, epidemic, war or outbreak of an infectious disease at a CMO could significantly interrupt our manufacturing capability. If necessary to avoid future disruption, we may have to establish alternative manufacturing sources. This would require substantial capital on our part, which we may not be able to obtain on commercially acceptable terms or at all. Additionally, we may experience manufacturing delays as we build or locate replacement facilities and seek and obtain necessary regulatory approvals. If this occurs, we will be unable to satisfy manufacturing needs on a timely basis, if at all. Also, operating any new facilities may be more expensive than operating our current facility. Further, business interruption insurance may not adequately compensate us for any losses that may occur and we would have to bear the additional cost of any disruption. For these reasons, a significant disruptive event affecting the manufacturing facility could have drastic consequences, including placing our financial stability at risk.

Even if we complete the necessary preclinical studies and clinical trials, we cannot predict whether or when we will obtain regulatory approval to commercialize a product candidate and we cannot, therefore, predict the timing of any revenue from a future product.

Neither we nor any strategic collaborator can commercialize a product until the appropriate regulatory authorities, such as the FDA, EMA or MHRA, have reviewed and approved the product candidate. The regulatory agencies may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval. Additional delays may result if an FDA Advisory Committee, or similar foreign governmental institution, recommends restrictions or conditions on approval or recommends non-approval. In addition, we or a strategic collaborator may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory agency policy during the period of product development, clinical trials and the review process.

Even if we obtain regulatory approval for a product candidate, we will still face extensive regulatory requirements and our products may face future development and regulatory difficulties.

Even if we obtain regulatory approval in the United States and the European Union, the FDA and the EMA may still impose significant restrictions on the indicated uses or marketing of our product candidates or impose ongoing requirements for potentially costly post-approval studies or post-market surveillance. The holder of an approved new drug application, or NDA, in the United States, or a marketing authorization, or MA, in the European Union is obligated to monitor and report adverse events, or AEs, or adverse reactions and any failure of a product to meet the

specifications in the NDA, or MA. The holder of an approved NDA or MA must also submit new or supplemental applications and obtain regulatory approval in order to make certain changes to the approved product, product labeling or manufacturing process. Advertising and promotional materials must comply with the relevant regulatory rules and, in the United States and in some EU Member States, are subject to FDA review or national regulatory review, in addition to other potentially applicable federal and state laws.

In addition, drug product manufacturers and their facilities are subject to payment of user fees or may require manufacturing and import authorizations, or MIAs in the European Union, and continual review and periodic inspections by regulatory authorities for compliance with current good manufacturing practices, or cGMP, including quality control, quality assurance, and the maintenance of records and documentation to ensure that approved products are safe and consistently meet applicable requirements, and adherence to commitments made in the NDA or MA. While we have not yet, and may not ever, obtain marketing approval for any of our products, when we do, we or any third party manufacturers we engage may be unable to comply with these cGMP and with other regulatory authority requirements. These requirements are enforced by regulatory authorities through periodic inspections of manufacturing facilities. If we or a regulatory agency discovers previously unknown problems with a product such as AEs of unanticipated severity or frequency, adverse reactions, or product quality issues, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions relative to that product or the manufacturing facility. A negative outcome from such inspection or a failure to provide adequate and timely corrective actions in response to deficiencies identified could result in enforcement action, including warning letters, fines and civil penalties, suspension of production, suspension or delay in product approval, product seizure or recall, plant shutdown, or the delay, withholding, or withdrawal of product approval. If the safety of any product is compromised due to a manufacturer's failure to adhere to applicable laws or for other reasons, we may not be able to obtain regulatory approval for or successfully commercialize our products, which would seriously harm our business.

If there are changes in the application of legislation or regulatory policies, or if problems are discovered with a product or our manufacture of a product, or if we or one of our distributors, licensees or co-marketers fails to comply with regulatory requirements, the regulators could take various actions such as:

- issuing a warning letter or untitled letter asserting that we are in violation of the law;
- seeking an injunction or imposing civil or criminal penalties or monetary fines;
- suspending or withdrawing regulatory approval;
- suspending any ongoing clinical trials;
- refusing to approve a pending NDA or MA or supplements to an NDA or MA submitted by us;
- seizing product; or
- refusing to allow us to enter into supply contracts, including government contracts.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize our future products and generate revenues.

Even if we obtain and maintain approval for our product candidates in one jurisdiction, we may never obtain approval for our product candidates with other regulatory authorities in other jurisdictions. Sales of our product candidates outside of the United States and the European Union will be subject to foreign regulatory requirements governing clinical trials and marketing approval and continual regulatory review. We will be subject to ongoing obligations and oversight by regulatory authorities, including adverse event reporting requirements, marketing restrictions and, potentially, other post-marketing obligations, all of which may result in significant expense and limit our ability to commercialize such products.

We may not be able to obtain or maintain orphan drug designations for any of our product candidates, and we may be unable to maintain the benefits associated with orphan drug designation, including the potential for market exclusivity.

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs or biologics for relatively small patient populations as orphan drugs. In the United States, under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biological product intended to treat a rare disease or condition. Such diseases and conditions are those that affect fewer than 200,000 individuals in the United States, or if they affect more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and making a drug available in the United States for these types of diseases or conditions will be recovered from sales of the drug. However, orphan drug designation must be requested before submitting an NDA and there can be no assurance that any such designation will be granted. If the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

In the United States, orphan drug designation recipients can take advantage of special incentives provided by the FDA such as (i) potential market exclusivity of the product for seven years as the first sponsor (ii) tax credits for qualified clinical research for a designated orphan product and (iii) waiver of associated fees when submitting a marketing application to the FDA.

Similarly, in the European Union, orphan designation is intended to promote the development of medicinal products that are intended for (i) the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions affecting not more than five in 10,000 persons in the European Union, or that are intended for the diagnosis, prevention, or treatment of a life-threatening, seriously debilitating or serious and chronic condition when, without incentives, it is unlikely that sales in Europe would be sufficient to justify the necessary investment, and (ii) there exists no satisfactory method of diagnosis, prevention or treatment of the condition that has been authorized in Europe or, if such method exists, that the medicinal product will be of significant benefit to those affected. In Europe, orphan designation entitles a party to a number of incentives, such as protocol assistance and scientific advice specifically for designated orphan medicines, and potential fee reductions depending on the status of the sponsor. European orphan medicines also benefit from ten years of market exclusivity, which precludes the EMA from approving another marketing application during this time period for a similar drug and for the same indication. This marketing exclusivity period can however, be reduced to six years if, at the time the marketing authorization is renewed after five years, a drug no longer meets the criteria for orphan designation or if the drug is sufficiently profitable, such that market exclusivity is no longer justified.

Our product candidate SLN124 has received orphan drug designation from the EMA for the treatment of beta-thalassemia and from the FDA for the treatment of beta-thalassemia, myelodysplastic syndrome, or MDS, and polycythemia vera, or PV. Our drug candidate SLN501 (collaboration with Mallinckrodt) has received orphan drug designation from the FDA for complement 3 glomerulopathy, or C3G. The EMA will reassess eligibility for SLN124 orphan exclusivity at the time of MA review and can remove orphan status if the drug no longer meets the eligibility criteria, including offering a significant benefit to those affected, at that time. Moreover, even if we obtain orphan drug exclusivity in the future for a product candidate for these or other indications, such exclusivity may not effectively protect the product candidate from competition because different therapies can be approved for the same condition and the same therapies can be approved for different conditions but used off-label. Even after an orphan drug is approved, the FDA or EMA can subsequently approve a different or a similar drug for the same condition if such regulatory authority concludes that the later drug is clinically superior because it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug exclusivity may also be lost if the regulatory authority later determines that the initial request for designation was materially defective. In addition, orphan drug exclusivity does not prevent the regulatory authority from approving competing drugs for the same disease or condition containing a different active ingredient. In addition, if a subsequent drug is approved for marketing for the same disease or condition as any of our product candidates that receive marketing approval, we may face increased competition and lose market share regardless of orphan drug exclusivity.

Although we have obtained Rare Pediatric Disease Designation for SLN124 for the treatment of beta-thalassemia, we may not realize the expected benefits of this designation.

In 2012, Congress authorized the FDA to award priority review vouchers to sponsors of certain rare pediatric disease product applications. This provision 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.

SLN124 has been granted rare pediatric disease designation, but designation of a drug for a rare pediatric disease does not guarantee that an NDA will meet the eligibility criteria for a rare pediatric disease priority review voucher at the time the application is approved. Specifically, on December 27, 2020, the Rare Pediatric Disease Priority Review Voucher Program was extended by Congress; 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 drug, and that designation was granted by September 30, 2024. After September 30, 2026, FDA may not award any rare pediatric disease priority review vouchers. Furthermore, a Rare Pediatric Disease Designation does not lead to faster development or regulatory review of the product, or increase the likelihood that it will receive marketing approval. We may or may not realize any benefit from receiving a voucher.

We may use our financial and human resources to pursue a particular research program or product candidate and fail to capitalize on programs or product candidates that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and human resources, we intend to leverage our existing licensing and collaboration agreements and may enter into new strategic collaboration agreements for the development and commercialization of our programs and potential product candidates in indications with potentially large commercial markets while focusing our internal development resources, and any future internal sales and marketing organization that we may establish, on research programs and product candidates intended for selected markets or patient populations, such as rare diseases. As a result, and even as we prioritize rare indications with expansion opportunities to large populations, we may forego or delay pursuit of other programs or product candidates or other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through strategic collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate, or we may allocate internal resources to a product candidate in a therapeutic area in which it would have been more advantageous to enter into a collaboration arrangement.

Any of our product candidates may cause adverse effects or have other properties that could delay or prevent their regulatory approval or limit the scope of any approved label or market acceptance.

AEs caused by our product candidates could cause us, other reviewing entities, clinical trial sites or regulatory authorities to interrupt, delay or halt clinical trials and could result in the denial of regulatory approval. Certain oligonucleotide therapeutics have been observed to result in injection site reactions and pro-inflammatory effects and may also lead to impairment of kidney or liver function. There is a risk that our future product candidates may induce similar AEs.

If AEs are observed in any clinical trials of our product candidates, including those that a strategic collaborator may develop under an agreement with us, our or our collaborators' ability to obtain regulatory approval for product candidates may be negatively impacted.

Further, if any of our future products, if and when approved for commercial sale, cause serious or unexpected side effects, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw their approval of the product or impose restrictions on our distribution in the form of a risk evaluation and mitigation strategy;
- regulatory authorities may require the addition of labeling statements, such as warnings or contraindications;
- we may be required to change the way the product is administered or conduct additional clinical trials;
- we could be sued and held liable for harm caused to patients; or
- our reputation may suffer.

Any of these events could prevent us or our collaborators from achieving or maintaining market acceptance of the affected product and could substantially increase the costs of commercializing our future products and impair our ability to generate revenues from the commercialization of these products either on our own or with the collaborator.

Even if any of our product candidates receive marketing approval, they may fail to achieve the degree of market acceptance by physicians, patients, third party payers and others in the medical community necessary for commercial success.

The product candidates that we are developing are based upon new technologies or therapeutic approaches. Key participants in pharmaceutical marketplaces, such as physicians, third-party payers and consumers, may not accept a product intended to improve therapeutic results based on RNAi technology. As a result, it may be more difficult for us to convince the medical community and third-party payers to accept and use our product, or to provide favorable reimbursement and market access. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy, safety and potential advantages of any of our product candidates compared to alternative treatments;
- our ability to offer our products for sale at competitive prices;
- the stability, shelf life, convenience and ease of storage and administration compared to alternative treatments;
- the willingness of the target patient population to try new treatments and of physicians to prescribe these treatments;
- our ability to hire and retain a sales force, or to engage one or more third party distributors for our products;
- the strength of marketing and distribution support;
- the availability of third party payer coverage and adequate reimbursement for our product candidates;
- the prevalence and severity of any side effects; and
- any restrictions on the use of our products together with other medications.

Risks Related to Our Business Operations and Compliance with Government Regulations

We face competition from other companies that are working to develop novel drugs and technology platforms using technologies similar to ours. If these companies develop drugs more rapidly than we do or their technologies, including delivery technologies, are more effective, our ability to successfully commercialize drugs may be adversely affected.

We face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions, governmental agencies and public and private research institutions. Many of our competitors may have greater experience in research and development, manufacturing, managing clinical trials and/or regulatory compliance than we do, and may be better resourced financially. Any product candidates that we successfully develop and commercialize will compete with existing products and new products that may become available in the future. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and recruiting lead clinical trial investigators and establishing clinical study sites and patient registration for clinical studies, as well as in acquiring technologies complementary to, or necessary for, our programs.

Companies that complete clinical trials, obtain required regulatory authority approvals and commence commercial sale of their drugs before we do may achieve a significant competitive advantage, and our commercial opportunity could be reduced or eliminated if competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop and commercialize. Because our products and many potential competing products are in various stages of preclinical and clinical development, and given the inherent unpredictability of drug development, it is difficult to predict which third parties may provide the most competition, and on what specific basis.

In addition to the competition we face from competing drugs in general, we also face competition from other companies working to develop novel drugs using technology that competes more directly with our own. We are aware of several other companies that are working to develop RNAi therapeutic products and other companies may develop alternative treatments for the diseases we have identified as being potentially treated with our siRNA molecules. To the extent those alternative treatments are more efficacious, less expensive, more convenient or produce fewer side effects, our market opportunity would be reduced.

Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on principal members of our executive team, the loss of whose services may adversely impact the achievement of our objectives. Certain of our executive officers are “at will” employees and may terminate their employment with us at any time upon prior written notice. Recruiting and retaining other qualified employees for our business, including scientific and technical personnel, will also be critical to our success. There is currently a shortage of skilled executives in our industry, which is likely to continue. As a result, competition for skilled personnel is intense and the turnover rate can be high. We may not be able to attract and retain personnel on acceptable terms given the competition among numerous life sciences companies for individuals with similar skill sets. In addition, failure to succeed in preclinical studies and clinical trials may make it more challenging to recruit and retain qualified personnel.

The inability to recruit or loss of the services of any executive or key employee might impede the progress of our research, development and commercialization objectives.

We may need to expand our organization and may experience difficulties in managing this growth, which could disrupt our operations.

As of December 31, 2022 we had 122 employees. In the future we may expand our employee base to increase our managerial, scientific, operational, commercial, financial and other resources and to hire more consultants and contractors. Future growth would impose significant additional responsibilities on our management, including the need to identify, recruit, maintain, motivate and integrate additional employees, consultants and contractors. Also, our

management may need to divert a disproportionate amount of its attention away from its day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. Moreover, if our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and/or grow revenues could be reduced, and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth.

If we fail to introduce new products or keep pace with advances in technology, our business, financial condition and results of operations could be adversely affected.

We spend a relatively low amount on technological innovation compared to our larger competitors. There is a risk that competitors will be quicker to develop new technologies, new products for the same gene targets or new delivery methods of nucleic acids into novel cell types, particularly once competitors learn about new gene targets that we or our collaborators have selected for development of siRNA molecules. We will need to successfully introduce new products to achieve our strategic business objectives. Our successful product development will depend on many factors, including our ability to attract strong talent to lead our research and development efforts, adapt to new technologies, obtain regulatory approvals on a timely basis, demonstrate satisfactory clinical results, manufacture products in an economical and timely manner, obtain appropriate intellectual property protection for our products, gain and maintain market acceptance of our products, and differentiate our products from those of our competitors. In addition, patents attained by others may preclude or delay our commercialization of a product. There can be no assurance that any products now in development or that we may seek to develop in the future will achieve technological feasibility, obtain regulatory approval or gain market acceptance. If we cannot successfully introduce new products or adapt to changing technologies, our products may become obsolete and our revenue and profitability could suffer.

We face potential product liability and other claims, and, if successful claims are brought against us, we may incur substantial liability and costs.

The use of our product candidates in clinical trials and the sale of any products for which we obtain marketing approval exposes us to the risk of product liability claims, including claims related to impurities in our products or potential product recalls. Certain single-stranded oligonucleotide therapeutics have led to injection site reactions and pro-inflammatory effects and may also lead to impairment of kidney or liver function. There is a risk that our current and future product candidates, although double-stranded, may induce similar or other adverse events. Product liability claims might be brought against us by consumers, healthcare providers, life sciences companies or others selling or otherwise coming into contact with our products; other claims may be brought against us by third parties with whom we contract, or by current or former employees or consultants, including claims of wrongful terminations, discrimination, other violations of labor law or other alleged conduct. If we cannot successfully defend against such claims, we could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, such claims may result in, among other things:

- impairment of our business reputation;
- withdrawal of clinical trial participants with respect to product liability claims;
- costs due to related litigation;
- distraction of management's attention from our primary business;
- substantial monetary awards to claimants;
- the inability to commercialize our product candidates; and

- decreased demand for our product candidates, if approved for commercial sale.

We maintain product liability insurance relating to the use of our therapeutics in clinical trials. However, such insurance coverage may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive and in the future we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If and when we obtain marketing approval for product candidates, we intend to expand our insurance coverage to include the sale of commercial products; however, we may be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. On occasion, large judgments have been awarded in class action lawsuits based on drugs that had unanticipated adverse effects. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business.

Cybersecurity risks and the failure to maintain the confidentiality, integrity, and availability of our computer hardware, software, and internet applications and related tools and functions could result in damage to our reputation and/or subject us to costs, fines or lawsuits.

Our business requires manipulating, analyzing and storing large amounts of data. We also maintain personally identifiable information about our employees. Our business therefore depends on the continuous, effective, reliable, and secure operation of our computer hardware, software, networks, internet servers, third party technology service providers and related infrastructure. To the extent that our hardware or software malfunctions or access to our data by internal research personnel is interrupted, our business could suffer. The integrity and protection of our employee and company data is critical to our business and employees have a high expectation that we will adequately protect their personal information. The regulatory environment governing information, security and privacy laws is increasingly demanding and continues to evolve, as further described below. Maintaining compliance with applicable security and privacy regulations may increase our operating costs. Although our computer and communications hardware are protected through physical and software safeguards, we are still vulnerable to fire, storm, flood, power loss, earthquakes, telecommunications failures, physical or software break-ins, software viruses, accidental or malicious insider-action and similar events. These events could lead to the unauthorized access, disclosure and use of non-public information. The techniques used by criminal elements to attack computer systems are sophisticated, change frequently and may originate from less regulated and remote areas of the world and increasingly involve highly resourced threat actors such as organized criminals and nation states. As a result, we cannot provide assurance that our efforts to address these techniques proactively or implement adequate preventative measures will always be successful. If our computer systems are compromised, we could be subject to fines, damages, litigation and enforcement actions, and we could lose trade secrets, the occurrence of which could harm our business. In addition, any sustained disruption in internet systems or network access provided by other companies could harm our business.

The collection, processing and cross-border transfer of personal information is subject to restrictive laws and regulations.

We are subject to privacy and data protection laws and regulations that apply to the collection, transmission, storage and use of personally identifiable information. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing amount of focus on compliance in this area, with the potential to affect our business.

In the European Union and the United Kingdom, the collection and use of personal data (including health data) is governed by the provisions of the EU and U.K. General Data Protection Regulations, or collectively, the GDPR. The GDPR applies to the processing of personal data (i) by businesses established in the European Union or the United Kingdom, regardless of whether the processing takes place in the European Union or the United Kingdom, or (ii) of individuals located in the European Union or the United Kingdom, by businesses established outside of the European Union or the United Kingdom, where they process personal data to (a) offer goods or services to individuals in the European Union or the United Kingdom, or (b) monitor their behavior, as it takes place in the European Union or the United Kingdom (e.g., carrying out clinical trial activities in the European Union or the United Kingdom).

The GDPR imposes data protection obligations on organizations processing personal data, including:

- disclosures to individuals, about, among others, how their personal data are processed, and the legal basis for such processing,
- limitations on the retention of personal data,
- mandatory data breach notification requirements in certain circumstances,
- data processing obligations on service providers who process personal data on behalf of other organizations,
- additional conditions when processing "sensitive data" under the GDPR (which includes health and genetic data of individuals located in the European Union or the United Kingdom),
- having security measures in place appropriate to the risk of processing, and
- responding to individuals exercising their data subject rights under the GDPR (i.e., right of access, erasure, rectification, restriction, objection, and data portability).

The GDPR also imposes strict rules on the transfer of personal data out of the European Economic Area, or EEA, or United Kingdom to third countries, including the United States. In order to transfer personal data outside of the EEA/United Kingdom, businesses will need to rely on (i) an adequacy decision (i.e., a finding by the European Commission or the United Kingdom that the destination country offers an "adequate" level of data protection), (ii) an appropriate safeguard (e.g., Standard Contractual Clauses), or (iii) a derogation. Failure to comply with the requirements of the EU's GDPR may result in fines of up to 4% of an undertaking's total global annual turnover for the preceding financial year, or €20,000,000, whichever is greater. In addition to administrative fines, a wide variety of other potential enforcement powers are available to data supervisory authorities in respect of potential and suspected violations of the GDPR, including extensive audit and inspection rights, and powers to order temporary or permanent bans on all or some processing of personal data carried out by noncompliant actors. While we have taken steps to comply with the GDPR, and implementing legislation in applicable EU member states and the United Kingdom, including seeking to establish appropriate lawful bases for the various processing activities we carry out as a controller, adopting an international transfer mechanism, where applicable, reviewing our security procedures, and entering into data processing agreements with relevant vendors and business partners, we cannot guarantee that our efforts to achieve and remain in compliance have been, and/or will continue to be, fully successful.

Additionally, the United Kingdom has transposed the GDPR into U.K. domestic law by way of the U.K. GDPR, As a result, we are exposed to two parallel regimes, each with enforcement powers. Failure to comply with the U.K. GDPR may result in fines of up to 4% of total global annual turnover or £17,500,000 for violations of the U.K. GDPR. Also, following the expiry of the post-Brexit transitional arrangements, the U.K. Information Commissioner's Office cannot be our "lead supervisory authority" in respect of any "cross border processing" for the purposes of the EU's GDPR. For so long as we are unable to, and/or do not, designate a lead supervisory authority in an EEA member state, we are not able to benefit from the GDPR's "one stop shop" mechanism. Among other things, this would mean that, in the event of a violation of the GDPR affecting data subjects across the United Kingdom and the EEA, we could be investigated by, and ultimately fined by the U.K. Information Commissioner's Office and the supervisory authority in each and every EEA member state where data subjects have been affected by such violation. Other countries have also passed or are considering passing laws requiring local data residency and/or restricting the international transfer of data.

Similarly, failure to comply with federal and state laws in the United States regarding privacy and security of personal information could further expose us to penalties under privacy and data protection laws. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our business.

Our employees, consultants and contractors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements or insider trading violations, which could significantly harm our business.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees, consultants or contractors could include intentional failures to comply with governmental regulations, comply with healthcare fraud and abuse and anti-kickback laws and regulations in the United States, the United Kingdom and other jurisdictions, or failure to report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. 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. Employee misconduct could also involve the improper use of, including improper trading based upon, information obtained in the course of clinical studies, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a code of business conduct and ethics and a robust compliance program, but it is not always possible to identify and deter employee misconduct, 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 these laws or regulations. 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 fines or other sanctions.

Healthcare legislative reform measures may have a negative impact on our business and results of operations.

In the United States, there have been, and continue to be, legislative and regulatory developments regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities, and affect our ability to profitably sell any product candidates for which we obtain marketing approval. Additionally, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent congressional inquiries and proposed and enacted federal and state legislation 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 products. While any proposed measures will require authorization through additional legislation to become effective, Congress and the current administration have each indicated that they will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures are increasingly 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. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or successfully commercialize our drugs.

The withdrawal of the United Kingdom from the European Union, commonly referred to as "Brexit," may adversely impact our ability to obtain regulatory approvals of our product candidates in the European Union, result in restrictions or imposition of taxes and duties for importing our product candidates into the European Union, may require additional licenses and procedural steps and may require us to incur additional expenses in order to develop, manufacture and commercialize our product candidates in the European Union.

Following the result of a referendum in 2016, the United Kingdom left the European Union on January 31, 2020, commonly referred to as Brexit. Pursuant to the formal withdrawal arrangements agreed between the United Kingdom and the EU, the United Kingdom was subject to a transition period until December 31, 2020, or the Transition Period, during which EU rules continued to apply. The Trade and Cooperation Agreement, which outlines the future trading relationship between the United Kingdom and the EU was agreed in December 2020 and entered into force on May 1, 2021.

Since a significant proportion of the regulatory framework in the United Kingdom applicable to our business and our product candidates is derived from EU directives and regulations, Brexit has had, and may continue to have, a material impact upon the regulatory regime with respect to the development, manufacture, importation, approval and

commercialization of our product candidates in the United Kingdom or the EU. For example, while Northern Ireland continues to be subject to EU pharmaceutical laws and is covered by centralized authorizations, Great Britain is no longer covered by the centralized procedures for obtaining EU-wide marketing authorization from the EMA and a separate marketing authorization will be required to market our product candidates in Great Britain. (referred to as a UKMA(GB)). Therefore, applicants must undergo two separate procedures to obtain marketing authorizations valid in the EU/EEA and Great Britain. The MHRA has established a number of accelerated procedures to allow those applying for a UKMA(GB) to fast-track their application if the applicant has already obtained a marketing authorization(s) through the mutual recognition or decentralized procedure or has a centralized marketing authorization. In these cases the MHRA provides for reliance procedures that allow applicants to obtain a UKMA(GB) within 67 days of marketing authorization validation. However, this procedure can be delayed if there are any major issues (leading to the application being switched to the standard 210-day timetable). Conversely, the EU does not provide for any mutual recognition or reliance routes based on U.K. marketing authorizations. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, could make it more difficult for us to commercialize our product candidates in the European Union or in the United Kingdom and restrict our ability to generate revenue and achieve and sustain profitability. While the Trade and Cooperation Agreement provides for the tariff-free trade of medicinal products between the United Kingdom and the EU, there may be additional non-tariff costs to such trade which did not exist prior to the end of the Transition Period. Although the United Kingdom currently remains aligned with EU pharmaceutical laws, should the United Kingdom diverge from the European Union from a regulatory perspective in relation to medicinal products, additional non-tariff barriers could arise on such trade. We could therefore, both now and in the future, face significant additional expenses (when compared to the position prior to the end of the Transition Period) to operate our business, which could significantly and materially harm or delay our ability to generate revenues or achieve profitability of our business. As Brexit means that the U.K. is a third country, there are also additional requirements around importing and exporting investigational medicinal products, medicinal products and active substances between the U.K and EU that might require additional licenses (e.g. an importation license rather than a wholesale dealers' license) and additional steps (e.g. batch release in the EU).

Additionally, there are potential changes to the regulatory framework in the United Kingdom. Notably, the U.K Government has introduced the Retained EU Law (Revocation and Reform) Bill into Parliament, which proposes that all retained European Union law will expire on December 31, 2023 (or at the latest June 23, 2026), which would include all key pharmaceutical legislative instruments. The Bill proposes to grant certain powers to Government Ministers to make regulations in the affected areas. While the U.K. Government and European Commission have finalized negotiations regarding the terms of the Northern Ireland Protocol, the Windsor Framework will need to be approved in the British Parliament. As such, there could be further uncertainty about the regulatory position in the United Kingdom.

While the Trade and Cooperation Agreement provides for the tariff-free trade of medicinal products between the United Kingdom and the EU, there may be additional non-tariff costs to such trade, which did not exist prior to the end of the Transition Period. Although the United Kingdom currently remains aligned with EU pharmaceutical laws, should the United Kingdom diverge from the European Union from a regulatory perspective in relation to medicinal products, additional non-tariff barriers could arise on such trade. We could therefore, both now and in the future, face significant additional expenses (when compared to the position prior to the end of the Transition Period) to operate our business, which could significantly and materially harm or delay our ability to generate revenues or achieve profitability of our business.

Any further changes in international trade, tariff and import/export regulations as a result of Brexit or otherwise may impose unexpected duty costs or other non-tariff barriers on us. These developments, or the perception that any of them could occur, may significantly reduce global trade and, in particular, trade between the impacted nations and the United Kingdom.

It is also possible that Brexit may negatively affect our ability to attract and retain employees, particularly those from the European Union, and make travel and staff transfers between our United Kingdom and German offices more difficult, time-consuming and expensive than previously was the case.

Legal, political and economic uncertainty surrounding Brexit may be a source of instability in international markets, create significant currency fluctuations, adversely affect our operations in the United Kingdom and pose additional risks to our business, revenue, financial condition, and results of operations.

The lack of clarity on future U.K. laws and regulations, including financial laws and regulations, tax and free trade agreements, intellectual property rights, data protection laws, supply chain logistics, environmental, health and safety laws and regulations, immigration laws and employment laws, after the expiration of the Transition Period may negatively impact foreign direct investment in the United Kingdom, increase costs, depress economic activity and restrict access to capital.

There is a risk that the Windsor Framework will not be approved and that disagreements over the application of a Protocol to the Trade and Cooperation Agreement to Northern Ireland may continue and may lead to the suspension of the Trade and Cooperation Agreement as a whole, or parts thereof. This may lead to new tariffs or non-tariff barriers applying to such trade in the future. The uncertainty concerning the United Kingdom's long-term legal, political and economic relationship with the European Union may be a source of instability in the international markets, create significant currency fluctuations, and/or otherwise adversely affect trading agreements or similar cross-border co-operation arrangements (whether economic, tax, fiscal, legal, regulatory or otherwise). These developments, or the perception that any of them could occur, have had, and may continue to have, a significant adverse effect on global economic conditions and the stability of global financial markets, and could significantly reduce global market liquidity and limit the ability of key market participants to operate in certain financial markets. In particular, it could also lead to a period of considerable uncertainty in relation to the U.K. financial and banking markets, as well as on the regulatory process in Europe. Asset valuations, currency exchange rates and credit ratings may also be subject to increased market volatility.

These developments, or the perception that any of them could occur, have had, and may continue to have, a significant adverse effect on global economic conditions and the stability of global financial markets, and could significantly reduce global market liquidity and limit the ability of key market participants to operate in certain financial markets. In particular, it could also lead to a period of considerable uncertainty in relation to the U.K. financial and banking markets, as well as on the regulatory process in Europe. Asset valuations, currency exchange rates and credit ratings may also be subject to increased market volatility.

If other EU member states pursue withdrawal from the European Union, barrier-free access between the United Kingdom and those EU member states or among countries within the current European Economic Area overall could be diminished or eliminated.

There may continue to be economic uncertainty surrounding the longer-term consequences of Brexit, which could adversely impact third party confidence resulting in collaborators reducing their spending budgets on our product candidates, which could adversely affect our business, revenue, financial condition, results of operations and could adversely affect the market price of our ADSs.

The ongoing effects of the COVID-19 pandemic and post-pandemic effects could adversely affect our clinical trial operations, as well as our supply chain.

Our planned clinical trials may be negatively affected by the COVID-19 pandemic. Clinical site initiation, patient enrollment and first dosing have been delayed due to prioritization of hospital resources toward the COVID-19 pandemic, delays and difficulties in enrolling patients, and staffing issues at clinical trial sites. Our clinical development timelines may be further delayed if our CMOs, CROs and other service providers upon whom we rely experience delays in providing services. Some patients may not be able to comply with clinical trial protocols if quarantines impede patient movement or interrupt healthcare services. We may also experience supply chain constraints as a result of the COVID-19 pandemic, which could impact our ability to conduct clinical trials and develop our products.

While the extent to which the ongoing COVID-19 pandemic impacts our business, our clinical development and regulatory efforts will depend on future developments that are highly uncertain and cannot be predicted with confidence, such as impacts of new variants on the disease, the duration of the outbreak, travel restrictions, quarantines, social distancing requirements, the continued effectiveness of the available vaccines and treatments, the

potential for additional business disruptions and the effectiveness of actions taken in the United States and other countries to continue to manage and treat the disease. Although many states and countries made decisions to relax social distancing requirements and lift travel and other restrictions, local resurgence of COVID-19 infection may occur and could result in prolonged significant disruption of global financial markets, reducing our ability to access capital, which could in the future negatively affect our liquidity a recession or market correction resulting from the ongoing effects of COVID-19 could materially affect our business and the value of our ADSs. Accordingly, we do not yet know the full extent of potential delays or impacts on our business, our clinical and regulatory activities, healthcare systems or the global economy as a whole. However, these impacts could adversely affect our business, financial condition, results of operations and growth prospects.

In addition, to the extent the ongoing COVID-19 pandemic adversely affects our business and results of operations, it may also have the effect of heightening many of the other risks and uncertainties described in this “Risk Factors” section.

Exchange rate fluctuations may adversely affect our results of operations and cash flows.

Our functional currency is pounds sterling, and our transactions are commonly denominated in that currency. However, we receive payments under our collaboration agreements in U.S. dollars and we incur a portion of our expenses in other currencies, primarily Euros. As a result, fluctuations in exchange rates, particularly between the pound sterling on the one hand and the U.S. dollar and Euro on the other hand, may adversely affect our reported results of operations and cash flows. Our business and the price of our ADSs may be affected by fluctuations in foreign exchange rates between the pound sterling and these and other currencies, any of which may have a significant impact on our results of operations and cash flows from period to period.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers’ compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials or other work-related injuries, this insurance may not provide adequate coverage against potential liabilities. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Inflation may adversely affect our operations, including increases in the prices of goods and services required for our operations.

High rates of inflation resulting from global events may adversely affect our operations in the event of increased prices of goods and services, such as energy and other operating costs, labor costs, materials costs and shipping costs, all of which may impact our direct costs. We are also experiencing increases in the cost of services provided by CMOs, CROs and other third parties with whom we do business, including significant increases in the cost of non-human primates required for studies. Such high inflation rates may result in unexpected and unbudgeted cost increases and may require changes to planned investments.

Risks Related to our Intellectual Property

If we are unable to obtain or protect intellectual property rights related to our current or future products and product candidates, we may not be able to compete effectively in our markets.

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our current and future products and product candidates. The strength of patents in the biotechnology and life sciences field involves complex legal and scientific questions and can be uncertain. The patent applications that we own may fail to result in patents with claims that cover our current and future product candidates in the United States, European countries or in other territories. Even if patents do successfully issue, third parties may challenge their validity, enforceability or scope, which may result in such patents being narrowed or invalidated and our patents and patent applications may not adequately protect our intellectual property, or our current and future product candidates, and may not prevent others from designing around our claims.

If the patent applications we hold and/or have out-licensed with respect to our product candidates fail to issue or if their breadth or strength of protection is threatened, it could dissuade companies from collaborating with us to develop product candidates, and threaten our ability to commercialize, future products. We cannot offer any assurances about which, if any, patents will issue or whether any issued patents will be found invalid and unenforceable or will be threatened by third parties. A patent may be challenged through one or more of several administrative proceedings including Inter Partes Review, Post Grant Review, re-examination or opposition before the U.S. Patent and Trademark Office, or the USPTO, or European Patent Office, or the EPO, and by way of similar proceedings in certain other jurisdictions. For example, re-examination of, or oppositions to, patents owned by us have previously been initiated, and while we believe these concluded proceedings did not result in a commercially relevant impact on the individual patents, any successful challenge of patents or any other patents owned by us could deprive us of rights necessary for the successful commercialization of any product candidates that we or our strategic alliance partners may develop. Since patent applications in the United States and most other countries are confidential for a period of up to 18 months after filing, and some remain confidential until issued, we cannot be certain that we were the first to file any patent application related to a product candidate or an siRNA related technology or method. Furthermore, in certain situations, if we and one or more third parties have filed patent applications in the United States claiming the same subject matter, an administrative proceeding, known as a derivation proceeding (previously known as an interference), can be initiated to determine which applicant is entitled to the patent on that subject matter. Such administrative proceedings provoked by third parties or brought by us may be necessary to determine the priority of inventions with respect to our patents or patent applications, or those of our alliance partners. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to us from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms or at all. Our defense of a patent or patent application in such a proceeding may not be successful and, even if successful, may result in narrowed claims, and at substantial costs and distraction to our management and other employees.

In addition, patents have a limited lifespan. In the United States and many other countries and regions of the world including Europe, the natural expiration of a patent is generally 20 years after it is filed as a non-provisional patent application, or a PCT international patent application. Various extensions may be available, however, the life of a patent and the protection it affords is limited. Once the patent life has expired for a product, we may be open to competition from generic medications. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate under patent protection could be reduced.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable, processes for which patents are difficult to enforce and any other elements of our drug discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. Although each of our Silence Therapeutics GmbH employees either has to assign their inventions to us under German Employee Invention Law, or agrees to assign their inventions to us through an employee inventions agreement, and all of our employees, consultants, advisers and any third parties who have access to our proprietary know-how, information or technology enter into confidentiality agreements, we cannot provide any assurances that all such agreements have been duly executed or that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or confidential proprietary information, or independently develop substantially equivalent information and techniques. In addition, others may independently discover our trade secrets, proprietary know-how and

information. For example, the FDA, as part of its transparency initiative, is currently considering whether to make additional information publicly available on a routine basis, including information that we may consider to be trade secrets or other proprietary information, and it is not clear at the present time how the FDA's disclosure policies may change in the future, if at all.

Further, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property in the United States, Europe and in other jurisdictions. If we are unable to prevent material disclosure of the non-patented intellectual property related to our technologies to third parties, and there is no guarantee that we will have any such enforceable trade secret protection, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, results of operations and financial condition.

Third-party claims of intellectual property infringement may prevent or delay our development and commercialization efforts.

Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and life sciences industries, including patent infringement lawsuits. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we and our strategic collaborators are pursuing development candidates and technologies.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to sequences, structures, materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates that are broad enough to cover one of our product candidates or use of our technologies. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in patents with claims that our product candidates or use of our technologies may infringe. In addition, third parties may have or may obtain in the future patents and assert that our product candidates or use of our technologies infringes upon one or more claims of these patents. If any third-party patents were held by a court of competent jurisdiction to be valid and enforceable and to cover the manufacturing process of any of our product candidates, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable patents, or until such patents expire. Similarly, if any third-party patents were held by a court of competent jurisdiction to be valid and enforceable and to cover aspects of our compositions, formulations, processes for manufacture or methods of use, including combination therapy, the holders of any such patents may be able to block our ability to develop and commercialize the applicable product candidate unless we obtained a license or until such patent expires. In either case, such a license may not be available on commercially reasonable terms or at all.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of our management, other employees and resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including up to treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time-consuming and unsuccessful.

Competitors may infringe our patents or the patents of our licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming, even if we ultimately prevail. For example, in 2017, we commenced patent infringement litigation against Alnylam Pharmaceuticals Inc., or Alnylam. In December 2018, we and Alnylam entered into a settlement and license agreement to settle the litigation, which was related to Alnylam's RNAi product ONPATTRO. As part of the settlement, we now

license specified patents to Alnylam, and Alnylam pays us a tiered royalty of up to one percent of its net sales of ONPATTRO in the European Union.

In addition to the costs and potential distraction associated with enforcing our patents in a lawsuit, in an infringement proceeding, a court may decide that a patent of ours or our licensors is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing.

Our efforts in a litigation may fail and, even if successful, may result in substantial costs and be a distraction to our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our ADSs.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties.

We employ individuals who were previously employed at other biotechnology or life sciences companies. We may be subject to claims that our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed confidential information of our employees' former employers or other third parties. We may also be subject to claims that former employers or other third parties have an ownership interest in our patents. Litigation may be necessary to defend against these claims. There is no guarantee of success in defending these claims, and if we are successful, litigation could result in substantial cost and be a distraction to our management and other employees.

Risks Related to Our ADSs and Shares

An active trading market for our ADSs may not develop and you may not be able to resell your ADSs at or above the price you pay for them, if at all.

Our ADSs have been listed on Nasdaq since September 8, 2020. There can be no assurance that an active trading market for the ADSs will be sustained. The lack of an active trading market may also reduce the fair market value of the 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 securities include:

- the commencement, enrollment or results of our planned and future clinical trials;
- positive or negative results from, or delays in, testing and clinical trials by us, collaborators or competitors;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates and technologies;

- the loss of any of our key scientific or management personnel;
- regulatory, legal or tax developments in the United States, United Kingdom, the European Union and other countries;
- the success of competitive products or technologies;
- adverse actions taken by regulatory agencies with respect to our clinical trials or manufacturers;
- changes or developments in laws or regulations applicable to our product candidates or technologies;
- changes to our relationships with collaborators, manufacturers or suppliers;
- concerns regarding the safety of our product candidates;
- announcements concerning our competitors or the pharmaceutical industry in general;
- actual or anticipated fluctuations in our operating results;
- changes in financial estimates or recommendations by securities analysts;
- potential acquisitions, financings, collaborations or other corporate transactions;
- the trading volume of our ADSs on Nasdaq;
- coordinated trading in our ordinary shares and/or ADSs by third parties, including market manipulation;
- publication of information in the media, including online blogs and social media, about our company by third parties;
- sales of our ADSs or ordinary shares by us, members of our senior management and directors or our shareholders;
- general economic, political, and market conditions and overall fluctuations in the financial markets in the United States, the United Kingdom, the European Union, and other countries, including impact of the Ukraine-Russia War and further global and regional impacts of the COVID-19 pandemic;
- stock market price and volume fluctuations of comparable companies and, in particular, those that operate in the biopharmaceutical industry; and
- investors' general perception of us and our business.

These and other market and industry factors may cause the market price and demand for our ADSs to fluctuate substantially, regardless of our actual operating performance, which may limit or prevent investors from selling their ADSs at or above the price paid for the ADSs and may otherwise negatively affect the liquidity of our ADSs.

Some companies that have experienced volatility in the trading price of their shares have been the subject of securities class action litigation. Any lawsuit to which we are a party, with or without merit, may result in an unfavorable judgment. We also may decide to settle lawsuits on unfavorable terms.

Any such negative outcome could result in payments of substantial damages or fines, damage to our reputation or adverse changes to our business practices. Defending against litigation is costly and time-consuming and could divert our management's and key employees' attention and our resources. Furthermore, during the course of litigation,

there could be negative public announcements of the results of hearings, motions or other interim proceedings or developments, which could have a negative effect on the market price of our ADSs.

Future sales, or the possibility of future sales, of a substantial number of our ADSs or our ordinary shares could adversely affect the price of such securities.

Future sales of a substantial number of ADSs or ordinary shares, or the perception that such sales will occur, could cause a decline in the market price of our ADSs. If holders sell substantial amounts of ADSs on Nasdaq, or if the market perceives that such sales may occur, the market price of the ADSs and our ability to raise capital through an issue of equity securities in the future could be adversely affected.

If equity research analysts do not publish research or reports, or publish unfavorable research or reports, about us, our business or our market, the price and trading volume of our ADSs could decline.

The trading market for our ADSs will be influenced by the research and reports that equity research analysts publish about us and our business. As a company admitted to trading on Nasdaq, our equity securities are currently subject to coverage by a number of analysts. However, we do not currently have and may never obtain broad research coverage by equity research analysts published in the United States. Equity research analysts may elect not to provide research coverage of our ADSs, and such lack of research coverage may adversely affect the market price of our ADSs. We will not have any control over the analysts or the content and opinions included in their reports. The price of our ADSs could decline if one or more equity research analysts downgrade our ADSs or issue other unfavorable commentary or research about us. If one or more equity research analysts ceases coverage of us or fails to publish reports on us regularly, demand for our ADSs could decrease, which in turn could cause the trading price or trading volume of our ADSs to decline.

Concentration of ownership of our ordinary shares (including ordinary shares represented by ADSs) among our existing senior management, directors and principal shareholders may prevent new investors from influencing significant corporate decisions and matters submitted to shareholders for approval.

Members of our senior management, directors and current beneficial owners of 5% or more of our ordinary shares and their respective affiliates, in the aggregate, beneficially owned approximately 71% of our issued and outstanding ordinary shares, based on the number of ordinary shares issued and outstanding as of March 1, 2023. As a result, depending on the level of attendance at general meetings of our shareholders, these persons, acting together, would be able to significantly influence all matters requiring shareholder approval, including the election, re-election and removal of directors, any merger, scheme of arrangement, or sale of all or substantially all of our assets, or other significant corporate transactions, and amendments to our articles of association. In addition, these persons, acting together, may have the ability to control the management and affairs of our company. Accordingly, this concentration of ownership may harm the market price of our ADSs by:

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

In addition, some of these persons or entities may have interests different than yours. For example, because many of these shareholders purchased their shares at prices substantially below the current market price of our ordinary shares and have held their shares for a longer period, they may be more interested in selling our company to an acquirer than other investors, or they may want us to pursue strategies that deviate from the interests of other shareholders.

Because we do not anticipate paying any cash dividends on our ordinary shares (including ordinary shares represented by ADSs) in the foreseeable future, capital appreciation, if any, will be your sole source of gains and you may never receive a return on your investment.

You should not rely on an investment in our ADSs to provide dividend income. Under current English law, a company's accumulated realized profits must exceed its accumulated realized losses (on a non-consolidated basis) before dividends can be paid. Therefore, we must have distributable profits before issuing a dividend. We have never declared or paid a dividend on our ordinary shares in the past, and we currently intend to retain our future earnings, if any, to fund the development of our technologies and product candidates and the growth of our business. As a result, capital appreciation, if any, on our ADSs will be your sole source of gains for the foreseeable future. Investors seeking cash dividends should not purchase our ADSs.

We incur increased costs as a result of having our ADSs listed in the United States, and our senior management will be required to devote substantial time to new compliance initiatives and corporate governance practices.

As a company whose securities are publicly listed in the United States, and particularly after we no longer qualify as an "emerging growth company," or EGC, we incur significant legal, accounting and other expenses that we did not incur prior to the listing of the ADSs on Nasdaq in the third quarter of 2020. For example, the Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and the Consumer Protection Act, the listing requirements of Nasdaq and other applicable U.S. 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 need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased our legal and financial compliance costs and have made some activities more time-consuming and costly. For example, it has become more difficult and more expensive for us to obtain director and officer liability insurance.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, regardless of whether or not we are an EGC we will be required to furnish a report by our senior management on our internal control over financial reporting. However, while we remain an EGC we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To prepare for eventual compliance with Section 404, including the attestation report required once we no longer qualify as an EGC, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants, 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.

As a result of the enhanced disclosure requirements of the U.S. securities laws, business and financial information that we report is broadly disseminated and highly visible to investors, which we believe may increase the likelihood of threatened or actual litigation, including by competitors and other third parties, which could, even if unsuccessful, divert financial resources and the attention of our management and key employees from our operations.

We have previously identified material weaknesses in our internal control over financial reporting that have since been remediated. If we experience additional material weaknesses or deficiencies in the future or otherwise fail to maintain an effective system of internal controls, we may not be able to accurately or timely report our financial condition or results of operations, which may adversely affect our business.

In connection with the preparation of our financial statements for the year ended December 31, 2020, we identified material weaknesses in our internal controls over our financial close and reporting process. A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of annual or interim financial statements will not be prevented or detected and corrected on a timely basis. As previously disclosed in our Annual Report on Form 20-F for the year ended December 31, 2020, the material weaknesses identified related to controls to address timely reconciliation and analysis of certain key accounts, including those related to revenue recognition and the recognition and accrual of research and

development related expenses such as CRO and CMO activities. The material weaknesses arose because of insufficient business processes, related internal controls, and financial resources at the time to satisfy the additional accounting and financial reporting requirements required for a publicly U.S. listed company.

While we developed a detailed plan to address the material weaknesses and were successful in remediating them in the year ended December 31, 2021, there can be no assurance that we will not identify additional control deficiencies or material weaknesses in the future.

In addition, if we identify new material weaknesses in the future, if we are unable to comply with the requirements of Section 404, in a timely manner, if we are unable to assert that our internal control over financial reporting is effective or if our independent registered public accounting firm is unable to express an opinion as to the effectiveness of our internal control over financial reporting, the accuracy and timing of our financial reporting may be adversely affected, potentially resulting in restatements of our financial statements, we may be unable to maintain compliance with securities law requirements regarding timely filing of periodic reports and applicable Nasdaq listing requirements, investors may lose confidence in our financial reporting, and our share price may decline as a result.

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

We are an EGC as defined in the SEC's rules and regulations and we will remain an EGC until the earlier to occur of (1) the last day of 2025, (2) the last day of the fiscal year in which we have total annual gross revenues of at least $1.235 billion, (3) the last day of the fiscal year in which we are deemed to be a "large accelerated filer" under SEC rules, which means the market value of our equity securities that is held by non-affiliates exceeds $700 million as of the prior June 30th, and (4) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period. For so long as we remain an EGC, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not EGCs. These exemptions include:

- not being required to comply with the auditor attestation requirements of Section 404;
- not being required to comply with any requirement that has or may be adopted by the PCAOB 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
- an exemption from the requirement to seek nonbinding shareholder advisory votes on executive compensation or golden parachute arrangements.

We may choose to take advantage of some, but not all, of the available exemptions. We have taken advantage of reduced reporting burdens in this report. In particular, we have not included all of the executive compensation information that would be required if we were not an EGC. We cannot predict whether investors will find our ADSs less attractive if we rely on certain or all of these exemptions. If some investors find our ADSs less attractive as a result, there may be a less active trading market for our ADSs and our ADS price may be more volatile.

We qualify as a foreign private issuer and, as a result, we will not be subject to U.S. proxy rules and will be subject to Exchange Act reporting obligations that, to some extent, are more lenient and less frequent than those of a U.S. domestic public company.

We report under the Exchange Act as a non-U.S. company with foreign private issuer status. Because we qualify as a foreign private issuer under the Exchange Act, we are exempt from certain provisions of the Exchange Act that are applicable to U.S. domestic public companies, including (i) the sections of the Exchange Act regulating the solicitation of proxies, consents or authorizations in respect of a security registered under the Exchange Act; (ii) the sections of the Exchange Act requiring insiders to file public reports of their stock ownership and trading activities and liability for insiders who profit from trades made in a short period of time; and (iii) the rules under the Exchange

Act requiring the filing with the SEC of quarterly reports on Form 10-Q containing unaudited financial and other specified information, or current reports on Form 8-K upon the occurrence of specified significant events. In addition, foreign private issuers are not required to file their annual report on Form 20-F until 120 days after the end of each fiscal year, while U.S. domestic issuers that are accelerated filers are required to file their annual report on Form 10-K within 75 days after the end of each fiscal year. Foreign private issuers also are exempt from Regulation Fair Disclosure, aimed at preventing issuers from making selective disclosures of material information. As a result of the above, you may not have the same protections afforded to shareholders of companies that are not foreign private issuers.

As a foreign private issuer, we are permitted to adopt certain home country practices in relation to corporate governance matters that differ significantly from Nasdaq corporate governance listing standards. These practices may afford less protection to shareholders than they would enjoy if we complied fully with Nasdaq corporate governance listing standards.

As a foreign private issuer listed on Nasdaq, we are subject to corporate governance listing standards. However, Nasdaq rules permit a foreign private issuer like us to follow the corporate governance practices of its home country in lieu of certain Nasdaq corporate governance listing standards. Certain corporate governance practices in England, which is our home country, may differ significantly from Nasdaq corporate governance listing standards. For example, neither the corporate laws of England nor our articles of association require a majority of our directors to be independent; we may include non-independent directors as members of our nominations and remuneration committees; and our independent directors are not required to hold regularly scheduled meetings at which only independent directors are present. Therefore, our shareholders may be afforded less protection than they otherwise would have under Nasdaq corporate governance listing standards applicable to U.S. domestic issuers. See “Item 16.G. Corporate Governance” for the exemptions to the Nasdaq corporate governance rules applicable to foreign private issuers.

We may lose our foreign private issuer status, which would then require us to comply with the Exchange Act’s domestic reporting regime and cause us to incur significant legal, accounting and other expenses.

As a foreign private issuer, we are not required to comply with all of the periodic disclosure and current reporting requirements of the Exchange Act applicable to U.S. domestic issuers. We may no longer be a foreign private issuer as of June 30, 2023, which would require us to comply with all of the periodic disclosure and current reporting requirements of the Exchange Act applicable to U.S. domestic issuers as of January 1, 2024. In order to maintain our current status as a foreign private issuer, either (a) a majority of our voting securities must be either directly or indirectly owned of record by non-residents of the United States or (b)(i) a majority of our executive officers or directors cannot be U.S. citizens or residents, (ii) more than 50% of our assets must be located outside the United States and (iii) our business must be administered principally outside the United States. If we lose our status as a foreign private issuer, we would be required to comply with the Exchange Act reporting and other requirements applicable to U.S. domestic issuers, which are more detailed and extensive than the requirements for foreign private issuers. We may also be required to make changes in our corporate governance practices in accordance with various SEC and Nasdaq rules. The regulatory and compliance costs to us under U.S. securities laws if we are required to comply with the reporting requirements applicable to a U.S. domestic issuer may be significantly higher than the cost we would incur as a foreign private issuer. As a result, we expect that a loss of foreign private issuer status would increase our legal and financial compliance costs and would make some activities highly time consuming and costly. We also expect that if we were required to comply with the rules and regulations applicable to U.S. domestic issuers, it would make it more difficult and expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced coverage and/or incur substantially higher costs to obtain coverage. These rules and regulations could also make it more difficult for us to attract and retain qualified members of our board of directors.

Holders of our ADSs have fewer rights than our shareholders and must act through the depositary to exercise their rights.

Holders of our ADSs do not have the same rights as our shareholders who hold our ordinary shares directly and may only exercise their voting rights with respect to the underlying ordinary shares in accordance with the provisions of the deposit agreement. Holders of the ADSs will appoint the depositary or its nominee as their representative to exercise the voting rights attaching to the ordinary shares represented by the ADSs. When a general meeting is

convened, if you hold ADSs, you may not receive sufficient notice of a shareholders' meeting to permit you to withdraw the ordinary shares underlying your ADSs to allow you to vote with respect to any specific matter. We will use commercially reasonable efforts to cause the depositary to extend voting rights to you in a timely manner, but we cannot assure you that you will receive voting materials in time to instruct the depositary to vote, and it is possible that you, or persons who hold their ADSs through brokers, dealers or other third parties, will not have the opportunity to exercise a right to vote. Furthermore, the depositary will not be liable for any failure to carry out any instructions to vote, for the manner in which any vote is cast or for the effect of any such vote. As a result, you may not be able to exercise your right to vote and you may lack recourse if your ADSs are not voted as you request. In addition, in your capacity as an ADS holder, you will not be able to call a shareholders' meeting.

You may be subject to limitations on transfers of your ADSs.

Your ADSs are transferable on the books of the depositary. However, the depositary may close its transfer books at any time or from time to time when deemed necessary or advisable by it in good faith in connection with the performance of its duties or at our reasonable written request, subject in all cases to compliance with applicable U.S. securities laws. In addition, the depositary may refuse to deliver, transfer or register transfers of ADSs generally when our books or the books of the depositary are closed, or at any time if we or the depositary deems it advisable to do so because of any requirement of law or of any government or governmental body, or under any provision of the deposit agreement, or for any other reason, subject to certain rights to cancel ADSs and withdraw the underlying ordinary shares. Temporary delays in the cancellation of 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 or similar corporate actions.

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

The depositary for our ADSs is entitled to charge holders fees for various services, including annual service fees.

The depositary for our ADSs is entitled to charge holders fees for various services, including for the issuance of ADSs upon deposit of ordinary shares, cancellation of ADSs, distributions of cash dividends or other cash distributions, distributions of ADSs pursuant to share dividends or other free share distributions, distributions of securities other than ADSs and annual service fees. In the case of ADSs issued by the depositary into The Depository Trust Company, or DTC, the fees will be charged by the DTC participant to the account of the applicable beneficial owner in accordance with the procedures and practices of the DTC participant as in effect at the time. The depositary for our ADSs will not generally be responsible for any U.K. stamp duty or stamp duty reserve tax arising upon the issuance or transfer of ADSs.

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

Although we do not have any present plans to declare or pay any dividends, in the event we declare and pay any dividend, the depositary for the ADSs has agreed to pay to you the cash dividends or other distributions it or the custodian receives on our ordinary shares or other deposited securities after deducting its fees and expenses, or withholding of taxes. You will receive these distributions in proportion to the number of our 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 register under U.S. securities laws any offering of ADSs, ordinary shares or other securities received through such distributions. We also have no obligation to take any other action to permit distribution on the ADSs, ordinary shares, rights or anything else to holders of the 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 an adverse effect on the value of your ADSs.

Your right to participate in any future rights offerings may be limited, which may cause dilution to your holdings.

Under English law, shareholders usually have preemptive rights to subscribe on a pro rata basis in the issuance of new shares for cash. The exercise of preemptive 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. We may from time to time distribute rights to our shareholders, including rights to acquire our securities. However, we cannot make rights available to you in the United States unless we register the rights and the securities to which the rights relate under the Securities Act or an exemption from the registration requirements is available. Also, under the deposit agreement, the depositary bank will not make rights available to you unless either both the rights and any related securities are registered under the Securities Act, or the distribution of them to ADS holders is exempted from registration under the Securities Act. We are under no obligation to file a registration statement with respect to any such rights or securities or to endeavor to cause such a registration statement to be declared effective. Moreover, we may not be able to establish an exemption from registration under the Securities Act. If the depositary does not distribute the rights, it may, under the deposit agreement, either sell them, if possible, or allow them to lapse. Accordingly, you may be unable to participate in our rights offerings and may experience dilution in your holdings. We are also permitted under English law to disapply preemptive rights (subject to the approval of our shareholders by special resolution or the inclusion in our articles of association of a power to disapply such rights) and thereby exclude certain shareholders, such as overseas shareholders, from participating in a rights offering (usually to avoid a breach of local securities laws).

If we are a passive foreign investment company, there could be adverse U.S. federal income tax consequences to U.S. Holders.

Under the Internal Revenue Code of 1986, as amended, or the Code, we will be a passive foreign investment company, or PFIC, for any taxable year in which (i) 75% or more of our gross income consists of passive income, or (ii) 50% or more of the average quarterly value of our assets consists of assets that produce, or are held for the production of, passive income (including cash). For purposes of these tests, passive income includes dividends, interest, gains from the sale or exchange of investment property and certain rents and royalties. In addition, 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 and received directly its proportionate share of the income of such other corporation. If we are a PFIC for any taxable year during which a U.S. Holder (as defined below under “Item 10.E. Taxation—Material U.S. Federal Income Tax Considerations for U.S. Holders”) holds our ADSs, the U.S. Holder may be subject to adverse tax consequences regardless of whether we continue to qualify as a PFIC, including ineligibility for any preferred tax rates on capital gains or on actual or deemed dividends, interest charges on certain taxes treated as deferred, and additional reporting requirements.

Based on estimates of our income and assets, and certain assumptions with respect to the characterization of our assets as active or passive, we do not believe we were a PFIC for our taxable year ended December 31, 2022. However, no assurances regarding our PFIC status can be provided for any past, current or future taxable year. The determination of whether we are a PFIC is a fact-intensive determination made on an annual basis and the applicable law is subject to varying interpretation. Accordingly, our U.S. counsel expresses no opinion with respect to our PFIC status for any prior, current or future taxable year.

For further discussion of the PFIC rules and the adverse U.S. federal income tax consequences in the event we are classified as a PFIC, see the section titled “Taxation—Material U.S. Federal Income Considerations for U.S. Holders.”

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

For U.S. federal income tax purposes, if a United States person is treated as owning (directly, indirectly or constructively) 10% or more of our stock by vote or value, such U.S. holder will be treated as a “United States shareholder” with respect to each “controlled foreign corporation” in our group (if any). Because our group includes at least one U.S. subsidiary, our non-U.S. subsidiaries and any non-U.S. subsidiaries we were to form or acquire in the future will be treated as controlled foreign corporations.

A United States shareholder of a controlled foreign corporation will be required to annually report and include in its U.S. federal taxable income its pro rata share of "subpart F income," "global intangible low-taxed income" and investments in U.S. property by the controlled foreign corporations, regardless of whether we make any distributions of such income. Special rules, however, apply to United States persons that are partnerships or other pass-through entities. Certain deductions and credits for foreign income taxes paid or accrued by the controlled foreign corporation may be allowed to a corporate United States shareholder, but will not be allowed to an individual United States shareholder. We cannot provide any assurance that we will furnish to any United States shareholder the information required to comply with the reporting and tax-paying obligations discussed applicable to a United States shareholder in respect of controlled foreign corporations. Failure to comply with such reporting obligations may subject a holder of our ordinary shares that is a United States shareholder to significant monetary penalties and may prevent the statute of limitations with respect to its U.S. federal income tax return for the year for which reporting was due from starting. Holders of our ordinary shares that are United States persons should consult their tax advisors regarding the potential application of these rules to their investment in our ordinary shares.

We may be unable to use U.K. carryforward tax losses to reduce future tax payments or benefit from favorable U.K. tax legislation.

As a U.K. resident trading entity, we are subject to U.K. corporate taxation. Due to the nature of our business, we have generated losses since inception. As of December 31, 2022, we had cumulative carryforward tax losses of £167.8 million. Subject to any relevant restrictions (including those that limit the percentage of profits that can be reduced by carried forward losses and those that can restrict the use of carried forward losses where there is a change of ownership of more than half the ordinary shares of the company and a major change in the nature, conduct or scale of the trade), we expect these to be available to carry forward and offset against future operating profits.

As a company that carries out extensive research and development activities, we benefit from the U.K. research and development tax credit regime under the scheme for small and medium-sized enterprises, or SMEs. Under the SME scheme, we are currently able to surrender some of our trading losses that arise from our qualifying research and development activities for a cash rebate of up to 33.35% of such qualifying research and development expenditures. Changes to the SME scheme that have been recently enacted and expected to take effect in relation to expenditure incurred on or after April 1, 2023 will reduce the research and development cash rebate under the SME scheme to an amount up to 18.6% of qualifying research and development expenditures. Proposed changes to the SME scheme that would take effect from April 1, 2023 would introduce restrictions on relief that may be claimed for expenditure on sub-contracted research and development activity outside of the U.K. The rate reduction and the proposed restrictions on the scope of the regime may impact the quantum of research and development relief that we are able to claim in the future. Furthermore, the U.K. government is currently consulting on the potential replacement of the SME scheme with a regime that would operate similarly to the existing research and development expenditure credit scheme for large companies. If the proposals in the consultation document are enacted then this could change the present treatment of sub-contracted research and development work and introduce different thresholds and caps on expenditure and relief. If enacted, the new regime would be expected to impact expenditures incurred from April 2024 onward, and could have an impact on the quantum of research and development relief that we are eligible to claim. From April 1, 2021, for credit claims in excess of £20,000, the amount of payable credit that a qualifying loss-making SME business can receive through SME research and development relief in any one year has been capped at £20,000 plus three times the company's and certain connected parties' total pay-as-you-earn and National Insurance Contributions liability for that year, unless the company actively manages its intellectual property and does not outsource more than 15% of its R&D to a related party. We may not be able to continue to claim payable research and development tax credits in the future if we cease to qualify as an SME, based on size criteria concerning employee headcount, turnover and gross assets. We may also be restricted in our ability to claim payable research and development tax credits in the future if we become subject to the cap on available relief. Qualifying expenditures largely are comprised of employment costs for research staff, research materials, outsourced CRO costs and R&D consulting costs incurred as part of research projects. Specified subcontracted qualifying research expenditures are eligible for a cash rebate of up to 21.67% (12.09% from April 2023).

In the event we generate revenues in the future, we may benefit from the U.K. "patent box" regime that allows profits attributable to revenues from patents or patented products to be taxed at an effective rate of 10%. As of December 31, 2022, we are the exclusive licensee or owner of 26 patent families with each family comprising several patent applications which, if issued, would cover our product candidates, and accordingly, future upfront fees,

milestone fees, product revenues and royalties could be taxed at this tax rate. When taken in combination with the enhanced relief available on our research and development expenditures, we expect a long-term lower effective rate of corporation tax to apply to us. If, however, there are unexpected adverse changes to the U.K. research and development 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 carryforwards and certain built-in losses to reduce future tax payments, our business, results of operations, and financial condition may be adversely affected. This may impact our ongoing requirement for investment and the timeframes within which additional investment is required.

Changes and uncertainties in the tax system in the countries in which we have operations, could materially adversely affect our financial condition and results of operations, and reduce net returns to our shareholders.

We conduct business in the United Kingdom, Germany and the United States and file income tax returns in multiple jurisdictions. Our consolidated effective income tax rate could be materially adversely affected by several factors, including: changing tax laws, regulations and treaties, or the interpretation thereof; tax policy initiatives and reforms under consideration (such as those related to the Organization for Economic Co-Operation and Development's, or OECD, Base Erosion and Profit Shifting, or BEPS, Project, the European Commission's state aid investigations and other initiatives); the practices of tax authorities in jurisdictions in which we operate; the resolution of issues arising from tax audits or examinations and any related interest or penalties. Such changes may include (but are not limited to) the taxation of operating income, investment income, dividends received or (in the specific context of withholding tax) dividends paid.

Tax authorities may disagree with our positions and conclusions regarding certain tax positions, or may apply existing rules in an unforeseen manner, resulting in unanticipated costs, taxes or non-realization of expected benefits.

A tax authority may disagree with tax positions that we have taken, which could result in increased tax liabilities. For example, His Majesty's Revenue & Customs, or HMRC, the U.S. Internal Revenue Service or another tax authority could challenge our allocation of income by tax jurisdiction and the amounts paid between our affiliated companies pursuant to our intercompany arrangements and transfer pricing policies, including amounts paid with respect to our intellectual property development. Similarly, a tax authority could assert that we are subject to tax in a jurisdiction where we believe we have not established a taxable connection, often referred to as a "permanent establishment" under international tax treaties, and such an assertion, if successful, could increase our expected tax liability in one or more jurisdictions.

A tax authority may take the position that material income tax liabilities, interest and penalties are payable by us, for example where there has been a technical violation of contradictory laws and regulations that are relatively new and have not been subject to extensive review or interpretation, in which case we expect that we might contest such assessment. High-profile companies can be particularly vulnerable to aggressive application of unclear requirements. Many companies must negotiate their tax bills with tax inspectors who may demand higher taxes than applicable law appears to provide. Contesting such an assessment may be a lengthy and costly process and if we were unsuccessful in disputing the assessment, the implications could increase our anticipated effective tax rate, where applicable.

Protections found in provisions under the U.K. City Code on Takeovers and Mergers, or the Takeover Code, may delay or discourage a takeover attempt, including attempts that may be beneficial to holders of our ADSs.

The Takeover Code applies to an offer for a public company whose securities have been admitted to trading on a multilateral trading facility in the United Kingdom which includes AIM, at any time during the 10 years prior to the relevant date of an offer, provided that (i) the registered office of the company is in the United Kingdom and (ii) the company is considered by the Panel on Takeovers and Mergers, or the Takeover Panel, to have its place of central management and control in the United Kingdom. The way in which the test for central management and control is applied for the purposes of the Takeover Code may be different from the way in which it is applied by the U.K. tax authorities. Under the Takeover Code, the Takeover Panel looks to where the majority of the directors are resident, among other factors, for the purposes of determining where a company has its place of central management and control.

The Takeover Panel has confirmed that based on the current composition of our board, the Takeover Code will continue to apply to us. However, the Takeover Code could cease to apply in the future if any changes to the board composition result in the majority of the directors not being resident in the United Kingdom, Channel Islands and Isle of Man. Our articles of association have been amended to include certain important protections which would apply in the event that the Takeover Code ceases to apply.

The Takeover Code provides a framework within which takeovers of certain companies organized in the United Kingdom are regulated and conducted. The following is a brief summary of some of the most important rules of the Takeover Code:

- In connection with a potential offer, if, following an approach by or on behalf of a potential bidder, the company is "the subject of rumor or speculation" or there is an "untoward movement" in the company's share price, there is a requirement for the potential bidder to make a public announcement about a potential offer for the company, or for the company to make a public announcement about its review of a potential offer.

- When a person or group of persons acting in concert (a) acquires, whether by a series of transactions over a period of time or not, interests in shares carrying 30% or more of the voting rights of a company (which percentage is treated by the Takeover Code as the level at which effective control is obtained) or (b) increases the aggregate percentage interest they have when they are already interested in not less than 30% and not more than 50%, they must make a cash offer to all other shareholders at the highest price paid by them or any person acting in concert with them in the 12 months before the offer was announced.

- When interests in shares carrying 10% or more of the voting rights of a class have been acquired for cash by an offeror (i.e. a bidder) or any person acting in concert with them in the offer period (i.e. before the shares subject to the offer have been acquired) or within the previous 12 months, the offer must be in cash or be accompanied by a cash alternative for all shareholders of that class at the highest price paid by the offeror or any person acting in concert with them in that period. Further, if an offeror or any person acting in concert with them acquires for cash any interest in shares during the offer period, the offer must be in cash or accompanied by a cash alternative at a price at least equal to the price paid for such shares during the offer period.

- If after an announcement of a firm offer is made, the offeror or any person acting in concert with them acquires an interest in shares in an offeree company (i.e. a target) at a price higher than the value of the offer, the offer must be increased accordingly.

- The board of directors of the offeree company must appoint a competent independent adviser whose advice on the financial terms of the offer must be made known to all the shareholders, together with the opinion of the board of directors of the offeree company.

- Favorable deals for selected shareholders are not permitted, except in certain circumstances where independent shareholder approval is given and the arrangements are regarded as fair and reasonable in the opinion of the financial adviser to the offeree company.

- All shareholders must be given the same information.

- Those issuing documents in connection with a takeover must include statements taking responsibility for the contents thereof.

- Profit forecasts, quantified financial benefits statements and asset valuations must be made to specified standards and must be reported on by professional advisers.

- Misleading, inaccurate or untrue statements made in documents or to the media must be publicly corrected immediately.

- Actions during the course of an offer by the offeree company which might frustrate the offer are generally prohibited unless shareholders approve these plans. Frustrating actions would include, for example, lengthening the notice period for directors under their service contract or agreeing to sell off material parts of the target group.

- Stringent requirements are laid down for the disclosure of dealings in relevant securities during an offer, including the prompt disclosure of positions and dealings in relevant securities by the parties to an offer and any person who is interested (directly or indirectly) in 1% or more of any class of relevant securities.

- Employees of both the offeror and the offeree company and the trustees of the offeree company's pension scheme must be informed about an offer. In addition, the offeree company's employee representatives and pension scheme trustees have the right to have a separate opinion on the effects of the offer on employment appended to the offeree board of directors' circular or published on a website.

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 our 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. See "Description of Share Capital and Articles of Association—Differences in Corporate Law" filed as Exhibit 2.3 to this report for a description of the principal differences between the provisions of the Companies Act applicable to us and, for example, the Delaware General Corporation Law relating to shareholders' rights and protections.

As an English company, certain capital structure decisions will require shareholder approval, which may limit our flexibility to manage our capital structure.

English law provides that a board of directors may only allot shares (or grant rights to subscribe for, or to convert any security into, shares) with the prior authorization of shareholders by ordinary resolution, being a resolution passed by a simple majority of votes cast, such authorization stating the aggregate nominal amount of shares that it covers and being valid for a maximum period of five years, each as specified in the articles of association or relevant shareholder resolution. In either case, this authorization would need to be renewed by our shareholders upon expiration (i.e., at least every five years). Typically, English public companies renew the authorization of their directors to allot shares on an annual basis at their annual general meeting.

English law also generally provides shareholders with preemptive rights when new shares are issued for cash. However, it is possible for the articles of association, or for shareholders to pass a special resolution at a general meeting, being a resolution passed by at least 75% of the votes cast, to disapply preemptive rights. Such a disapplication of preemptive rights may be for a maximum period of up to five years from the date of adoption of the articles of association, if the disapplication is contained in the articles of association, or from the date of the shareholder special resolution, if the disapplication is by shareholder special resolution, but not longer than the duration of the authority to allot shares to which the disapplication relates. In either case, this disapplication would need to be renewed by our shareholders upon its expiration (i.e., at least every five years). Typically, English public companies renew the disapplication of preemptive rights on an annual basis at their annual general meeting.

English law also generally prohibits a public company from repurchasing its own shares without the prior approval of shareholders by ordinary resolution, being a resolution passed by a simple majority of votes cast, and other formalities. Such approval may be for a maximum period of up to five years. See "Description of Share Capital and Articles of Association" filed as Exhibit 2.3 to this report.

Claims of U.S. civil liabilities may not be enforceable against us.

We are incorporated under English law. Substantially all of our assets are located outside the United States. The majority of our senior management and board of directors reside outside the United States. As a result, it may not be

possible for investors to effect service of process within the United States upon such persons or to enforce judgments obtained in U.S. courts against them or us, including judgments predicated upon the civil liability provisions of the U.S. federal securities laws.

The United States and the United Kingdom do not currently have a treaty providing for the reciprocal recognition and enforcement of judgments (other than arbitration awards) in civil and commercial matters. Consequently, a final judgment for payment given by a court in the United States, whether or not predicated solely upon U.S. securities laws, would not automatically be recognized or enforceable in England and Wales. In addition, uncertainty exists as to whether the English and Welsh courts would entertain original actions brought in England and Wales against us or our directors or senior management predicated upon the securities laws of the United States or any state in the United States. Any final and conclusive monetary judgment for a definite sum obtained against us in U.S. courts would be treated by the courts of England and Wales as a cause of action in itself and sued upon as a debt so that no retrial of the issues would be necessary, provided that certain requirements are met consistent with English law and public policy. Whether these requirements are met in respect of a judgment based upon the civil liability provisions of the U.S. securities laws is an issue for the English court making such decision. If an English court gives judgment for the sum payable under a U.S. judgment, the English judgment will be enforceable by methods generally available for this purpose.

As a result, U.S. investors may not be able to enforce against us or our senior management, board of directors or certain experts named herein who are residents of the United Kingdom or countries other than the United States any judgments obtained in U.S. courts in civil and commercial matters, including judgments under the U.S. federal securities laws.

Our articles of association provide that the U.S. federal district courts are the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act.

Our articles of association provide that the U.S. federal district courts are the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. However, the enforceability of similar federal court choice of forum provisions has been challenged in legal proceedings in the United States, and it is possible that a court could find this type of provision to be inapplicable, unenforceable, or inconsistent with other documents that are relevant to the filing of such lawsuits. In addition, the Securities Act provides that both federal and state courts have jurisdiction over suits brought to enforce any duty or liability under the Securities Act or the rules and regulations thereunder. Accepting or consent to this forum selection provision does not constitute a waiver by you of compliance with federal securities laws and the rules and regulations thereunder. You may not waive compliance with federal securities laws and the rules and regulations thereunder. If a court were to find the choice of forum provision contained in our articles of association to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our results of operations and financial condition. This choice of forum provision may limit a shareholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits.

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 owners and holders 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 the 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 the ADSs.

In addition, New York courts will not enforce a jury trial waiver provision in order to bar a viable setoff or counterclaim of 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 owner or holder of our ADSs brings a claim against us or the depositary in connection with matters arising under the deposit agreement or the ADSs, including claims under U.S. federal securities laws, such owner or holder 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.

ITEM 4: INFORMATION ON THE COMPANY

A. History and Development of the Company.

We were incorporated as a public limited company under the laws of England and Wales on November 18, 1994 under the name Stanford Rook Holdings plc with company number 2992058. In July 2005, we acquired Atugen AG, a company specializing in siRNA. On April 26, 2007, we changed our name to Silence Therapeutics plc. Our principal executive offices are located at 72 Hammersmith Road, London W14 8TH, United Kingdom and our telephone number is +44 (0)20-3457-6900. Our registered office address is 27 Eastcastle Street, London, W1W 8DH, United Kingdom. Our ADSs were listed on the Nasdaq Capital Market under the symbol "SLN" in September 2020. In June 2021, we moved our Nasdaq listing from the Nasdaq Capital Market tier to the Nasdaq Global Market tier. The SEC maintains a website at www.sec.gov which contains in electronic form each of the reports and other information that we have filed electronically with the SEC. Our website address is www.silence-therapeutics.com. Our agent for service of process in the United States is Harvard Business Services, Inc., 16192 Coastal Hwy, Lewes, Delaware 19958, USA.

Capital Expenditures

Our capital expenditures for the years ended December 31, 2022, 2021, and 2020 were £0.4 million, £1.3 million, and £0.5 million, respectively. These capital expenditures consisted primarily of lab and computer equipment.

B. Business Overview

We are a biotechnology company focused on discovering and developing novel molecules incorporating short interfering ribonucleic acid, or siRNA, to inhibit the expression of specific target genes thought to play a role in the pathology of diseases with significant unmet medical need. Our siRNA molecules are designed to harness the body's natural mechanism of RNA interference, or RNAi, by specifically binding to and degrading messenger RNA, or mRNA, molecules that encode specific targeted disease-associated proteins in a cell. By degrading the message that encodes the disease-associated protein, the production of that protein is reduced and its level of activity is lowered. In the field of RNAi therapeutics, this reduction of disease-associated protein production and activity is referred to as "gene silencing." Our proprietary mRNAi GOLD™ (**G**alNAc **Ol**igonucleotide **D**iscovery) platform consists of precision engineered product candidates designed to accurately target and 'silence' specific disease-associated genes in the liver. Using our mRNAi GOLD™ platform, we have generated siRNA product candidates both for our internal development pipeline as well as for out-licensed programs with third-party collaborators. Our wholly owned pipeline is currently focused in three therapeutic areas of high unmet need: cardiovascular disease, hematology and rare diseases.

SLN360, an siRNA targeting the *LPA* gene, is our wholly owned product candidate currently in phase 2 clinical development (ALPACAR-360 trial), to reduce high levels of lipoprotein(a), or Lp(a), a genetically determined cardiovascular risk factor affecting up to 20% of the world's population. In February 2022, we reported positive results

from the single-ascending dose portion of the APOLLO phase 1 program evaluating SLN360 in 32 healthy adults with high Lp(a) ≥150 nmol/L. In the APOLLO trial, participants in the top two SLN360 single dose groups (300 mg and 600 mg) were observed to have experienced up to a 96% and 98% median reduction in Lp(a) levels, respectively, and median reductions of up to 71% and 81% from baseline persisted at 150 days. Those receiving a placebo saw no change in Lp(a) levels. Further analysis showed median time-averaged Lp(a) reductions over 150 days exceeded 80% in the SLN360 300 mg and 600 mg dose groups. At day 365, some participants still exhibited substantially reduced levels of Lp(a) of approximately 50% compared to baseline. SLN360 was well tolerated with no serious safety concerns reported. The multiple-ascending dose portion of the APOLLO program in subjects with high Lp(a) and stable ASCVD is ongoing and expected to readout in the fourth quarter of 2023. In January 2023, we started dosing in the ALPACAR-360 phase 2 trial evaluating subjects with high Lp(a) ≥125 nmol/L at high risk of atherosclerotic cardiovascular disease, or ASCVD, events and we expect to complete enrollment by the end of 2023.

SLN124, an siRNA targeting the *TMPRSS6* gene, is our wholly owned product candidate that has shown the potential to address a range of hematological conditions by modulating endogenous hepcidin, a peptide hormone that is the master regulator of systemic iron balance. SLN124 is being evaluated in the SANRECO phase 1/2 trial in patients with polycythemia vera, or PV, and the GEMINI II phase 1 trial in patients with non-transfusion dependent, or NTD, thalassemia. SLN124 demonstrated proof of mechanism in the GEMINI phase 1 trial in healthy volunteers completed in May 2021, or the GEMINI trial, representing the first clinical data from our mRNAi GOLD™ platform. SLN124 has FDA Fast Track and orphan drug designations for PV as well as orphan drug and rare pediatric disease designations for beta-thalassemia. The European Medical Agency has also granted SLN124 orphan drug designation and rare pediatric disease designation for beta-thalassemia.

The potential of our mRNAi GOLD™ platform has been validated through ongoing research and development collaborations with leading pharmaceutical companies, such as AstraZeneca, Mallinckrodt and Hansoh. These collaborations collectively represent up to 16 pipeline programs and approximately $7.5 billion in potential milestones plus royalties.

We believe the potential for our mRNAi GOLD™ platform to address disease-associated genes in the liver is substantial. Only around one percent of the approximately 14,000 liver expressed genes have been targeted by publicly known siRNAs. Once in the clinic, early-stage N-acetylgalactosamine, or GalNAc, conjugated RNAi programs have shown a greater likelihood of advancement from the current phase of development compared to the pharmaceutical industry average, according to a 2020 industry analysis based on phase transition success rates. We aim to maximize our mRNAi GOLD™ platform by advancing both our proprietary and partnered pipelines.

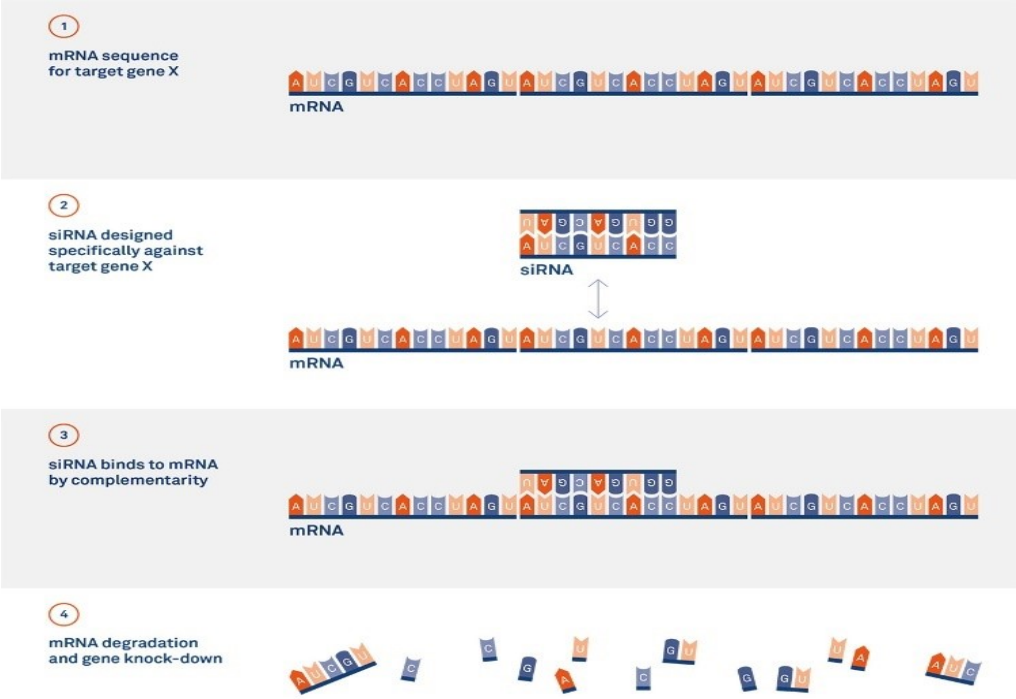
Background on siRNA Molecules and RNA Interference

Messenger RNA (mRNA) plays an essential role in the process used by cells to translate genetic information from DNA to create proteins. Transcription from DNA in the cell nucleus generates different types of RNA, including mRNA, which carries in the sequence of its nucleotides the genetic information which serves as molecular blueprints required for translation, or protein synthesis, outside of the nucleus where proteins are made. In some cases, cells produce mRNA erroneously, resulting in synthesis of too much of a particular protein or a mutated protein variant, which can lead to disease. Our siRNAs are designed to bind to undesirable mRNA, whereupon a natural process known as RNA interference, or RNAi, is triggered, resulting in catalytic degradation of the mRNA and reduced production and activity of the disease-associated protein.

RNAi is a naturally occurring biological pathway within cells for sequence-specific silencing and regulation of gene expression. RNAi was discovered by Andrew Fire and Craig Mello, for which they were awarded the 2006 Nobel Prize in Physiology or Medicine. RNAi therapeutics represent a novel advance in drug development that has the potential to transform the care of patients with genetic and other diseases. Historically, the pharmaceutical industry had developed only small molecules or recombinant proteins to inhibit the activity of disease-associated proteins. While this approach is effective for many diseases, a number of proteins cannot be inhibited by either small molecules or recombinant proteins. Some proteins lack the binding pockets small molecules require for interaction. Other proteins are solely intracellular and are therefore inaccessible to recombinant protein-based therapeutics, which are limited to cell surface and extracellular proteins. The unique advantage of RNAi is that, instead of targeting proteins, RNAi silences the expression of genes themselves via the targeted destruction of the mRNAs made from the gene. Rather than seeking to inhibit a protein directly, the RNAi approach works upstream to prevent its creation in the first place.

Once inside a cell, siRNA molecules are recognized by the endogenous RNAi cellular machinery, which removes one of the strands, referred to as a passenger strand, of the siRNA construct thereby allowing the other strand, referred to as a guide strand, to find its target mRNA and bind to it through Watson-Crick base pairing. This site-specific binding triggers the biological process of RNAi interference, by which natural cellular machinery degrades target mRNA bound by the guide strand and thereby prevents it from being translated into functional proteins.

Our medicines are designed to harness this natural pathway to develop a new generation of therapeutics by designing tailored siRNA sequences that are able to bind through Watson-Crick base pairing to mRNAs that code for specific disease-associated genes, or genes that regulate them. Our siRNA molecules are administered by subcutaneous injection. Once administered, our siRNA molecules are taken up specifically by target liver cells or cleared from the body within hours. A single siRNA molecule, once in the liver and incorporated into the RNAi cellular machinery, can degrade large numbers of targeted mRNAs due to the catalytic nature of the cell's RNAi machinery. Because the catalytic activity of the RNAi pathway eventually fades with gradual degradation of the guide strands, RNAi-mediated protein reduction is not permanent. In our preclinical studies, we have observed a durable, dose-dependent silencing effect with our product candidates, with the highest dose resulting in reductions of between 50% and 85% or more of the target protein level over the course of several weeks to months following subcutaneous injection. As a result of the phase 1 clinical data we have generated in both our SLN360 and SLN124 programs, we believe that these observed results suggest that our product candidates could lead to similar results in humans. The graphic below shows the steps involved in the pairing of our siRNA molecules with the bases contained in the mRNA sequence for a particular target gene.



We believe that siRNA molecules can, in theory, be engineered to bind specifically to and silence almost any gene in the human genome to which siRNA can be delivered. This potentially broad application of siRNA therapeutics could allow them to become a new major class of drugs. We are currently able to deliver siRNA molecules to liver cells using GalNAc for receptor-mediated targeting. GalNAc is an amino-modified monosaccharide that binds to asialoglycoprotein receptors, or ASGPRs, with high affinity and specificity. When GalNAc-conjugated siRNA molecules reach the surface of liver cells, they are internalized in those cells, with those not internalized being excreted. Once internalized, the siRNAs specifically bind to their target mRNAs, degrading them through the cell's natural RNAi pathway. This GalNAc-siRNA drug modality is intended to enable precision medicine through the accuracy of Watson-Crick base pairing of the siRNA to its target gene mRNA, coupled with the specificity of GalNAc-mediated delivery to the target gene-containing liver cell.

Our mRNAi GOLD™ platform uses a novel structure of double-stranded RNA with chemical modifications designed to improve the stability and efficacy of our siRNA molecules as well as to enhance delivery to targeted liver cells. We incorporate proprietary chemical modifications to enhance drug properties of our siRNA molecules, such as potency, stability and tissue distribution. We believe this approach results in a powerful modular technology that will be well-suited to tackle life-changing diseases. Particular siRNA molecules are designed to reduce the levels of a disease-associated protein directly, such as in the case of SLN360. In preclinical studies and our phase 1 single-ascending dose study, SLN360 was shown to directly reduce Lp(a) expression. Alternatively, in cases in which a disease-associated protein is normally subject to inhibition by a regulatory protein, siRNA molecules are designed to increase the levels of the disease-associated protein by silencing the inhibitory protein, thereby relieving inhibition and indirectly increasing levels of the protein normally subject to inhibition. In preclinical studies and in a phase 1 clinical trial in healthy volunteers, SLN124 was shown to indirectly up-regulate hepcidin levels by reducing the expression of a specific gene, TMPRSS6, which normally inhibits the production of hepcidin. We will use this approach to address 'iron loading' anemia conditions in which hepcidin expression is typically low. Using these

techniques, we believe we can design siRNA molecules to decrease high protein levels, and in some cases, to increase low protein levels, depending on the particular disease genes being targeted.

Our mRNAi GOLD™ Platform

Our mRNAi GOLD™ platform comprises elements of our GalNAc-siRNA toolbox, our liver cell targeting technology and our target selection and screening process.

GalNAc-siRNA Toolbox. Our mRNAi GOLD™ platform is a toolbox comprising several different elements that can be incorporated into our double-stranded siRNA structure, known as blunt-ended 19-mers, either singly or in different combinations depending on individual siRNA sequences. The toolbox elements include:

- sugar modifications of one or more select individual nucleotides;
- stabilizing modifications of one or more internucleoside linkages in the sense and antisense strands;
- stabilizing modifications at one or more of the ends of the siRNA molecules; and
- a versatile linker chemistry for GalNAc ligand conjugation in various numbers and configurations.

When applying these elements of our toolbox, we also aim to reduce the overall content of the sugar modifications and the number of undefined stereogenic centers in the siRNA molecule.

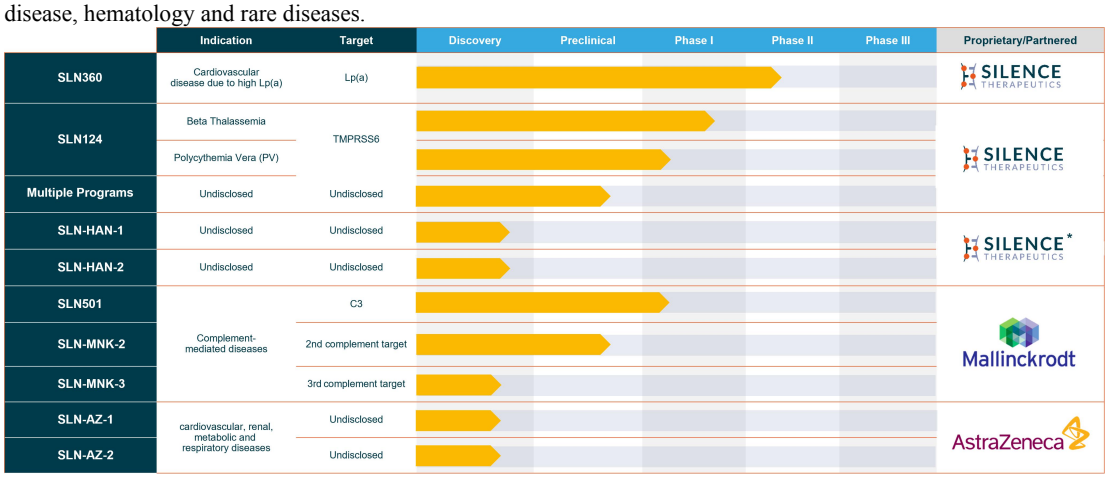
Liver Cell Targeting Technology. Blood flow and fenestra, or small openings in the endothelium, result in a large amount of the injected dose of a conjugated siRNA passing through the liver and reaching the main cell type of the liver known as a hepatocyte. Hepatocytes are cuboidal epithelial cells that line the liver sinusoids. Individual hepatocytes have approximately 0.5 to 1.0 million cell surface ASGPRs. GalNAc binds to ASGPRs with high affinity so that when GalNAc-conjugated siRNA reach the hepatocytes, they are internalized into the cells where siRNA can bind and, as a result, can degrade the target mRNA, which in turn reduces production of the encoded protein and that protein's activity, thereby silencing the respective gene. Only a small fraction of the initial dose reaches the hepatocyte and the right compartment of the cell, but once the siRNA is there, it can stay active and intact for several months, allowing a small number of internalized siRNA molecules to exert a potent effect on the target mRNA. We apply the toolbox elements in the lead optimization phase to identify candidates that we believe will be potent with a long duration of action and have a favorable safety profile.

Target Selection and Screening Process. We are able to source potential product candidates through a proprietary target selection process. The selection of new targets involves a careful analysis of the biology underlying an indication, disease epidemiology and addressable population, the current standard of care and resulting medical need, the commercial landscape and the envisaged clinical path.

Our screening process relies on a proprietary *in silico* algorithm that seeks to predict the most efficacious and specific siRNAs for any given target. This bioinformatics function is designed to continuously improve *in silico* predictions for finding potentially potent and safe siRNA sequences. The highest scoring drug candidates subsequently undergo a multi-step evaluation process involving several rounds of *in vitro* screening in cell lines and primary hepatocytes to identify the most potent molecules. Top candidates identified *in vitro* are then tested for safety and potential efficacy in animal models. At this point in the process, additional modification patterns and new chemistries are introduced for improvement of activity and duration of action while maintaining the desired safety profile. To be selected as a drug candidate for clinical trials, it further needs to be shown that a molecule is well tolerated, elicits no serious adverse effects, and achieves strong and long-lasting knockdown of the targeted gene in a study with non-human primates.

Our Pipeline

Our pipeline is centered around our liver-targeting mRNAi GOLD™ platform and consists of a diversified set of therapeutic areas, including cardiovascular disease, hematology and rare diseases.



*Silence retains exclusive rights to this program outside of the China region, which includes Hong Kong, Macau and Taiwan.

Our siRNA Product Candidates

SLN360

Overview

SLN360 is an siRNA molecule designed for the treatment of cardiovascular disease associated with elevated Lp(a), a lipoprotein in the blood. Available human data validate Lp(a) as an independent risk factor increasing the chances of developing premature cardiovascular diseases, including coronary heart disease and unstable angina, as well as myocardial infarction and ischemic stroke. SLN360 has the potential to reduce these diseases by specifically binding to and inducing RNAi-mediated degradation of the mRNAs made from *LPA*, the gene that encodes apolipoprotein(a), a protein specifically found in Lp(a). SLN360's mode of action creates an opportunity to develop this product candidate for several indications for which Lp(a) has been shown to be a causal, independent risk factor.

We believe SLN360 could be beneficial in addressing increased cardiovascular risk associated with raised levels of Lp(a) greater than 50mg/dL, which is considered to affect up to 20% of the world's population. The incidence of elevated Lp(a) is thought to be higher in people with established cardiovascular disease and calcific aortic valvular stenosis. Additionally, elevated Lp(a) concentrations are associated with an increased risk of myocardial infarction and ischemic stroke, particularly in stroke patients 55 years of age and younger. There is a genetic link between plasma Lp(a) level and cardiovascular risk. Mutations that genetically cause elevated Lp(a) levels have been linked with increases in myocardial infarction, ischemic stroke, carotid stenosis, peripheral arterial disease (including femoral artery stenosis), abdominal aortic aneurysm, obstructed coronary vessels (i.e. coronary atherosclerotic burden), earlier onset of coronary artery disease, cardiovascular and all-cause mortality, increased risk of heart failure and reduced longevity. Importantly, these causal relationships are independent of concentrations of other lipids and lipoproteins, including low-density lipoprotein, or LDL, and conventional cardiovascular disease risk factors. Conversely, a genetically determined decrease in Lp(a) has been associated with a 29% lower risk of coronary artery disease, 31% lower risk of peripheral vascular disease, 17% lower risk of heart failure, 13% lower risk of stroke and a 37% lower risk of aortic stenosis.

SLN360 is administered by subcutaneous injection and was observed to have a long duration of action in the APOLLO trial, potentially allowing for infrequent dosing, such as every three months or less frequently. In April 2022, results from the single-ascending dose portion of the APOLLO program in 32 healthy adults with high Lp(a) ≥150 nmol/L were simultaneously presented in a late-breaking presentation at the American College of Cardiology Annual Meeting and published in *The Journal of the American Medical Association,* or JAMA. In January 2023, we

started dosing in the ALPACAR-360 phase 2 clinical trial evaluating subjects with high Lp(a) ≥125 nmol/L at high risk of ASCVD events and we expect to complete enrollment in the fourth quarter of 2023.

Disadvantages of existing treatment options

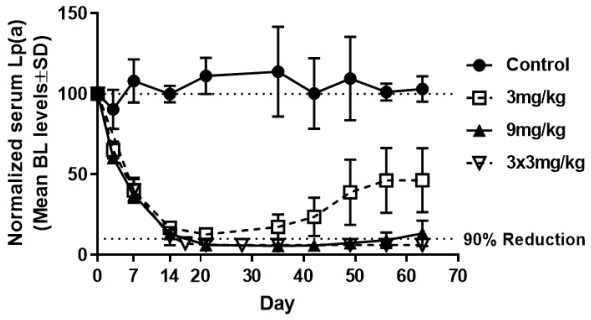
Lp(a) is not susceptible to lifestyle changes and there are no currently available pharmacological treatments that cause an appreciable reduction in Lp(a). The only existing treatment to reduce Lp(a) is apheresis, which involves the removal of blood plasma from the body by the withdrawal of blood, its separation into plasma and cells, and the reintroduction of the cells, used especially to remove antibodies in treating autoimmune diseases. This process can take between two and four hours and is performed every one to two weeks. Consequently, it is invasive and burdensome for patients, and it is only available at limited centers at a high cost. Apheresis is primarily used in Europe and it is not incorporated in the treatment guidelines in the United States.

There are currently no approved lipid-lowering agents specific to Lp(a). Several non-specific agents, largely targeting LDL cholesterol, have been observed to have only marginal or modest Lp(a) reductions, including ezetimibe (7%), niacin therapy (23%), cholesteryl ester transfer protein, or CETP, inhibitors (25-60%), and antisense oligonucleotide-mediated inhibition of apolipoprotein B (ApoB) by mipomersen (26%). Additionally, two monoclonal antibodies that inhibit proprotein convertase subtilisin/kexin type 9, or PCSK9, have been observed to reduce Lp(a) levels by 20%-30%. However, randomization studies have suggested that to produce a clinically significant reduction in cardiovascular risk, a larger reduction in Lp(a) may be required, something that we believe may be achieved by targeted RNA-based approaches such as ours.

Preclinical Data

In a proof of mechanism study in cynomolgus monkeys, non-human primates also known as long-tailed macaques, administration of SLN360 lowered blood serum Lp(a) levels in a sustained manner. The chart below shows changes from baseline, or BL, levels with each data plot shown as an arithmetic mean plus or minus one standard deviation, or SD. As shown in the chart below, over nine weeks following administration of either a single dose of SLN360 (3 mg/kg or 9 mg/kg) on day 0 or three doses (of 3 mg/kg each) on days 0, 7 and 14, the largest dose resulted in a 95% reduction in Lp(a) levels. Individual animals observed in the study had their serum Lp(a) normalized to their own baseline levels, which are expressed as a nominal value of 100 in the chart below.

SLN360-Induced Reduction in Serum Lp(a) in Cynomolgus Monkeys



SLN360 has undergone an extensive nonclinical safety and pharmacokinetic evaluation, including rat biodistribution, repeat dose toxicity in two animal species (rat and the pharmacologically relevant cynomolgus monkey), including safety pharmacology investigations, and in vitro and in vivo genetic toxicity studies. SLN360 has displayed a typically short pharmacokinetic profile, where the compound is almost completely cleared from circulation in the blood after 24 hours. SLN360 distribution was largely restricted to the liver and kidney, with levels in other organs (including reproductive organs) at less than 1% of peak liver levels. SLN360 was shown to be non-genotoxic in the standard battery of genotoxic tests. In good laboratory practice (GLP) toxicology studies, SLN360 was well

tolerated up to the maximum dose administered. All findings in both species were considered to be non-adverse. In the cynomolgus monkey, the most relevant species, the No Observed Adverse Effect Level, or NOAEL, was 60 times the pharmacologically active dose, and no dose-related changes in clinical chemistry, hematology, circulatory and electrocardiography, or ECG, parameters, respiratory rate, neurobehavior, plasma cytokines, complement activation or c-reactive protein levels were noted.

Phase 1 Clinical Program (APOLLO)

The APOLLO phase 1 clinical program is a global randomized, double-blind, placebo controlled, single-ascending dose and multiple-ascending dose study to investigate the safety, tolerability, pharmacodynamic and pharmacokinetic response of SLN360 administered subcutaneously in up to 88 people total with high Lp(a) levels of approximately ≥ 60mg/dL or ≥ 150 nmol/L.

In February 2022, we reported positive results from the single-ascending dose portion of the APOLLO phase 1 program evaluating SLN360 in 32 healthy adults with high Lp(a) ≥150 nmol/L. In April 2022, results from the APOLLO trial were simultaneously presented in a late-breaking presentation at the ACC Annual Meeting and published in JAMA. In the APOLLO trial, participants in the top two SLN360 single dose groups (300 mg and 600 mg) were observed to have experienced up to a 96% and 98% median reduction in Lp(a) levels, respectively, and median reductions of up to 71% and 81% from baseline persisted at 150 days. Those receiving a placebo saw no change in Lp(a) levels. Other efficacy measures included the effects of SLN360 on low-density lipoprotein cholesterol (LDL cholesterol) and ApoB, both of which are associated with an increased risk of cardiovascular events. The highest doses of SLN360 reduced LDL cholesterol and ApoB by about 25%. SLN360 was well tolerated with no serious safety concerns reported. In November 2022, we presented a further analysis from the APOLLO trial up to 365 days in a moderated poster session at the American Heart Association 2022 Annual Meeting. The analysis showed median time-averaged Lp(a) reductions over 150 days exceeded 80% in the SLN360 300 mg and 600 mg dose groups. At day 365, some participants still exhibited substantially reduced levels of Lp(a) of approximately 50% compared to baseline. Additionally, extension data to day 365 showed no new drug related safety findings. The multiple-ascending dose portion of the APOLLO study in subjects with high Lp(a) and stable ASCVD is ongoing and expected to readout in the fourth quarter of 2023.

Phase 2 Clinical Program (ALPACAR-360)

The ALPACAR-360 phase 2 clinical trial is a randomized, double-blind, placebo-controlled trial enrolling approximately 160 patients with high Lp(a) ≥ 125nmol/L at high risk of ASCVD events. Study participants will be randomly assigned to receive either two or three doses of SLN360 or placebo administered subcutaneously. The primary endpoint is time averaged change in Lp(a) from baseline. In January 2023, we announced that we started dosing patients in the ALPACAR-360 trial and we expect to complete enrollment in the fourth quarter of 2023.

SLN124

Overview

SLN124 is an siRNA molecule designed to treat ineffective erythropoiesis, or the production of red blood cells, associated with iron overload disorders and with primary or secondary dysregulation of hepcidin synthesis. These constitute diseases associated with pathologically low hepcidin and diseases in which there is inadequate hepcidin response for the degree of iron loading, such as beta-thalassemia and PV. Left untreated, iron overload disorders cause damage to the heart, liver, pituitary gland, adrenal gland, testes, pancreas, ovaries and kidney and endocrine organs. Beta-thalassemia is often accompanied by the destruction of a large number of red blood cells, which causes the spleen to enlarge and work harder than normal, potentially worsening the anemia. Beta-thalassemia is a rare disease, with an overall prevalence of 1 per 100,000 persons, rising in certain regions (such as Mediterranean Europe, the Middle East and South East Asia) to 1 per 10,000 persons. Globally, there are over 60,000 new cases of beta-thalassemia each year, of which there are approximately 15,000 cases in the United States and the five major markets in Europe. PV is a chronic myeloproliferative neoplasm, where the body makes too many blood cells. This increases the thickness of the blood and can lead to an increased risk of thrombosis (blood clots). The disease often presents later in life (60-65 years) and affects approximately 44 per 100,000 persons in Europe and the United States. SLN124 has the potential to reduce systemic iron, prevent organ iron overload and normalize erythropoiesis. It does so by specifically binding

to and inducing RNAi-mediated degradation of mRNAs made from the gene TMPRSS6, a negative regulator of hepcidin, which is the main hormone controlling iron homeostasis.

SLN124 is administered by subcutaneous injection and has been observed to have a long duration of action in the GEMINI healthy volunteer trial completed in May 2021. Data from the trial showed that SLN124 was effective in reducing plasma iron levels and had a long duration of action. In September 2022, we reported preliminary safety data from the single dose component of the GEMINI II phase 1 trial of SLN124 in patients with NTD thalassemia. Data showed SLN124 was well tolerated with no serious safety issues identified. The multiple dose component of the GEMINI II trial is ongoing and expected to readout in the fourth quarter of 2023. SLN124 is also being evaluated in the SANRECO phase 1/2 trial in PV patients.

In 2019, the EMA granted SLN124 orphan drug designation for the treatment of beta-thalassemia. In 2020, the FDA granted rare pediatric disease designation for the treatment of beta-thalassemia and orphan drug designations for the treatment of MDS and adult beta-thalassemia. In 2022, the FDA granted Fast Track and orphan drug designations for SLN124 in PV.

Disadvantages of existing treatment options

The cornerstone of treatment for iron loading anemias, like beta-thalassemia, is the regular transfusion of packed red blood cell, or RBC, units. Despite providing immediate symptomatic relief by boosting hemoglobin levels (therefore reducing anemia), RBC transfusions are burdensome, require frequent hospital visits (every two to five weeks) and carry the risk of further iron overload. Iron chelators are the standard of care for the prevention of iron overload and can be administered by intravenous or subcutaneous twice daily injections (deferoxamine) or taken orally once (deferasirox) to three times daily (deferiprone). While orally available chelators, particularly Deferasirox (Exjade) are currently prescribed due to their ease of administration, some patients still need to receive deferoxamine infusions. Regardless of administration profile, chelator use carries a known risk of severe side effects with several restrictions of use and black box warnings regarding potential renal, ophthalmic, hepatic and gastrointestinal, or GI, toxicity/failure, with common acute GI side effects including abdominal pain, diarrhea, nausea and vomiting. The side effect profile as well as frequency of administration and perceived bad taste are reported as drivers of poor patient compliance with this existing treatment option.

Luspatercept (Reblozyl) is approved for the treatment of adults with transfusion-dependent beta-thalassemia, and adults with erythropoiesis-stimulating agent (ESA) refractory MDS with ringed sideroblasts. We believe that the limited response rates observed in the MEDALIST and BELIEVE pivotal studies suggest that there remains a substantial unmet need among these patients. Lentiglobin (Zynteglo) is a gene therapy approved in the U.S. and Europe for the treatment of a subset of patients with transfusion-dependent beta-thalassemia. We believe that outstanding questions surrounding the cost, safety and durability of gene therapies and their associated pre-conditioning regimens will limit their uptake, leaving a substantial unmet need for the treatment of beta-thalassemia.

The primary treatment goal in PV is to reduce the risk of thrombotic events by reducing hematocrit (the number of blood cells in a given volume) to within target levels. The mainstay of treatment is therapeutic phlebotomy to reduce the number of blood cells by regularly removing blood from the patient. Phlebotomy results in erratic, suboptimal control of hematocrit, and regular phlebotomies can be burdensome to the patient. Patients over 60, or those with prior thrombotic events or additional cardiovascular risk factors are also treated with chemotherapy drugs (cytoreductive agents) to suppress blood cell production. The majority of these patients are treated with hydroxyurea, which is poorly tolerated and carries the risk of potential long term side effects. Patients who are resistant or intolerant to hydroxyurea may be treated with the JAK2 inhibitor ruxolitinib (Jakafi), which carries the risk of thrombocytopenia (low platelet count). Finally, some patients are treated with synthetic hepcidin mimetic dosed weekly by subcutaneous injection in clinical trials. In contrast to synthetic hepcidin mimetics, SLN124 elevates endogenous hepcidin produced and secreted by the liver, avoiding high local concentrations of hepcidin at the injection site. We believe the sustained duration of action will allow SLN124 to be dosed monthly, or less frequently, bringing additional value to patients.

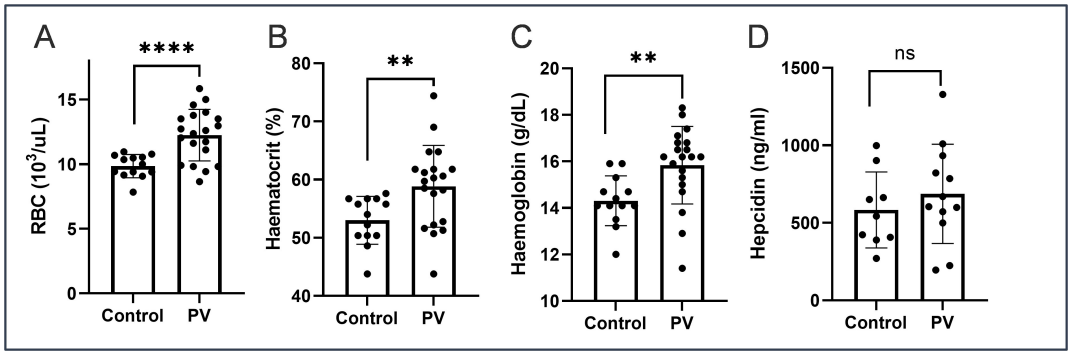
Preclinical Data

Preclinical data in a PV transgenic mouse model

A proof-of-concept study was conducted with an inducible PV mouse model to determine if TMPRSS6 siRNA can attenuate disease progression and severity by raising endogenous hepcidin levels and restricting iron from erythropoiesis.

A majority of PV patients have a *JAK2* gene gain of function mutation, $JAK2^{V617F}$. Since JAK-STAT signaling is involved in the regulation of hepcidin in the liver, it was imperative to create a PV model that restricted the expression of mutant JAK2 allele to the bone marrow. A pharmacodynamic study was conducted using a tamoxifen inducible (CreERT2) bone marrow transplant mouse model of PV with the human $JAK2^{V617F}$allele. Control mice lacked the inducible CreERT2. The PV model recapitulated human disease with increased red blood cells, hematocrit and hemoglobin compared to control animals. Importantly, our model animals displayed hepcidin levels in line with control animals, again corresponding to what has been previously reported in PV patients.

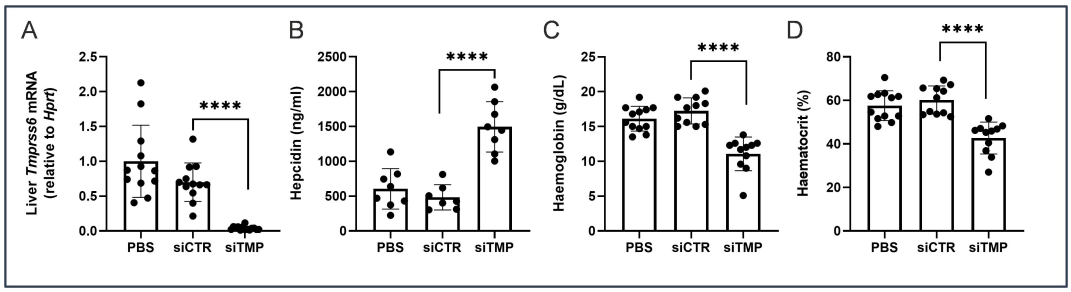
Inducible bone marrow transplant model of polycythemia vera



(A) Red blood cells (RBC), (B) hematocrit, (C) hemoglobin and (D) serum hepcidin in control (n=13) and PV mice (n=20). Data are presented as mean +/- SD. *p ≤ 0.05; **p ≤ 0.01; ***p ≤ 0.001; ****p ≤ 0.0001.

Treatment of the PV mice with TMPRSS6 siRNA resulted in an approximately 95% reduction in *TMPRSS6* mRNA levels which also resulted in a 3.1-fold increase in hepcidin levels in comparison to mice treated with non-targeting control siRNA, or siCTR. The increased hepcidin levels caused a 25% and 32% reduction in hematocrit and hemoglobin, respectively, in comparison to siCTR.

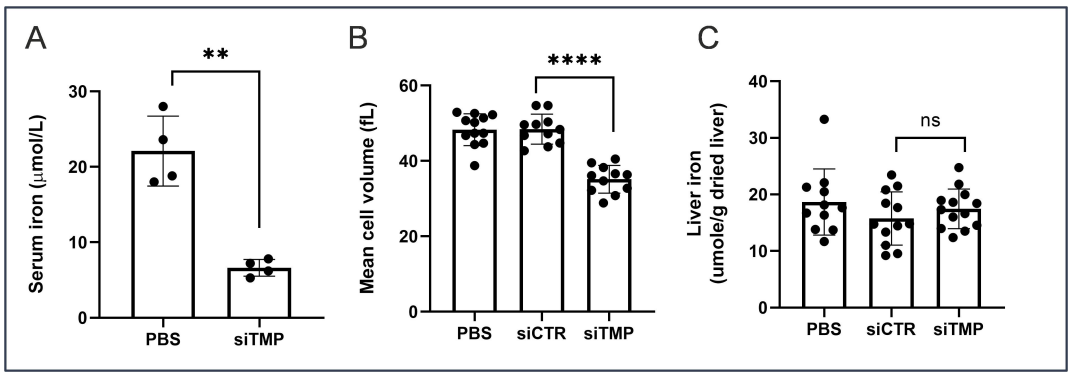
TMPRSS6 siRNA increases hepcidin and decreases erythron



(A) Liver TMPRSS6 mRNA, (B) serum hepcidin, (C) hemoglobin and (D) hematocrit of PV mice treated by subcutaneous injections of PBS (n=12), non-targeting control siRNA, siCTR (n=11) or Tmprss6 siRNA, siTMP (n=13). Data are presented as mean +/- SD. *p ≤ 0.05; **p ≤ 0.01; ***p ≤ 0.001; ****p ≤ 0.0001.

Mice treated with TMPRSS6 siRNA had decreased mean cell volume compared to siCTR treated mice, which is indicative of iron restricted erythropoiesis. TMPRSS6 siRNA significantly decreased serum iron levels, however it did not have an effect on liver iron levels, in comparison to siCTR treated mice.

TMPRSS6 siRNA treatment decreases serum iron



(A) Serum iron, (B) Mean cell volume and (C) liver iron in PV mice treated with subcutaneous injections of PBS (n=12), siCTR (n=11) and siTMP (n=13). Data are presented as mean +/- SD. *p ≤ 0.05; **p ≤ 0.01; ***p ≤ 0.001; ****p ≤ 0.0001.

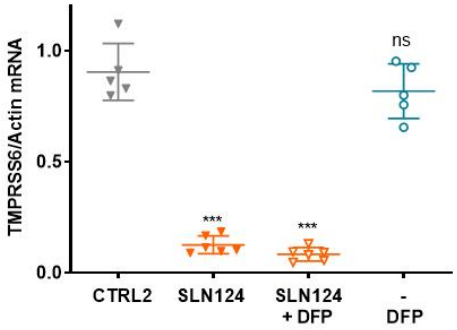
Preclinical data in a beta thalassemia rodent disease model

In a beta-thalassemia rodent disease model, mice treated with SLN124 showed reduced expression of the target gene, *TMPRSS6*, in the liver after 35 days, and increased serum hepcidin levels and lowered transferrin saturation. On days 1 and 15 of the study, mice with heterozygous deletion of two different β-globin genes, also known as $Hbbth^{3/+}$, were treated with either 3 mg/kg of SLN124 subcutaneously as monotherapy or with the same dose of SLN124 in combination with 1.25 ng/mL of deferiprone supplied in drinking water. One cohort of mice was treated with deferiprone alone. The control group consisted of mice having TMPRSS6 siRNA without a ligand.

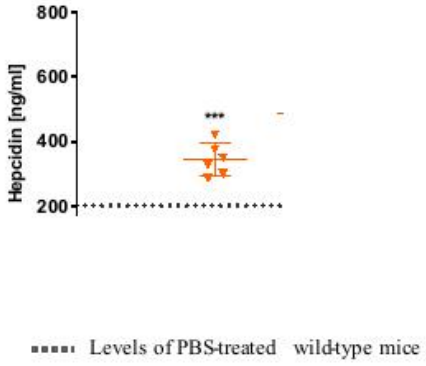
TMPRSS6 mRNA levels were assessed by quantitative Reverse Transcription Polymerase Chain Reaction, or qRT-PCR, a common laboratory technique, and were normalized to the endogenous reference actin relative to their expression levels in control treated animals. These TMPRSS6 mRNA levels are shown in the left panel of the figure below. Serum hepcidin levels were determined using an ELISA assay and are shown in the middle panel of the figure below. Transferrin saturation, a clinical biomarker for serum iron levels, was calculated based on total serum iron and total iron binding capacity, and the observations from the study are shown in the right panel of the figure below.

In the figure below, we show the results from administration on individual animals as well as the mean for each group plus or minus one standard deviation. The figures show that administration of SLN124, either as monotherapy or in combination with deferiprone, reduced TMPRSS6 mRNA levels as compared to the control group or treatment with deferiprone alone. The two mouse groups receiving SLN124 also experienced comparatively higher hepcidin levels and lower transferrin saturation levels than the control group or the deferiprone only group (the deferiprone only control data being non-statistically significant or "ns"). However, because this is a preclinical study, the observed results will need to be confirmed in human clinical trials.

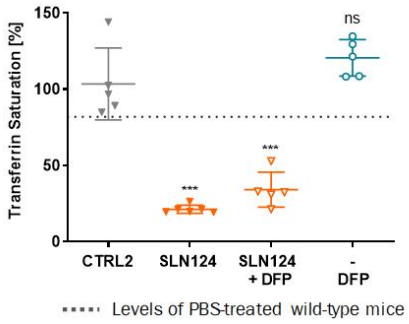
SLN124 reduced liver TMPRSS6 mRNA levels in β-thalassemic mice compared to deferiprone



SLN124 increased serum hepcidin levels in β-thalassemic mice compared to deferiprone

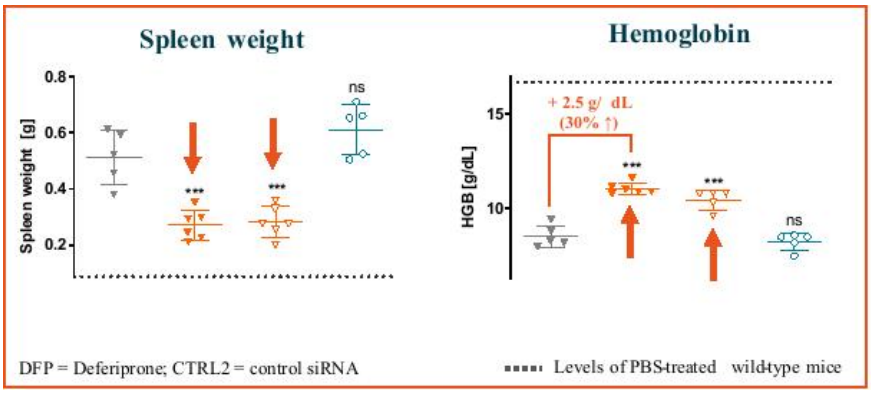


SLN124 reduced transferrin saturation in β-thalassemic mice compared to deferiprone



In our preclinical studies of beta-thalassemic mice, we also observed that administration of SLN124 improved anemia, which led to reduced extramedullary erythropoiesis, evident by the reduction in spleen weight shown in the left panel of the figure below. In these studies, mice were dosed twice over two weeks, following which their spleen weight and hemoglobin levels were measured over five weeks. As shown in the right panel of the figure below, we observed a median increase of 2.5 g/dL in hemoglobin levels, or 30% more than the control group, in the mice receiving SLN124 in this study. Increases of at least 1.5 g/dL are generally considered to be clinically relevant responses, based on 2018 International Working Group standardized response criteria for showing hematologic improvement in patients with MDS.

SLN124 reduced spleen weight and improved anemia in β-thalassemic mice



Data based on collaboration with Dr. J. Vadolas, Australia, Monash Medical Centre/Melbourne.

SLN124 has undergone an extensive nonclinical safety and pharmacokinetic evaluation including mouse biodistribution, single and repeat dose toxicity in two relevant animal species (mouse and cynomolgus monkey) including safety pharmacology investigations, and in vitro genetic toxicity studies. Drug-drug interaction studies have also been performed. The toxicological data obtained so far are regarded as adequate to support single and repeated intermittent monthly treatment in humans.

In these nonclinical evaluations, SLN124 was highly absorbed within hours, while its pharmacodynamic effects were sustained over weeks. SLN124 was distributed to the liver and kidney with little or no detectable tissue concentrations in other tissues, including brain and reproductive organs. The nonclinical safety has been assessed in a series of GLP pharmacology studies. In these studies, ECG, blood pressure and respiration were assessed in cynomolgus monkeys without any test-article related observations. Evaluation of SLN124 in weekly repeat dose GLP studies in mouse and non-human primates has not revealed any unexpected findings. The NOAEL was more than 25 times the predicted efficacious pharmacological dose in both the mouse and monkey species. In vitro experiments in mammalian assay systems confirmed the lack of genotoxicity. In drug-drug interaction studies, SLN124 was not a direct or time-dependent inhibitor of analyzed cytochrome enzymes and was neither an inhibitor nor a substrate of analyzed transporters under the conditions examined.

Healthy Volunteer Trial (GEMINI)

The GEMINI trial, was a randomized, double-blind, placebo controlled, single-ascending dose study to investigate the safety, tolerability, PK and PD response of SLN124 (1.0, 3.0 and 4.5 mg/kg doses) administered subcutaneously in 24 healthy volunteers. In May 2021, we reported positive data from the GEMINI trial, which was the first clinical data from our mRNAi GOLD™ platform. In December 2021, we presented further clinical data from the study at the American Society of Hematology (ASH) Annual Meeting. Key outcomes included:

- All 3 dose levels were well tolerated with no serious or severe treatment emergent adverse events, or TEAEs, leading to withdrawal.
- Average hepcidin, a key endogenous regulator of iron balance and distribution, increased up to ~4-fold after a single dose with effect sustained for at least 2 months.
- Serum iron reduced by ~50% after a single dose with effect sustained for at least 2 months.
- SLN124 was rapidly distributed (median t_{max} was 4.0 or 5.0 hours) and largely eliminated from plasma within 24 hours post-dose in all dosing groups. SLN124 plasma concentrations increased in a greater than dose-linear fashion between dosing groups.
- All SLN124 doses induced marked reductions in transferrin saturation, or TSAT; absolute levels of TSAT achieved (10–16%) are below the level (< 20%) where iron availability to tissue is restricted and at or below that (< 16%) required to support normal erythropoiesis in health.

Thalassemia Phase 1 Program (GEMINI II)

The GEMINI II phase 1 trial is a global, randomized, single-blind, placebo controlled, single-ascending and multiple-ascending dose studies to investigate the safety, tolerability, PK and PD response of SLN124 in approximately 24 adults with NTD thalassemia. In September 2022, we reported preliminary safety results from the single-ascending dose portion of the trial showing SLN124 was well tolerated with no serious adverse events, or AEs, no severe treatment emergent AEs that were SLN124 related and no TEAEs leading to withdrawal identified. Effects on hepcidin, serum iron, transferrin saturation and hemoglobin are being evaluated in the ongoing multiple-dose arm expected to readout in the fourth quarter of 2023.

PV Phase 1/2 Program (SANRECO)

The SANRECO phase 1/2 trial is a two-part clinical trial which includes a phase 1 open-label, dose finding trial followed by a phase 2 randomized, double-blind, placebo-controlled parallel arm study of SLN124 in PV patients. The trial is expected to enroll approximately 65 participants total. The primary endpoint for the phase 1 portion of the trial is safety/tolerability and the assessment of the number of phlebotomies at different intervals. The phase 2 portion of the trial will evaluate the number of patients who are phlebotomy free after treatment. In January 2023, we announced that sites are open for enrollment.

Collaborations

In July 2019, we announced a strategic collaboration with Mallinckrodt to develop and commercialize RNAi drug targets designed to silence the complement cascade in complement-mediated disorders. Under the agreement, we granted Mallinckrodt an exclusive worldwide license to our C3 targeting program, SLN501, with options to license additional complement-mediated disease targets from us, with Mallinckrodt exercising the option for two additional targets in July 2020. We are responsible for preclinical activities, and for conducting each development program until the end of phase 1 clinical trials, after which Mallinckrodt will assume clinical development and responsibility for global commercialization. In connection with the execution of the agreement, Mallinckrodt made an upfront cash payment to us of $20 million (£16.4 million) and purchased $5 million of our ordinary shares. We are eligible to receive up to $10 million in potential research milestone payments, in addition to funding for the phase 1 clinical development of SLN501 including GMP manufacturing. We will fund all other preclinical activities. We received a $2 million (equivalent to £1.6 million based on the exchange rate at the payment date) research milestone payment in October 2019 upon the initiation of work on the first C3 target. In September 2020, we received another $2 million (£1.4 million) research milestone payment following the initiation of work on a second complement target. In February 2021, we initiated work on the third complement target which triggered another $2 million (£1.5 million) research milestone payment. In April 2021, we received $2 million (£1.5 million) for the second research milestone related to the SLN501 C3 targeting program and triggered another $3 million milestone payment following the submission of the SLN501 clinical trial application in March 2022. The collaboration provides for potential additional development and regulatory milestone payments in aggregate of up to $100 million for the initial C3 target and up to $140 million for each of the two optioned complement-mediated disease targets, with such milestones relating to the initiation of specified clinical trials in specified jurisdictions, and upon the receipt of regulatory approvals by specified authorities, in each case for multiple indications. We are also eligible to receive potential commercial milestone payments of up to $562.5 million upon the achievement of specified levels of annual net sales of licensed products for each program. In addition, we are eligible to receive tiered, low double-digit to high-teen percentage royalties on net sales for licensed products for each program.

In March 2020, we announced a strategic collaboration with AstraZeneca to discover, develop and commercialize siRNA therapeutics for the treatment of cardiovascular, renal, metabolic and respiratory diseases. AstraZeneca made an upfront cash payment to us of $20 million (equivalent to £17.1 million based on the exchange rate at the payment date) in May 2020 and an additional cash payment of $40 million (equivalent to £30.8 million based on the exchange rate at the payment date) in May 2021. AstraZeneca also made an equity investment of $20 million in our company in March 2020. The collaboration covers five targets initially, with AstraZeneca having the option to extend the collaboration to a further five targets. AstraZeneca has agreed to pay us $10 million for each selected target at the point of candidate nomination. For each target selected under the collaboration, we will be eligible to receive up to $140 million in milestone payments upon the achievement of milestones relating to the initiation of specified clinical trials, the acceptance of specified regulatory filings and the first commercial sale in specified jurisdictions. For each target selected, we will also be eligible to receive up to $250 million in milestone payments as well as tiered royalties as a percentage of net sales ranging from the high single digits to the low double digits.

On October 15, 2021, we announced a collaboration agreement with Hansoh, one of the leading biopharmaceutical companies in China, to develop siRNAs for three undisclosed targets leveraging Silence's proprietary mRNAi GOLD™ platform. Under the terms of the agreement, we retain exclusive rights to the first two targets in all territories except the China Region (Greater China, Hong Kong, Macau and Taiwan). Hansoh has the exclusive option to license rights to those two targets in the China Region following the completion of phase 1 studies. Silence will be responsible for all activities up to option exercise and will retain responsibility for development outside the China region post phase 1 studies. Hansoh will also have the exclusive option to license global rights to a third target at the point of IND filing. Hansoh will be responsible for all development activities post option exercise for the third target. Hansoh made a $16 million upfront payment to us in December 2021. We achieved our first $2 million research milestone payment in the Hansoh collaboration in April 2022. We are eligible to receive up to $1.3 billion in additional development, regulatory and commercial milestones. We will also receive royalties tiered from low double-digit to mid-teens on Hansoh net product sales. In December 2022, we initiated work on the second target which we retain global rights to outside the China Region.

SLN501: Complement Factor C3 Program

SLN501 is our siRNA partnered with Mallinckrodt that targets C3 and is in development for complement-mediated diseases. In June 2022, we initiated a phase 1 trial in healthy volunteers.

Overview of the complement system

The complement system plays a pivotal role in both innate and adaptive immune systems. Complement proteins are produced primarily by the liver and circulate in the blood and through the body's tissues. The complement system may be activated through three principal pathways, known as the classical, lectin and alternative pathways, each of which requires the C3 protein to enable three principal immune responses: opsonization, inflammation and formation of the membrane attack complex, or MAC. When C3 is activated, C3 fragments, such as C3b, tag cell surfaces in a process called opsonization, which marks the cells for removal from tissues or the bloodstream. Two other fragments, C3a and C5a, are released, contributing to inflammation in the surrounding tissues. Further complement activation causes MAC formation on cell surfaces, piercing holes and causing cells to lyse, or rupture.

Under conditions of excessive or uncontrolled activation, the complement system is believed to play a key role in the incidence and progression of several autoimmune and inflammatory diseases. In these diseases, the complement system acts directly through tissue destruction by the MAC and indirectly by signaling other elements of the immune system to inappropriately target otherwise healthy tissues. Because the contribution of complement activation to the development and progression of these diseases is not fully understood, it has been difficult to develop therapeutics that ameliorate the conditions contributing to these diseases by targeting only one of the complement activation pathways.

Competition

The life sciences industry is characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. We face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions, governmental agencies and public and private research institutions. Many of our competitors may have greater experience in research and development, manufacturing, managing clinical trials and/or regulatory compliance than we do, and may be better resourced financially. Any product candidates that we successfully develop and commercialize will compete with existing products and new products that may become available in the future. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and recruiting lead clinical trial investigators and establishing clinical study sites and patient registration for clinical studies, as well as in acquiring technologies complementary to, or necessary for, our programs.

Companies that complete clinical trials, obtain required regulatory authority approvals and commence commercial sale of their drugs before their competitors may achieve a significant competitive advantage, and our commercial opportunity could be reduced or eliminated if competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop and commercialize. Our competitors also may obtain FDA, EMA or other regulatory approval for their products more rapidly than we obtain approval, which could result in our competitors establishing a strong market position for either the product or a specific indication before we are able to enter the market. Drugs resulting from our research and development efforts or from our joint efforts with collaboration partners therefore may not be commercially competitive with our competitors' existing products or products under development. Because our products and many potential competing products are in various stages of preclinical and clinical development, and given the inherent unpredictability of drug development, it is difficult to predict which third parties may provide the most competition, and on what specific basis.

We consider a number of companies to be our competitors in developing RNAi therapeutic products. Some of these companies are seeking, as we are, to develop chemically synthesized siRNA molecules as drugs. Others are following a gene therapy approach, with the goal of treating patients not with synthetic siRNAs but with synthetic, exogenously-introduced genes designed to produce siRNA-like molecules within cells. Additionally, other companies may also develop alternative treatments for the diseases we have identified as being potentially treated with our siRNA molecules. To the extent those alternative treatments are more efficacious, less expensive, more convenient or produce fewer side effects, our market opportunity would be reduced.

We anticipate that we will face intense and increasing competition as new products and therapies enter the market and advanced technologies become available. We expect any treatments that we develop and commercialize to

compete on the basis of, among other things, efficacy, safety, delivery, patient friendliness, price and the availability of reimbursement from government and other third-party payers.

Intellectual Property

Patents

We actively seek to protect the intellectual property and proprietary technology that we believe is important to our business, including seeking, maintaining, enforcing and defending patent rights and protecting our related know-how for our siRNA platform technologies such as siRNA stabilization chemistries, as well as for our specific siRNA targeting sequences and related therapeutics and processes, whether developed internally or licensed to third parties. Our success will depend on our ability to obtain and maintain patent and other protections including data/market exclusivity for our product candidates and platform technology, preserve the confidentiality of our know-how and operate without infringing the valid and enforceable patents and proprietary rights of third parties. See the "*Risk Factors-Risks Related to Intellectual Property*" section of this report.

Our policy is to seek to protect our proprietary position early, generally by filing an initial priority filing in the European Patent Office. This is followed by the filing of one or more international patent applications, including a patent application under the Patent Cooperation Treaty, or PCT, claiming priority from the initial application(s) and then filing regional and national applications for patent grant in territories including, for example, the United States and Europe. In each case, we determine the strategy and territories required after discussion with our patent attorneys and collaboration partners so that we obtain relevant coverage in territories that are commercially important to our technologies and product candidates. With respect to our product candidates and related methods that we intend to develop and commercialize in the normal course of business, we will seek patent protection covering, when legally possible, siRNA sequences alone and with chemical modifications, compositions, methods of use, dosing and formulations. We may also pursue patent protection with respect to manufacturing and drug development processes when possible. We intend to additionally rely on data exclusivity, market exclusivity, other regulatory exclusivities and patent term extensions when available. We also rely on trade secrets and know-how relating to our underlying platform technology and product candidates. In each case, we seek to balance the value of patent protection against the advantage of keeping know-how confidential.

Issued patents can provide exclusivity on claimed subject matter for varying periods of time, typically starting on the date of patent grant and expiring at the end of the legal term of a patent in the country in which it is granted. In general, patents provide exclusionary rights for 20 years from the effective filing date of a non-provisional patent application in a particular country, or for a PCT international patent application, from the international filing date, assuming all maintenance fees are paid. In some instances, patent terms may be increased or decreased, depending on the laws and regulations of the country or jurisdiction that grants the patent. In the United States, a patent term may be shortened if a patent is terminally disclaimed over another patent or as a result of delays in patent prosecution by the patentee. A U.S. patent's term may be lengthened by a patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office, or USPTO, in granting a patent. The patent term of a European patent is 20 years from its effective filing date, which, unlike in the United States, is not subject to patent term adjustments in the same way as U.S. patents.

The level of protection afforded by a patent may vary and depends upon many factors, including the type of patent, the scope of its claim coverage, claim interpretation and patent law in the country or region that granted the patent, the validity and enforceability of the patent under such laws, and the availability of legal remedies in each particular country.

In certain regions or countries, regulatory-related patent extensions may be available to extend the term of a patent that claims an approved product or method. Regulatory-based patent term extensions allow patentee to recapture a portion of patent term effectively lost as a result of the regulatory review period for a product candidate. The term of a U.S. patent that covers an FDA-approved drug or biologic, for example, may be eligible for patent term extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug or biologic is under regulatory review. Patent extension cannot extend the

remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be extended. Similar provisions are available in Europe, Japan, China and other jurisdictions to extend the term of a patent that covers an approved drug, for example Supplementary Protection Certificates in Europe. In very few jurisdictions (such as in the U.S. and Europe), patent or regulatory exclusivities may potentially be further extended by a pediatric extension, to give an additional six months' extension, if pre-defined clinical trial data for a pediatric indication are timely submitted and accepted. In the future, if and when our products receive FDA approval, we expect to apply for regulatory patent term extensions on patents covering those products. We anticipate that some of our issued patents may be eligible for patent term extensions in certain jurisdictions based on an approved product or method, but such extensions may not be available and therefore its commercial monopoly may be restricted solely to patent term.

As of December 31, 2022, we solely owned 44 granted patents, of which 21 are U.S.-issued patents. We also owned 178 pending patent applications, of which 11 are co-owned and 22 are U.S. pending patent applications. Commercially or strategically important non-U.S. jurisdictions in which we hold issued or pending patent applications include (in addition to Europe): Australia, Brazil, Canada, China, Egypt, Hong Kong, India, Indonesia, Israel, Japan, Mexico, New Zealand, Philippines, Russia, Singapore, South Africa, South Korea, Taiwan and Vietnam. We also solely owned seven priority applications (priority year pending), of which four are first priority applications.

Our granted patents and pending patent applications include compositions of matter claims directed to siRNA molecules and compositions. They also include claims directed to siRNA molecules having specific nucleic acid modifications and linkers as well as specific nucleic acid sequences. In addition, our pending patent applications with an effective filing date after 2003 also include claims directed to methods of use and processes relating to such siRNA molecules and compositions.

Our earliest filed patent applications directed to 19-mer blunt-ended siRNAs with particular siRNA modification patterns expire in August 2023, subject to potential extension. Our current patent application families directed to toolbox elements, if and when granted, would not be expected to expire until at least 2036. Our current patent families covering siRNA sequences directed to specific target genes and associated uses for our SLN360, SLN124 and SLN501 product candidates, if and when granted, would not be expected to expire until at least 2038.

Government Regulation and Product Approval

Review and Approval of New Drug Products in the United States

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and non-U.S. 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 drug 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 a pending NDA, withdrawal of an approval, imposition of a clinical hold, issuance of warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties.

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

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, at each clinical site before each trial may be initiated;

- performance of adequate and well-controlled clinical trials, in accordance with GCP requirements to establish the safety and efficacy of the proposed drug for each indication;
- payment of user fees;
- submission to the FDA of an NDA;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with cGMP requirements, and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- satisfactory completion of an FDA inspection of selected clinical sites to assure compliance with GCPs and the integrity of the clinical data; and
- FDA review and approval of the NDA.

Preclinical Studies

Preclinical studies include laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies to assess potential pharmacology and toxicology. An IND sponsor must submit the results of the nonclinical tests, together with manufacturing information, analytical data and any available clinical data or literature, among other things, to the FDA as part of an IND. Some nonclinical 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 result in the FDA not allowing clinical trials to commence.

Clinical Trials

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, 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 of the trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, an IRB at each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must continue to oversee the clinical trial while it is being conducted.

Human clinical trials are typically conducted in three sequential phases, which may overlap or be combined. In phase 1, the drug is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an initial indication of its effectiveness. In phase 2, the drug typically 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. In phase 3, the drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the safety and efficacy of the product for approval, to establish the overall risk-benefit profile of the product and to provide adequate information for the labeling of the product.

Progress reports detailing the results of the clinical trials must be submitted, at least annually, to the FDA, and more frequently if SAEs occur. Phase 1, phase 2 and phase 3 clinical trials might not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not

being conducted in accordance with the IRB's requirements, or if the drug has been associated with unexpected serious harm to patients.

Marketing Approval

Assuming successful completion of the required clinical testing, the results of the preclinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. In most cases, the submission of an NDA is subject to a substantial application user fee. Under the Prescription Drug User Fee Act, or PDUFA, guidelines that are currently in effect, the FDA has a goal of ten months from the date of "filing" of a standard NDA for a new molecular entity to review and act on the submission. This review typically takes twelve months from the date the NDA is submitted to the FDA because the FDA has approximately two months to make a "filing" decision.

In addition, under the Pediatric Research Equity Act, certain NDAs or supplements to an NDA must contain data that are adequate to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Unless otherwise required by regulation, the pediatric data requirements do not apply to a product for an indication with orphan designation.

The FDA also may require submission of a risk evaluation and mitigation strategy, or REMS, to ensure that the benefits of the drug outweigh its risks. The REMS could include medication guides, physician communication plans, assessment plans, and/or elements to assure safe use, such as restricted distribution methods, patient registries or other risk minimization tools.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA reviews an NDA to determine, among other things, whether the drug is safe and effective and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and purity.

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

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

The testing and approval process for an NDA requires substantial time, effort and financial resources, and takes several years to complete. Data obtained from preclinical and clinical testing are not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. The FDA may not grant approval of an NDA on a timely basis, or at all.

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval

letter, or, in some cases, a complete response letter. A complete response letter generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA and may require additional clinical or preclinical testing in order for FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

Even if the FDA approves a product, it may limit the approved indications for use of the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including phase 4 clinical trials, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes, and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug intended to treat a rare disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000, there is no reasonable expectation that sales of the drug in the United States will be sufficient to offset the costs of developing and making the drug available in the United States. Orphan drug designation must be requested before submitting an NDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If the FDA approves a sponsor's marketing application for a designated orphan drug for use in the rare disease or condition for which it was designated, the sponsor is eligible for a seven-year period of marketing exclusivity, during which the FDA may not approve another sponsor's marketing application for a drug with the same active moiety and intended for the same disease or condition as the approved orphan drug, except in limited circumstances, such as if a subsequent sponsor demonstrates its product is clinically superior. During a sponsor's orphan drug exclusivity period, competitors, however, may receive approval for drugs with different active moieties for the same disease or condition as the approved orphan drug, or for drugs with the same active moiety as the approved orphan drug, but for different diseases or conditions. A competitor's orphan drug exclusivity could block the approval of one of our products for seven years if the competitor obtains approval for a drug with the same active moiety intended for the same disease or condition before we do, unless we are able to demonstrate that grounds for revocation of the competitor's orphan drug designation and orphan drug exclusivity exist, or that our product is clinically superior. Further, if a designated orphan drug receives marketing approval for an indication broader than the rare disease or condition for which it received orphan drug designation, it may not be entitled to exclusivity.

Rare Pediatric Disease, or RPD, designation by FDA may enable priority review voucher, or PRV, eligibility upon U.S. market approval of a designated drug for rare pediatric diseases. The RPD-PRV program is intended to encourage development of therapies to prevent and treat rare pediatric diseases. The voucher, which is awarded upon NDA approval to the sponsor of a designated RPD, can be sold or transferred to another entity and used by the holder to receive priority review for a future NDA or BLA submission, which reduces the FDA's target review time of such future submission from ten to six months from the date of "filing" of an NDA for a new molecular entity. However, priority review does not guarantee that the FDA will review and approve an application within six months of filing.

Post-approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, many changes to the approved product, such as adding new indications, manufacturing changes or certain

labeling changes, are subject to further testing requirements and prior FDA review and approval. There also are continuing annual user fee requirements for any marketed products.

Even if the FDA approves a product, it may limit the approved indications for use of the product, require that contraindications, warnings or precautions be included in the product labeling, including a boxed warning, require that post-approval studies, including phase 4 clinical trials, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms under a REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP 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 AEs 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 or effectiveness information; imposition of post-market studies or clinical trials to assess 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, untitled letters, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label, although physicians, in the practice of medicine, may prescribe approved drugs for unapproved indications. 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.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution.

Federal and State Fraud and Abuse, Data Privacy and Security, and Transparency Laws and Regulations

In addition to FDA restrictions on marketing of pharmaceutical products, federal and state healthcare laws and regulations restrict business practices in the biopharmaceutical industry. These laws may impact, among other things, our current and future business operations, including our clinical research activities, and proposed sales, marketing and education programs and constrain the business or financial arrangements and relationships with healthcare providers and other parties through which we market, sell and distribute our products for which we obtain marketing approval. These laws include anti-kickback and false claims laws and regulations, data privacy and security, and transparency laws and regulations, including, without limitation, those laws described below.

The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce or in return for purchasing, leasing, ordering or arranging for or recommending the purchase, lease or order of any item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The term "remuneration" has been broadly interpreted to include anything of value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other. Although there are a number of statutory exemptions and regulatory safe harbors protecting some common activities from prosecution, the exemptions 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 qualify for an exemption or safe harbor. 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.

A person or entity does not need to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act or the civil monetary penalties statute, which imposes penalties against any person who is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

Federal false claims laws, including the federal civil False Claims Act, prohibits any person or entity from knowingly presenting, or causing to be presented, a false claim for payment to the federal government or 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. A claim includes "any request or demand" for money or property presented to the U.S. government. Several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of products for unapproved, and thus non-reimbursable, uses.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created additional federal criminal statutes that prohibit, among other things, knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private third-party payers 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. Also, many states 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 payer.

In addition, we may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their respective implementing regulations, imposes specified requirements on certain types of individuals and entities relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's security standards directly applicable to "business associates," defined as independent contractors or agents of covered entities that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions

in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in certain circumstances, many of which are not preempted by HIPAA, differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

The federal Physician Payments Sunshine Act requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services, or CMS, information related to payments or other transfers of value made to physicians and teaching hospitals, and applicable manufacturers and applicable group purchasing organizations to report annually to CMS ownership and investment interests held by the physicians and their immediate family members.

We may also be subject to state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, as well as state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures.

Because of the breadth of these laws and the narrowness of available statutory and regulatory exemptions, it is possible that some of our business activities could be subject to challenge under one or more of such laws. If our operations are found to be in violation of any of the federal and state laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including criminal and significant civil monetary penalties, damages, fines, individual imprisonment, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, contractual damages, reputational harm, diminished profits and future earnings, disgorgement, exclusion from participation in government healthcare programs and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that any of our products are sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

Coverage and Reimbursement in the United States

The future commercial success of our product candidates or any of our collaborators' ability to commercialize any approved product candidates successfully will depend in part on the extent to which governmental payer programs at the federal and state levels, including Medicare and Medicaid, private health insurers and other third-party payers provide coverage for and establish adequate reimbursement levels for our product candidates. Government health administration authorities, private health insurers and other organizations generally decide which drugs they will pay for and establish reimbursement levels for healthcare. In particular, in the United States, private health insurers and other third-party payers often provide reimbursement for products and services based on the level at which the government, through the Medicare or Medicaid programs, provides reimbursement for such treatments. In the United States, the European Union, and other potentially significant markets for our product candidates, government authorities and third-party payers are increasingly attempting to limit or regulate the price of medical products and services, particularly for new and innovative products and therapies, which often has resulted in average selling prices lower than they would otherwise be. Further, the increased emphasis on managed healthcare in the United States will put additional pressure on product pricing, reimbursement and usage, which may adversely affect our future product sales and results of operations. These pressures can arise from rules and practices of managed care groups, judicial decisions and laws and regulations related to Medicare, Medicaid and healthcare reform, pharmaceutical coverage and reimbursement policies and pricing in general.

Third-party payers are increasingly imposing additional requirements and restrictions on coverage and limiting reimbursement levels for medical products. For example, federal and state governments reimburse covered prescription drugs at varying rates generally below average wholesale price. These restrictions and limitations influence the purchase of healthcare services and products. Third-party payers may limit coverage to specific drug products on an approved list, or formulary, which might not include all of the FDA-approved drug products for a particular indication. Third-party payers are increasingly challenging the price and examining the medical necessity

and cost-effectiveness of medical products and services, in addition to their safety and efficacy. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain the FDA approvals. Our product candidates may not be considered medically necessary or cost-effective. A payer's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Further, one payer's determination to provide coverage for a drug product does not assure that other payers will also provide coverage for the drug product. 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 drug development. Legislative proposals to reform healthcare or reduce costs under government insurance programs may result in lower reimbursement for our products and product candidates or exclusion of our product candidates from coverage. The cost containment measures that healthcare payers and providers are instituting and any healthcare reform could significantly reduce our revenues from the sale of any approved product candidates. We cannot provide any assurances that we will be able to obtain and maintain third-party coverage or adequate reimbursement for our product candidates in whole or in part.

There have been several U.S. government initiatives over the past several years to fund and incentivize certain comparative effectiveness research, including creation of the Patient-Centered Outcomes Research Institute under the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the PPACA. It is also possible that comparative effectiveness research demonstrating benefits in a competitor's product could adversely affect the sales of our product candidates. If third-party payers do not consider our product candidates to be cost-effective compared to other available therapies, they may not cover our product candidates, once approved, as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our product on a profitable basis.

In addition, there has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed federal and proposed and enacted state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. These and other healthcare reform initiatives may result in additional reductions in Medicare and other healthcare funding. On March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate price cap, currently set at 100% of a drug's average manufacturer price for single source and innovator multiple source products, beginning on January 1, 2024. Further, in July 2021, the Biden Administration released an executive order that included multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, U.S. Department of Health & Human Services, or HHS, released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug price reform. The plan sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions by HHS. No legislative or administrative actions have been finalized to implement these principles. In addition, Congress is considering drug pricing as part of the budget reconciliation process. Additionally, the Inflation Reduction Act of 2022, or the IRA, among other things, (i) directs HHS to negotiate the price of certain high-expenditure, single-source drugs and biologics covered under Medicare, and subject drug manufacturers to civil monetary penalties and a potential excise tax by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law, and (ii) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. The IRA permits HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. These provisions will take effect progressively starting in fiscal year 2023, although they may be subject to legal challenges. It is currently unclear how the IRA will be effectuated but it is likely to have a significant impact on the pharmaceutical industry. Individual states in the United States also have increasingly passed legislation and implemented regulations designed to control 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.

Foreign Corrupt Practices Act, the Bribery Act and Other Laws

The Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering, or authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the

United States to comply with accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations. Activities that violate the FCPA, even if they occur wholly outside the United States, can result in criminal and civil fines, imprisonment, disgorgement, oversight, and debarment from government contracts.

Our operations are also subject to non-U.S. anti-corruption laws such as the Bribery Act. As with the FCPA, these laws generally prohibit us and our employees and intermediaries from authorizing, promising, offering, or providing, directly or indirectly, improper or prohibited payments, or anything else of value, to government officials or other persons to obtain or retain business or gain some other business advantage. Under the Bribery Act, we may also be liable for failing to prevent a person associated with us from committing a bribery offense.

We are also subject to other laws and regulations governing our international operations, including regulations administered by the governments of the United Kingdom and the United States and authorities in the European Union, including applicable export control regulations, economic sanctions and embargoes on certain countries and persons, anti-money laundering laws, import and customs requirements and currency exchange regulations, collectively referred to as trade control laws.

Failure to comply with the Bribery Act, the FCPA and other anti-corruption laws and trade control laws could subject us to criminal and civil penalties, disgorgement and other sanctions and remedial measures, and legal expenses.

Review and Approval of New Drug Products in the European Union

In the European Union, medicinal products, including advanced therapy medicinal products, or ATMPs, are subject to extensive pre- and post-market regulation by regulatory authorities at both the European Union and national levels. ATMPs comprise gene therapy products, somatic-cell therapy products and tissue engineered products, which are cells or tissues that have undergone substantial manipulation and that are administered to human beings in order to regenerate, repair or replace a human tissue. We anticipate that our siRNA products will be regulated as ATMPs in the European Union. There is legislation at a European Union level relating to the standards of quality and safety for the collection and testing of human blood and blood components for use in cell-based therapies, which could apply to our products. Additionally, there may be local legislation in various EU Member States, which may be more restrictive than the EU legislation, and we would need to comply with such legislation to the extent it applies.

Clinical Trials

Clinical trials of medicinal products in the European Union must be conducted in accordance with EU and national regulations and the International Conference on Harmonization, or ICH, guidelines on GCP. Additional GCP guidelines from the European Commission, focusing in particular on traceability, apply to clinical trials of ATMPs. The sponsor must take out a clinical trial insurance policy, and in most EU countries, the sponsor is liable to provide “no fault” compensation to any study subject injured in the clinical trial.

Prior to commencing a clinical trial, the sponsor must obtain a clinical trial authorization from the competent authority, and a positive opinion from an independent ethics committee. The application for a clinical trial authorization 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. Since the new Clinical Trials Regulation took effect in January 2022, there is now a centralized application procedure where applications are submitted via a portal maintained by the EMA and where one national authority takes the lead in reviewing the application and the other national authorities have more limited involvement. Any substantial changes to the trial protocol or other information submitted with the clinical trial applications must be notified to or approved by the relevant competent authorities and ethics committees. Medicines used in clinical trials must be manufactured in accordance with cGMP. Other national and EU-wide regulatory requirements also apply.

During the development of a medicinal product, the EMA and national medicines regulators within the European Union provide the opportunity for dialogue and guidance on the development program. At the EMA level, this is usually done in the form of scientific advice, which is given by the Scientific Advice Working Party of the Committee for Medicinal Products for Human Use, or CHMP. A fee is incurred with each scientific advice procedure, but this

can be eliminated for orphan medicinal products. Advice from the EMA is typically provided based on questions concerning, for example, quality (chemistry, manufacturing and controls testing), nonclinical testing and clinical studies, and pharmacovigilance plans and risk-management programs. Given the current stage of the development of our product candidates, we have not yet sought any such advice from the EMA. However, to the extent that we do obtain such scientific advice in the future, while both the company and the EMA are expected to respect the outcome of the scientific advice procedure, such advice will, in accordance with the EMA's policy, be not legally binding with regard to any future marketing authorization application of the product concerned.

Marketing Authorizations

In order to market a new medicinal product in the European Union, a company must submit and obtain approval from regulators of a marketing authorization application, or MAA. The process for doing this depends, among other things, on the nature of the medicinal product.

The centralized procedure results in a single marketing authorization, or MA, granted by the European Commission that is valid across the European Union and by extension to the EEA (i.e., the European Union as well as Iceland, Liechtenstein and Norway). The centralized procedure is compulsory for human drugs that are: (i) derived from biotechnology processes, such as genetic engineering, (ii) contain a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, diabetes, neurodegenerative diseases, autoimmune and other immune dysfunctions, and viral diseases, (iii) officially designated orphan medicines and (iv) ATMPs, such as gene therapy, somatic cell therapy or tissue-engineered medicines. The centralized procedure may at the request of the applicant also be used in certain other cases. Therefore, the centralized procedure would be mandatory for the products we are developing.

The Committee for Advanced Therapies, or CAT, is responsible in conjunction with the CHMP for the evaluation of ATMPs. The CAT is primarily responsible for the scientific evaluation of specific issues that typically arise for ATMPs and prepares a draft opinion on the quality, safety and efficacy of each ATMP for which a marketing authorization application is submitted. The CAT's opinion is then taken into account by the CHMP when giving its final recommendation regarding the authorization of a product in view of the balance of benefits and risks identified. Although the CAT's draft opinion is submitted to the CHMP for final approval, the CHMP may depart from the draft opinion, if it provides detailed scientific justification. The CHMP and CAT are also responsible for providing guidelines on ATMPs and have published numerous guidelines, including specific guidelines on gene therapies and cell therapies. These guidelines provide additional guidance on the factors that the EMA will consider in relation to the development and evaluation of ATMPs and include, among other things, the preclinical studies required to characterize ATMPs; the manufacturing and control information that should be submitted in a marketing authorization application; and post-approval measures required to monitor patients and evaluate the long term efficacy and potential adverse reactions of ATMPs. Although these guidelines are not legally binding, we believe that our compliance with them is likely necessary to gain and maintain approval for any of our product candidates.

Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of an MAA by the EMA is 210 days. This excludes so-called clock stops, usually at day 120 and day 180 of the procedure, during which additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP. At the end of the review period, the CHMP provides an opinion to the European Commission. If this is opinion favorable, the Commission may then adopt a decision to grant an MA. In exceptional cases, the CHMP might perform an accelerated review of an MAA in no more than 150 days. This is usually when the product is of major interest from the point of view of public health and, in particular, from the viewpoint of therapeutic innovation.

The European Commission may grant a so-called "marketing authorization under exceptional circumstances". Such authorization is intended for products for which the applicant can demonstrate that it is unable to provide comprehensive data on the efficacy and safety under normal conditions of use, because the indications for which the product in question is intended are encountered so rarely that the applicant cannot reasonably be expected to provide comprehensive evidence, or in the present state of scientific knowledge, comprehensive information cannot be provided, or it would be contrary to generally accepted principles of medical ethics to collect such information. Consequently, marketing authorization under exceptional circumstances may be granted subject to certain specific obligations, which may include the following:

- the applicant must complete an identified program of studies within a time period specified by the competent authority, the results of which form the basis of a reassessment of the benefit/risk profile;

- the medicinal product in question may be supplied on medical prescription only and may in certain cases be administered only under strict medical supervision, possibly in a hospital and in the case of a radiopharmaceutical, by an authorized person; and

- the package leaflet and any medical information must draw the attention of the medical practitioner to the fact that the particulars available concerning the medicinal product in question are as yet inadequate in certain specified respects.

A marketing authorization under exceptional circumstances is subject to annual review to reassess the risk-benefit balance in an annual reassessment procedure. Continuation of the authorization is linked to the annual reassessment and a negative assessment could potentially result in the marketing authorization being suspended or revoked. The renewal of a marketing authorization of a medicinal product under exceptional circumstances, however, follows the same rules as a "normal" marketing authorization. Thus, a marketing authorization under exceptional circumstances is granted for an initial five years, after which the authorization will become valid indefinitely, unless the EMA decides that safety grounds merit one additional five-year renewal.

The European Commission may also grant a so-called "conditional marketing authorization" prior to obtaining the comprehensive clinical data required for an application for a full marketing authorization. Such conditional marketing authorizations may be granted for product candidates (including medicines designated as orphan medicinal products), if (i) the risk-benefit balance of the product candidate is positive, (ii) it is likely that the applicant will be in a position to provide the required comprehensive clinical trial data, (iii) the product fulfills an unmet medical need, and (iv) the benefit to public health of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required. A conditional marketing authorization may contain specific obligations to be fulfilled by the marketing authorization holder, including obligations with respect to the completion of ongoing or new studies, and with respect to the collection of pharmacovigilance data. Conditional marketing authorizations are valid for one year, and may be renewed annually, if the risk-benefit balance remains positive, and after an assessment of the need for additional or modified conditions and/or specific obligations. The timelines for the centralized procedure described above also apply with respect to the review by the CHMP of applications for a conditional marketing authorization.

The EU medicines rules expressly permit the EU Member States to adopt national legislation prohibiting or restricting the sale, supply or use of any medicinal product containing, consisting of or derived from a specific type of human or animal cell, such as embryonic stem cells. While the products we have in development do not make use of embryonic stem cells, it is possible that the national laws in certain EU Member States may prohibit or restrict us from commercializing our products, even if they have been granted an EU marketing authorization.

Data Exclusivity

Marketing authorization applications for generic medicinal products do not need to include the results of preclinical and clinical trials, but instead can refer to the data included in the marketing authorization of a reference product for which regulatory data exclusivity has expired. If a marketing authorization is granted for a medicinal product containing a new active substance, that product benefits from eight years of data exclusivity, during which generic marketing authorization applications referring to the data of that product may not be accepted by the regulatory authorities, and a further two years of market exclusivity, during which such generic products may not be placed on the market. The two-year period may be extended to three years if during the first eight years a new therapeutic indication with significant clinical benefit over existing therapies is approved.

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 European Union. 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.

Pediatric Development

In the European Union, companies developing a new medicinal product must agree to a Pediatric Investigation Plan, or PIP, with the EMA and must conduct pediatric clinical trials in accordance with that PIP, unless a deferral or waiver applies, (e.g., because the relevant disease or condition occurs only in adults). The marketing authorization application for the product must include the results of pediatric clinical trials conducted in accordance with the PIP, unless a waiver applies, or a deferral has been granted, in which case the pediatric clinical trials must be completed at a later date. Products that are granted a marketing authorization on the basis of the pediatric clinical trials conducted in accordance with the PIP are eligible for a six-month extension of patent protection under a supplementary protection certificate (if any patent or supplementary protection certificate is in effect at the time of approval) or, in the case of orphan medicinal products, a two year extension of the orphan market exclusivity. This pediatric reward is subject to specific conditions and is not automatically available when data in compliance with the PIP are developed and submitted.

Post-Approval Controls

The holder of a marketing authorization must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance, or QPPV, who is responsible for oversight of that system. Key obligations include expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports, or PSURs.

All new marketing authorization applications must include a risk management plan, or 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 regulatory authorities may also impose specific obligations as a condition of the marketing authorization. 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. RMPs and PSURs are routinely available to third parties requesting access, subject to limited redactions.

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 European Union. Although general requirements for advertising and promotion of medicinal products are established under EU directives, the details are governed by regulations in each EU Member State and can differ from one country to another.

Pricing and Reimbursement in the European Union

Governments influence the price of medicinal products in the European Union through their pricing and reimbursement rules and control of national healthcare systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost-effectiveness of a particular product candidate to currently available therapies. Other EU Member States allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on healthcare costs in general, particularly prescription medicines, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products.

Brexit and the Regulatory Framework in the United Kingdom

On June 23, 2016, the electorate in the United Kingdom voted in favor of Brexit and the United Kingdom officially withdrew from the European Union on January 31, 2020.

Pursuant to the formal withdrawal arrangements agreed between the United Kingdom and the European Union, the United Kingdom was subject to a transition period until December 31, 2020, during which European Union rules continued to apply. A trade and cooperation agreement, or the Trade and Cooperation Agreement, which outlines the future trading relationship between the United Kingdom and the European Union was agreed in December 2020.

Great Britain is no longer covered by the European Union's procedures for the grant of marketing authorizations (Northern Ireland is covered by the centralized authorization procedure and can be covered under the decentralized or mutual recognition procedures). A separate marketing authorization will be required to market drugs in Great Britain. Various national procedures are now available to place a drug on the market in the United Kingdom, Great Britain, or Northern Ireland. The standard procedure takes 210 days. However, there are a number of procedures with accelerated assessment timetables. For example, the MHRA offers a 150-day assessment timeline from validation for medicinal products with new active substances, biosimilars and existing active substances with "high-quality" new MA applications (excluding time taken to provide any further information or data required). The MHRA also offers a Decentralized and Mutual Recognition Reliance Procedure and a European Commission Decision Reliance Procedure, which means the MHRA may grant a marketing authorization for Great Britain within 67 days of validation. The data, market and pediatric exclusivity periods in the United Kingdom are currently in line with those in the European Union, but the Trade and Cooperation Agreement provides that the periods for both data and market exclusivity are to be determined by domestic law. It is likely these periods will diverge in future as the European Commission is in the process of redrafting the general pharmaceutical regulatory framework and its drafts indicate the Commission intends to change marketing and data exclusivity periods. The UK has not indicated it intends to mirror such changes in its national legislation yet.

Orphan designation criteria in Great Britain following Brexit are essentially identical to the position in the European Union, but are based on the prevalence of the condition in Great Britain. It is therefore possible that conditions that are currently designated as orphan conditions in Great Britain will no longer be and that conditions that are not currently designated as orphan conditions in the European Union will be designated as such in Great Britain. Also, unlike the European Union's procedure, in Great Britain there is no pre-marketing authorization orphan designation. The MHRA only reviews the orphan designation when an applicant submits a marketing authorization application.

The European Union's regulatory environment for clinical trials has been harmonized by the Clinical Trials Regulation which entered into application on January 31, 2022. The U.K. clinical trial legislation is being updated (the MHRA launched a public consultation on updating the legislation on January 17, 2022) and whilst the proposals are broadly in line with the European Union there are likely to be some divergences from the European Union in the final legislation. The impact of these divergences will need to be assessed.

In the short term, there is a risk of disrupted import and export processes due to a lack of administrative processing capacity by the respective U.K. and EU customs agencies that may delay time sensitive shipments and negatively impact supply chains. Additionally, expenses will be incurred due to increased licensing and administrative requirements around import and export, e.g. the need for a manufacturer/importer license (rather than a wholesale dealer's license) and the need to perform batch release in the EU to move product from the UK to the EMA.

However, there are potential changes to the regulatory framework in the United Kingdom. Notably, the UK Government has introduced the Retained EU Law (Revocation and Reform) Bill into Parliament, which proposes that all retained European Union law will expire on December 31, 2023 (or at the latest June 23, 2026), which would include all key pharmaceutical legislative instruments. The Bill proposes to grant certain powers to Government Ministers to make regulations in the affected areas. There are also ongoing discussions between the UK Government and European Union about renegotiating the terms of the Northern Ireland Protocol. As such, there could be further uncertainty about the regulatory position in the United Kingdom, and how it will diverge from the position in the European Union.

C. Organizational Structure.

A full list of our subsidiaries and the address of their registered offices as of December 31, 2022 is set forth below.

Name	Place of incorporation and operation	Registered Address	Principal technology area	Proportion of ownership interest
Silence Therapeutics GmbH	Germany	Robert-Rössle-Strasse 10, 13125 Berlin, Germany	RNA therapeutics	100 %
Silence Therapeutics (London) Ltd	England	27 Eastcastle Street, London W1W 8DH, England	Dormant	100 %
Innopeg Ltd	England	27 Eastcastle Street, London W1W 8DH, England	Dormant	100 %
Silence Therapeutics Inc.	USA	c/o Harvard Business Services Inc, 16192 Coastal Highway, Lewes, Delaware 19958, USA	RNA therapeutics	100 %

D. Property, Plants and Equipment.

We lease approximately 4,000 sq ft of office space in London, England for our corporate headquarters and other general and administrative functions under a lease with a term through September 2025. We also lease regional offices and laboratory space in Berlin, Germany (two leases: rolling contract basis with either party being able to end the lease upon 11.5 months' prior notice) and Hoboken, New Jersey, USA (three leases: current lease end dates of October 2023, November 2023 and February 2024, with either party being able to end the lease upon three months' prior notice).

We believe that our current facilities are adequate to meet our needs for the near future and that suitable additional or alternative space will be available on commercially reasonable terms to accommodate our foreseeable future operations.

Environmental Issues

For information on environmental issues that may affect our utilization of our facilities, see "Item 3.D. Risk Factors──Risks Related to Our Business Operations and Compliance with Government Regulations──*If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.*"

ITEM 4A: UNRESOLVED STAFF COMMENTS

None.

ITEM 5: OPERATING AND FINANCIAL REVIEW AND PROSPECTS

A. OPERATING RESULTS

You should read the following discussion and analysis of financial condition and operating results and our consolidated financial statements and the related notes to those financial statements included elsewhere in this Annual Report, which have been prepared in accordance with IFRS, as issued by the IASB.

The statements in this discussion with respect to our plans and strategy for our business, including expectations regarding our future liquidity and capital resources and other non-historical statements, are forward-looking statements. These forward-looking statements are subject to numerous risks and uncertainties, including the risks and uncertainties described in the section of this Annual Report titled "Risk Factors." Our actual results may differ materially from those contained in or implied by any forward-looking statements.

Overview

Silence Therapeutics plc ("we", "us", "our", "the Company" or "Silence") is a biotechnology company focused on discovering and developing novel molecules incorporating short interfering ribonucleic acid, or siRNA, to inhibit the expression of specific target genes thought to play a role in the pathology of diseases with significant unmet medical need. Our siRNA molecules are designed to harness the body's natural mechanism of RNA interference, or RNAi, by specifically binding to and degrading messenger RNA, or mRNA, molecules that encode specific targeted disease-associated proteins in a cell. By degrading the message that encodes the disease-associated protein, the production of that protein is reduced, and its level of activity is lowered. In the field of RNAi therapeutics, this reduction of disease-associated protein production and activity is referred to as "gene silencing." Our proprietary mRNAi GOLD™ (**G**alNAc **Ol**igonucleotide **D**iscovery) platform consists of precision engineered product candidates designed to accurately target and 'silence' specific disease-associated genes in the liver. Using our mRNAi GOLD™ platform, we have generated siRNA product candidates both for our internal development pipeline as well as for out-licensed programs with third-party collaborators. Our wholly owned pipeline is currently focused in three therapeutic areas of high unmet need: cardiovascular disease, hematology and rare diseases.

SLN360, an siRNA targeting the *LPA* gene, is our wholly owned product candidate currently in phase 2 clinical development (ALPACAR-360 trial) to reduce high levels of Lp(a), a genetically determined cardiovascular risk factor affecting up to 20% of the world's population. In February 2022, we reported positive results from the single-ascending dose portion of the APOLLO phase 1 program evaluating SLN360 in 32 healthy adults with high Lp(a) ≥150 nmol/L. In the APOLLO trial, participants in the top two SLN360 single dose groups (300 mg and 600 mg) were observed to have experienced up to a 96% and 98% median reduction in Lp(a) levels, respectively, and median reductions of up to 71% and 81% from baseline persisted at 150 days. Those receiving a placebo saw no change in Lp(a) levels. Further analysis showed median time-averaged Lp(a) reductions over 150 days exceeded 80% in the SLN360 300 mg and 600 mg dose groups. At day 365, some participants still exhibited substantially reduced levels of Lp(a) of approximately 50% compared to baseline. SLN360 was well tolerated with no serious safety concerns reported. The multiple-ascending dose portion of the APOLLO program in subjects with high Lp(a) and stable ASCVD is ongoing and expected to readout in the fourth quarter of 2023. In January 2023, we started dosing in the ALPACAR-360 trial evaluating subjects with high Lp(a) ≥125 nmol/L at high risk of atherosclerotic cardiovascular disease, or ASCVD, events and we expect to complete enrollment by the end of 2023. We are engaged in global partnership discussions for this program to ensure we are well positioned to scale up SLN360 development and future commercialization.

SLN124, an siRNA targeting the *TMPRSS6* gene, is our wholly owned product candidate that has shown the potential to address a range of hematological conditions by modulating endogenous hepcidin, a peptide hormone that is the master regulator of systemic iron balance. SLN124 is being evaluated in the SANRECO phase 1/2 trial in patients with PV and the GEMINI II phase 1 trial in patients with NTD thalassemia. In September 2022, we reported preliminary results from the single dose portion of the GEMINI II trial which showed SLN124 was well tolerated with no serious AEs, no severe treatment emergent AEs that were SLN124 related and no TEAEs leading to withdrawal. No dose limiting toxicity or drug related liver injury was observed. Effects on hepcidin, serum iron, transferrin saturation and hemoglobin are being evaluated in the ongoing multiple-dose arm expected to readout in the fourth quarter of 2023. SLN124 demonstrated proof of mechanism in the GEMINI trial in healthy volunteers completed in

May 2021, representing the first clinical data from our mRNAi GOLD™ platform. SLN124 has FDA Fast Track and orphan drug designations for PV as well as orphan drug and rare pediatric disease designations for beta-thalassemia. The European Medical Agency has also granted SLN124 orphan drug designation and rare pediatric disease designation for beta-thalassemia.

The potential of our mRNAi GOLD™ platform has been validated through ongoing research and development collaborations with leading pharmaceutical companies, such as AstraZeneca, Mallinckrodt and Hansoh. These collaborations collectively represent up to 16 pipeline programs and approximately $7.5 billion in potential milestones plus royalties.

We believe the potential for our mRNAi GOLD™ platform to address disease-associated genes in the liver is substantial. Only around one percent of the approximately 14,000 liver expressed genes have been targeted by publicly known siRNAs. Once in the clinic, early-stage GalNAc-conjugated RNAi programs have shown a much greater likelihood of advancement from the current phase of development compared to the pharmaceutical industry average. We aim to maximize our mRNAi GOLD™ platform by advancing both our proprietary and partnered pipelines.

Executive Summary

Our results of operations for the full fiscal year ended December 31, 2022 reflect the following:

SLN360 for cardiovascular disease

- In January 2022, we started dosing in the multiple-ascending dose portion of the APOLLO program in patients with high Lp(a) that have a history of stable ASCVD.
- In February 2022, we reported positive topline data in the single-ascending dose portion of the APOLLO program.
- In April 2022, results from the APOLLO program in healthy adults with high Lp(a) were simultaneously presented at the American College of Cardiology Annual Meeting and published in *The Journal of the American Medical Association*.
- In November 2022, we presented a further analysis up to 365 days from the APOLLO program in healthy adults with high Lp(a) in a moderated poster session at the American Heart Association Annual Meeting.
- In December 2022, SLN360's INN (international nonproprietary name) was approved – zerlasiran**.**

SLN124 for hematological conditions

- In March 2022, we received FDA orphan drug designation for SLN124 in PV.
- In March 2022, we discontinued further enrollment in the MDS arm of the SLN124 GEMINI trial and prioritized thalassemia and PV indications.
- In September 2022, we received FDA Fast Track Designation for SLN124 for the treatment of PV.
- In September 2022, we reported preliminary results from the single dose portion of the GEMINI II trial in NTD thalassemia patients.

Partnered Program Updates

- In March 2022, we achieved a $3.0 million milestone payment following the submission of the clinical trial application for SLN501, our complement program partnered with Mallinckrodt.
- In June 2022, we started dosing subjects in the SLN501 healthy volunteer study.
- In April 2022, we achieved a $2.0 million research milestone in our Hansoh collaboration.

- In December 2022, we initiated work on the second target under our Hansoh collaboration. We retain global rights to this target outside the China Region.

Corporate Updates

- In February 2022, we appointed Craig Tooman, previously Chief Financial Officer, as President, Chief Executive Officer and Board member. Rhonda Hellums, previously VP, Finance, was appointed as our Chief Financial Officer.
- In August 2022, we completed a registered direct offering of 5,950,000 ADSs, at a public offering price of $9.50 per ADS. Our aggregate gross proceeds from this offering were $56.5 million (approximately £46.4 million) before deducting $4.1 million (approximately £3.3 million) in underwriting discounts, commissions and estimated offering expenses.

Post Period Highlights

- In January 2023, we started dosing subjects in the ALPACAR-360 phase 2 clinical trial evaluating SLN360 in patients with high Lp(a) ≥ 125 nmol/L at high-risk of ASCVD events. We expect to complete enrollment in the fourth quarter of 2023.
- In January 2023, we opened sites for enrollment in the SANRECO phase 1/2 clinical program of SLN124 in PV patients.
- In February 2023, we started dosing the last subject in the multiple dose portion of the APOLLO phase 1 study of SLN360 in people with high Lp(a) and stable ASCVD. We remain on-track to report topline data in the fourth quarter of 2023.
- In March 2023, we dosed the final subject in the multiple dose portion of the GEMINI II phase 1 study of SLN124 in thalassemia patients. We remain on-track to report topline data in the fourth quarter of 2023.

Collaboration Agreement with AstraZeneca

In March 2020, we entered into a collaboration agreement with AstraZeneca to discover, develop and commercialize siRNA therapeutics for the treatment of cardiovascular, renal, metabolic and respiratory diseases. Under this agreement, AstraZeneca made an upfront cash payment to us of $20.0 million in May. AstraZeneca made an additional unconditional cash payment to us of $40.0 million which was received in May 2021. In March 2020, an affiliate of AstraZeneca also subscribed for 4,276,580 new ordinary shares for an aggregate subscription price of $20.0 million.

The collaboration covers five targets initially, with AstraZeneca having the option to extend the collaboration to a further five targets. AstraZeneca has agreed to pay us $10 million for each selected target at the point of candidate nomination. For each target selected, we will be eligible to receive up to $140.0 million in potential milestone payments upon the achievement of milestones relating to the initiation of specified clinical trials, the acceptance of specified regulatory filings and the first commercial sale in specified jurisdictions. For each target selected, we will also be eligible to receive up to $250.0 million in potential commercial milestone payments, upon the achievement of specified annual net sales levels, as well as tiered royalties as a percentage of net sales ranging from the high single digits to the low double digits.

Collaboration Agreement with Mallinckrodt

In July 2019, we entered into a collaboration agreement with Mallinckrodt to develop and commercialize RNAi drug targets designed to silence the complement cascade in complement-mediated disorders. Under the agreement, we granted Mallinckrodt an exclusive worldwide license to our C3 targeting program, SLN501, with options to license two additional complement-mediated disease targets from us, with Mallinckrodt exercising the option for two additional complement targets from us in July 2020.

While we are responsible for the phase 1 clinical trial in each case, Mallinckrodt will be funding all of our research personnel costs on a full-time equivalent, or FTE, basis associated with preparing for and conducting the phase 1 clinical trials. We are also responsible for the provision of drug product for preclinical activities and for the phase 1 clinical trials, but any manufacturing expense relating to the phase 1 trial will be paid for by Mallinckrodt. After completion of the phase 1 clinical trials, Mallinckrodt will assume clinical development and responsibility for potential global commercialization.

The collaboration provides for potential additional development and regulatory milestone payments in aggregate of up to $100 million for the initial C3 target and up to $140 million for each of the two optioned complement-mediated disease targets, with such milestones relating to the initiation of specified clinical trials in specified jurisdictions, and upon the receipt of regulatory approvals by specified authorities, in each case for multiple indications. We are also eligible to receive potential commercial milestone payments of up to $562.5 million upon the achievement of specified levels of annual net sales of licensed products for each program. We are also eligible to receive tiered, low double-digit to high-teen percentage royalties on net sales for licensed products for each program. We received a research milestone payment of $2 million in October 2019 upon the initiation of work for the first complement C3 target. In September 2020, we received another $2 million research milestone payment following the initiation of work on a second complement target. In February 2021, we initiated work on the third complement target which triggered another $2 million research milestone payment. In April 2021, we received $2 million for initiating IND-enabling studies in the SLN501 C3 targeting program and we triggered another $3 million milestone payment following the submission of the SLN501 clinical trial application in March 2022.

In connection with the execution of this agreement, Mallinckrodt made an upfront cash payment to us of $20.0 million (equivalent to £16.4 million as of the payment date). Under a separate subscription agreement, Cache Holdings Limited, a wholly owned subsidiary of Mallinckrodt, concurrently subscribed for 5,062,167 new ordinary shares for an aggregate subscription price of $5.0 million (equivalent to £4.0 million as of the payment date).

Collaboration Agreement with Hansoh

On October 15, 2021, we announced a collaboration agreement with Hansoh, one of the leading biopharmaceutical companies in China, to develop siRNAs for three undisclosed targets leveraging Silence's proprietary mRNAi GOLD™ platform. Under the terms of the agreement, we retain exclusive rights to the first two targets in all territories except the China Region (Greater China, Hong Kong, Macau and Taiwan). Hansoh has the exclusive option to license rights to those two targets in the China Region following the completion of phase 1 studies. Silence will be responsible for all activities up to option exercise and will retain responsibility for development outside the China region post phase 1 studies. Hansoh will also have the exclusive option to license global rights to a third target at the point of IND filing. Hansoh will be responsible for all development activities post option exercise for the third target. Hansoh made a $16 million upfront payment to us in December 2021. We achieved our first $2 million research milestone payment in the Hansoh collaboration in April 2022. We are eligible to receive up to $1.3 billion in additional development, regulatory and commercial milestones. We will also receive royalties tiered from low double-digit to mid-teens on Hansoh net product sales. In December 2022, we initiated work on the second target which we retain global rights to outside the China Region.

Financial Operations Overview

Revenue

We do not have any approved products. Accordingly, we have not generated any revenue from product sales, and we do not expect to generate any revenue from the sale of any products unless and until we obtain regulatory approvals for, and commercialize any of, our product candidates. In the future, we will seek to generate revenue primarily from product sales and, potentially, regional or global strategic collaborations with third parties.

Under our collaboration agreement with Mallinckrodt, we received an upfront cash payment of $20.0 million (£16.4 million as of the payment date) and are eligible to receive specified development, regulatory and commercial milestone payments. We received a milestone payment of $2.0 million (£1.7 million as of the payment date) during the year ended December 31, 2020. In February 2021, we initiated work on the third complement target which triggered another $2 million (£1.5 million) research milestone payment. In April 2021, we also received $2 million

(£1.5 million) for the second research milestone related to the first complement 3 target. During the year ended December 31, 2022 we received milestone payments totaling $3.0 million (£2.2 million). In addition to these potential payments, Mallinckrodt has agreed to fund some of our research personnel and preclinical development costs. We recognize the upfront payment, milestone payments, payments for personnel costs and other research funding payments over time, in accordance with IFRS 15 para 35 c). During the year ended December 31, 2022, we recognized a total of £11.7 million in revenue under this agreement.

Under our collaboration agreement with AstraZeneca, we received an upfront cash payment of £17.1 million ($20.0 million) and an additional payment of £30.8 million ($40.0 million) in May 2021. We are also eligible to receive specified development and commercial milestone payments as well as tiered royalties on net sales, if any. We recognize the upfront payment and milestone payments over time, in accordance with IFRS 15 para 35 c). During the year ended December 31, 2022, we recognized a total of £5.1 million in revenue under this agreement.

We entered into a collaboration agreement with Hansoh on October 15, 2021. We received a $16 million (equivalent to approximately £11.9 million based on the exchange rate at the payment date and $14.4 million or £10.7 million, net of taxes) upfront payment to us in December 2021. We are eligible to receive up to $1.3 billion in additional development, regulatory and commercial milestones. We will also receive royalties tiered from low double-digit to mid-teens on Hansoh net product sales. During the year ended December 31, 2022, we achieved milestone payments totaling $2.0 million (£1.5 million). We recognize the upfront payment and milestone payments over time, in accordance with IFRS 15 para 35 c). During the year ended December 31, 2022, we recognized a total of £0.2 million in revenue under this agreement.

In December 2018, we entered into a settlement and license agreement with Alnylam Pharmaceuticals Inc., or Alnylam, pursuant to which we settled outstanding patent litigation with Alnylam related to its RNAi product ONPATTRO. As part of the settlement, we license specified patents to Alnylam, and Alnylam pays us a tiered royalty of up to one percent of net sales of ONPATTRO in the European Union. We are eligible to receive these royalties until December 2023. We invoice Alnylam quarterly in arrears based on sales data for that quarter as reported to us by Alnylam. Royalty revenue is recognized based on the level of sales when the related sales occur. During the year ended December 31, 2022, we recognized a total of £0.6 million in royalty income from Alnylam.

Cost of sales

Cost of sales consists of research and development expenditure that is directly related to work carried out on revenue generating contracts. This includes salary costs that are apportioned based on time spent by employees working on these contracts as well as costs of materials and costs incurred under agreements with CROs.

Operating Expenses

We classify our operating expenses into two categories: research and development expenses and general and administrative expenses. Personnel costs, including salaries, benefits, bonuses and share-based payment expense, comprise a significant component of each of these expense categories. We allocate expenses associated with personnel costs based on the function performed by the respective employees.

Research and Development Expenses

The largest component of our total operating expenses since inception has been costs related to our research and development activities, including the preclinical and clinical development of our product candidates. We expense research and development costs as they are incurred and classify them as contracted development, personnel and other.

Our contracted development expense primarily consists of:

- costs incurred under agreements with CROs and investigative sites that conduct preclinical studies and clinical trials;

- costs related to manufacturing active pharmaceutical ingredients and drug products for preclinical studies and clinical trials; and
- costs for materials used for in-house research and development activities.

Our personnel research and development expense primarily consists of:

- salaries and personnel-related costs, including bonuses, benefits, recruitment costs and any share-based payment expense, for our personnel performing research and development activities or managing those activities that have been out-sourced; and
- consultants' costs associated with target selection, preclinical and clinical research activities, and the progression of programs towards clinical trials.

Our other research and development expense primarily consists of

- costs of related facilities, equipment and other overhead expenses that are considered directly attributable to research and development;
- costs associated with obtaining and maintaining patents for intellectual property; and
- depreciation of capital assets used for research and development activities.

The successful development of our product candidates is highly uncertain. Product candidates in later stages 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. Accordingly, we expect research and development costs to increase significantly for the foreseeable future as programs progress.

The duration, costs and timing of clinical trials and development of our product candidates will depend on a variety of factors, including:

- the scope, rate of progress, results and expenses of our ongoing and future clinical trials, preclinical studies and research and development activities;
- the potential need for additional clinical trials or preclinical studies requested by regulatory agencies;
- potential uncertainties in clinical trial enrollment rates or drop-out or discontinuation rates of patients;
- competition with other drug development companies in, and the related expense of, identifying and enrolling patients in our clinical trials and contracting with third-party manufacturers for the production of the drug product needed for our clinical trials;
- the achievement of milestones requiring payments under in-licensing agreements, if any;
- any significant changes in government regulation;
- the terms and timing of any regulatory approvals;
- the expense of filing, prosecuting, defending and enforcing patent claims and other intellectual property rights; and
- the ability to market, commercialize and achieve market acceptance for any of our product candidates, if they are approved.

We have not historically tracked research and development expenses on a program-by-program basis for our preclinical product candidates.

General and Administrative Expenses

General and administrative expenses consist of personnel costs, allocated expenses and other expenses for outside professional services, including legal, audit, tax and accounting services, public relations and investor relations services. Personnel costs consist of salaries, bonuses, benefits, recruitment costs and share-based payment expenses for personnel in executive, finance, business development and other support functions. Other administrative expenses include office space-related costs not otherwise allocated to research and development expense, insurance expenses, and costs of our information systems and costs for compliance with the day-to-day requirements of being a listed public company in the United States. We anticipate that our administrative expenses will continue to increase in the future as we increase our headcount to support our continued research and development and potential commercialization of our product candidates. We also expect to incur additional expenses as a public company in the United States, including expenses related to compliance with the rules and regulations of the SEC and Nasdaq, additional insurance expenses, expenses related to investor relations activities and other administrative and professional services.

Finance and Other Income (Expense)

Finance and other income primarily relates to interest earned on our cash, cash equivalents and short-term deposits, as well as foreign exchange gains. Finance and other expense primarily relates to lease liability interest expense and foreign exchange losses. Foreign exchange gains and losses relate to cash held in foreign currencies (primarily Euros).

Taxation

We are subject to corporate taxation in the United Kingdom, United States and Germany. Due to the nature of our business, we have generated losses since inception. Our income tax credit recognized represents the sum of the research and development, or R&D, tax credits recoverable in the United Kingdom. The U.K. R&D tax credit, as described below, is fully refundable to us. We have recorded the entire benefit from the U.K. R&D tax credit as a credit to “Taxation.”

As a company that carries out extensive research and development activities, we currently benefit from the U.K. research and development tax credit regime for small or medium-sized enterprises, or SMEs. Under the SME regime, we are able to surrender some of the trading losses that arise from qualifying R&D activities for a cash rebate of up to 33.4% of such qualifying R&D expenditures (starting on April 1, 2023, such rebate will be reduced to 18.6%). From 1 April 2021, for credit claims in excess of £20,000, the amount of payable credit that a qualifying loss-making SME business can receive through SME research and development relief in any one year will be capped at £20,000 plus three times the company’s and certain connected parties’ total pay-as-you-earn and National Insurance Contributions liability for that year, unless the company actively manages its intellectual property and does not outsource more than 15% of its R&D to a related party. Based on the implementation of the new rules, we do not currently expect the 2022 R&D tax claim to be restricted. Qualifying expenditures are net of any revenue contribution and largely comprise employment costs for research staff, materials, outsourced CRO costs and R&D consulting costs incurred as part of research projects, clinical trial and manufacturing costs, including outsourced CRO costs, employment costs for relevant staff and consumables incurred as part of research and development projects. Certain subcontracted qualifying research and development expenditures are eligible for a cash rebate of up to 21.7% (starting on April 1, 2023, such rebate will be reduced to 14.1%). A large portion of costs relating to our research and development, clinical trials and manufacturing activities are eligible for inclusion within these tax credit cash rebate claims. We recognize research and development tax credits when receipt is probable.

We may not be able to continue to claim research and development tax credits in the future under the current research and development tax credit scheme if we cease to qualify as a small or medium-sized company. However, we may be able to file under the U.K. research and development expenditure credit, or RDEC, regime for large companies. However, the relief available under RDEC is not as favorable as that of the SME regime.

Total estimated tax losses of £167.8 million and £154.1 million as of December 31, 2022 and 2021, respectively, were available for relief against our future profits. Unsurrendered U.K. tax losses may be carried forward indefinitely to be offset against future taxable profits, subject to numerous utilization criteria and restrictions. The amount that can be offset each year is limited to £5.0 million plus an incremental 50% of U.K. taxable profits. After accounting for tax credits receivable, we had accumulated tax losses for carry forward in the United Kingdom of £124.3 million as of December 31, 2022 (£107.6 million as of December 31, 2021). However, in the event of a change in ownership of a U.K. company, certain provisions may apply to restrict the utilization of carried forward tax losses in future periods. These provisions apply where there is a major change in the nature or conduct of a trade in connection with the change in ownership. For the avoidance of doubt, we do not recognize a deferred tax asset in respect of the accumulated tax losses. In addition to our accumulated tax losses in the United Kingdom, we also had £43.6 million of accumulated tax losses as of December 31, 2022 (£46.4 million as of December 31, 2021) related to our operations in Germany. We had had a foreign tax expense in Germany of £0.4 million (2021: £0.2 million). Tax losses in the U.S. were negligible.

In the event we generate revenues in the future, we may benefit from the U.K. “patent box” regime that allows profits attributable to revenues from patents or patented products to be taxed at an effective rate of 10%.

Value Added Tax, or VAT, is charged on all qualifying goods and services by VAT-registered businesses. Where applicable, an amount of 20% of goods and services is added to all sales invoices and is payable to the U.K. tax authorities. Similarly, VAT paid on purchase invoices is reclaimable from the U.K. tax authorities.

Results of Operations

Comparison of the years ended December 31, 2022, 2021 and 2020

The following tables summarize the results of our operations for the years ended December 31, 2022, 2021 and 2020.

Consolidated Income statements

	Year ended December 31,		
	2022	2021	2020
	£000s	£000s	£000s
Revenue	**17,501**	12,415	5,479
Cost of sales	**(10,880)**	(7,456)	(3,762)
Gross profit	**6,621**	4,959	1,717
Research and development costs	**(35,605)**	(30,765)	(20,209)
General and administrative expenses	**(19,609)**	(20,008)	(13,983)
Other losses - net	**-**	-	(3,372)
Operating loss	**(48,593)**	(45,814)	(35,847)
Finance and other expenses	**(47)**	(52)	(323)
Finance and other income	**1,272**	10	129
Loss for the year before taxation	**(47,368)**	(45,856)	(36,041)
Taxation	**6,879**	6,446	3,494
Loss for the year after taxation	**(40,489)**	(39,410)	(32,547)
Loss per ordinary equity share (basic and diluted)	**(41.9) pence**	(44.1) pence	(39.8) pence

Revenue

Revenue for the year ended December 31, 2022 was £17.5 million (2021: £12.4 million; 2020: £5.5 million). The increase was primarily due to the advancement of targets in our Mallinckrodt, AstraZeneca, and Hansoh collaborations which delivered £16.9 million to us in 2022, offset by the reduction in revenue due to the completion of other collaboration agreements (2021: £11.4 million; 2020: £3.8 million).

Research and Development Expenses

The following table summarizes our research and development costs for the years ended December 31, 2022, 2021 and 2020.

	Year ended December 31,		
	2022	2021	2020
	£000s	£000s	£000s
Research and development expenses			
Contracted development costs	**19,656**	16,482	11,703
Personnel costs	**13,902**	12,663	7,256
Other costs	**2,046**	1,620	1,250
Total	**35,605**	30,765	20,209

Research and development expenses for the year ended December 31, 2022 were £35.6 million as compared to £30.8 million for the year ended December 31, 2021 and £20.2 million for the year ended December 31, 2020. Contract development costs increased by £3.2 million from 2021 as a result of additional clinical trials and an increase in contract manufacturing activities for our proprietary programs. Personnel costs also increased by £0.8 million from 2021 associated with the increase of headcount related to the addition of new R&D programs.

Cost of sales consists of research and development expenditure that is directly related to work carried out on revenue generating contracts, which increased to £10.9 million for the year ended December 31, 2022 (2021: £7.5 million, 2020 £3.8 million). The increase was largely due to the further advancement of our collaboration programs.

General and administrative Expenses

General and administrative expenses were £19.6 million for the year ended December 31, 2022 as compared to £20.0 million for the year ended December 31, 2021 and £14.0 million for the year ended December 31, 2020. While there was an increase in payroll costs of £1.6 million, this was offset by a reduction in consulting and recruiting costs of £0.6 million as we continue to reduce reliance on consultants. The remainder of the decrease is due to finance, insurance, internal control, travel and legal costs as we continue to benefit from efficiencies gained and the monitoring of administrative costs.

Finance and Other Income (Expense)

Finance income represents bank interest and accretion from U.S. Treasury Bills. For December 31, 2022 this was £0.2 million (2021: £10 thousand and 2020: £0.1 million). The increase of finance income in 2022 can mainly be attributed to purchases of U.S. Treasury Bills in 2022.

Also included in the Finance and other Income total is foreign exchange gains of £1.0 million, £nil, and £nil for the years ended December 31, 2022, 2021 and 2020, respectively. Net foreign exchange gains and losses result primarily from foreign currency (Euro and USD) denominated bank accounts.

Finance expense for the year ended December 31, 2022 was £47 thousand, resulting from interest expense incurred in connection with lease liabilities, compared to £8 thousand for the prior year.

Also included in the Finance and other expense total is foreign exchange losses of £nil, £32 thousand, and £307 thousand for the years ended December 31, 2022, 2021 and 2020, respectively. Net foreign exchange gains and losses result primarily from foreign currency (Euro and USD) denominated bank accounts.

Taxation

During 2022 and 2021, we have recognized U.K. research and development tax credits of £7.4 million and £6.9 million, respectively in respect of R&D expenditures incurred; the higher tax credit in current year due to an increase in R&D expenditure compared to previous year. This amount was offset by tax charges in our foreign tax expense.

Critical Accounting Policies, Judgments and Estimates

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 are considered to be relevant. Actual results may differ from these estimates. Revisions to accounting estimates for the current and/or futures periods impacted, are recognized in the period in which the estimate is revised.

The following are our critical judgments that we have made in the process of applying our accounting policies and that have the most significant effect on the amounts recognized in our consolidated financial statements included elsewhere in this report.

Revenue Recognition under Collaboration Agreements

During the years ended December 31, 2022, 2021 and 2020, a significant portion of our revenue from collaboration agreements was derived from our agreements with Mallinckrodt, AstraZeneca, and Hansoh. Mallinckrodt obtained an exclusive worldwide license for three RNAi programs, AstraZeneca obtained an exclusive worldwide license for up to ten RNAi targets and Hansoh obtained an exclusive option to license up to two targets in Greater China, Hong Kong, Macau and Taiwan and a third target worldwide.

We have out-licensed the rights to some of our intellectual property associated with our siRNA stabilization chemistry technology to AstraZeneca in the context of a Research Collaboration, Option and License Agreement dated March 24, 2020, under which we and AstraZeneca will collaborate to discover, develop and commercialize siRNA therapeutics for the treatment of cardiovascular, renal, metabolic and respiratory diseases. AstraZeneca made an upfront cash payment of $60 million, of which $20 million was paid in May 2020 and the remaining $40 million was paid in May 2021. The upfront payment has been allocated evenly between the ten targets on the basis of a benchmarking exercise that took into account the standalone selling price per target, of similar precedent transactions that had been publicly announced by comparable companies. Subsequent milestones are allocated to the target to which they are related. The upfront and milestone payments will be recognized as revenue as the services are provided. We anticipate initiating work on up to five targets in the early stages of the collaboration, with AstraZeneca having the option to extend the collaboration to a further five targets. Under the collaboration, utilizing our technology, we are responsible for designing siRNA molecules against gene targets selected by AstraZeneca, and for manufacturing of material to support GLP toxicology studies and phase 1 clinical trials. We and AstraZeneca will collaborate during the discovery phase, and AstraZeneca will lead clinical development and commercialization of molecules arising from the collaboration. For each target selected under the collaboration, we will be eligible to receive up to $140 million in milestone payments upon the achievement of milestones relating to initiation of specified clinical trials, the acceptance of specified regulatory filings and the first commercial sale in specified jurisdictions. AstraZeneca has the right to terminate the agreement in its entirety or on a target-by-target basis, for any reason upon specified prior written notice to us. We may terminate the agreement on a target-by-target basis in the event that AstraZeneca begins a legal or administrative proceeding challenging the patentability, validity, ownership or enforceability of our patents. Either party may terminate the agreement on a target-by-target basis upon a material breach by the other party that is not cured within a specified period after receiving written notice, or in its entirety upon giving written notice following the other party's bankruptcy, insolvency or similar instance. The license of the intellectual property and the R&D services are not distinct, as AstraZeneca cannot benefit from the intellectual property absent the R&D services, as those R&D services are used to discover and develop a drug candidate and to enhance the value in the underlying intellectual property, which could not be performed by another party, indicating that the two are highly interrelated. On this basis, we have concluded that there is a single performance obligation covering both the R&D services and the license of the intellectual property in respect of each target (i.e., one for the initial target and one for each additional optioned complement-mediated disease target). We recognize revenue over the duration of the contract based on an input method based on percentage of cost incurred.

We granted an exclusive worldwide license to our C3 targeting program, SLN501, with options to license two additional complement-mediated disease targets, to Mallinckrodt in July 2019 to develop and commercialize RNAi drug targets designed to silence the complement cascade in complement-mediated disorders, with Mallinckrodt exercising the option for two additional targets from us in July 2020. The license of the intellectual property and the R&D services are not distinct, as Mallinckrodt cannot benefit from the intellectual property absent the R&D services,

as those R&D services are used to discover and develop a drug candidate and to enhance the value in the underlying intellectual property, which could not be performed by another party, indicating that the two are highly interrelated. On this basis, we have concluded that there is a single performance obligation covering both the R&D services and the license of the intellectual property in respect of each target (*i.e.,* one for the initial target and one for each additional optioned complement-mediated disease target). We recognize revenue over the duration of the contract based on an input method based on cost to cost.

The agreement with Mallinckrodt has four elements of consideration:

- a fixed upfront payment, which we received in July 2019;
- subsequent milestone payments, which are variable and depend upon our achievement of specified development, regulatory and commercial milestones;
- payments in respect of certain research personnel costs on an FTE, basis, which costs are variable depending on activity under the collaboration; and
- funding for phase 1 clinical development and certain preparatory activities, including GMP manufacturing, which costs are also variable.

The upfront payment has been allocated evenly between the initial target and the optioned complement-mediated disease targets, because the compounds are at a similar stage of development, on the basis of a benchmarking exercise that took into account the standalone selling price per target, of similar precedent transactions that had been publicly announced by comparable companies. Subsequent milestones are allocated to the target to which they are related. The upfront and milestone payments will be recognized as revenue as the services are provided.

We granted an exclusive option to license two targets in Greater China, Hong Kong, Macau and Taiwan following the completion of phase 1 trials to Hansoh on October 15, 2021. We will retain exclusive rights for those two targets in all other territories. Silence will be responsible for all activities up to option exercise and will retain responsibility for development outside the China region post phase 1 trials. Hansoh will also have the exclusive option to license global rights to a third target at the point of IND filing. Hansoh will be responsible for all development activities post option exercise for the third target. Hansoh made a $16 million upfront payment to us in December 2021 which has been allocated between the three targets based on geography for each option, amount of reimbursable costs for activities provided by Silence for each target, as well as a benchmarking exercise that took into account the standalone selling price per target based on similar precedent transactions that had been publicly announced by comparable companies. Subsequent milestones are allocated to the target to which they are related. The upfront payment and subsequent milestone payments, which are variable and depend upon probability of achievement of specified development, regulatory and commercial milestones, will be recognized as revenue as the services are provided. The license of the intellectual property and the R&D services are not distinct, as Hansoh cannot benefit from the intellectual property absent the R&D services, as those R&D services are used to discover and develop a drug candidate and to enhance the value in the underlying intellectual property, which could not be performed by another party, indicating that the two are highly interrelated. On this basis, we have concluded that there is a single performance obligation covering both the R&D services and the license of the intellectual property in respect of each target (*i.e.,* one for the initial target and one for each additional optioned complement-mediated disease target). We recognize revenue over the duration of the contract based on an input method based on cost to cost.

For all the collaboration agreements listed above, as there is only a single performance obligation per target, the revenue for each element of consideration will be recognized over the contract period based on a cost-to-cost method, which is considered to be the best available measure of our effort during the contract period. The total cost estimate for the contract includes costs expected to be incurred during the contract period. Other variable elements of consideration will only begin to be recognized when it is considered highly probable that a significant reversal of the amounts will not occur.

For the year ended December 31, 2022, 2021 and 2020, we determined actual costs and forecast costs for the remainder of the contract. We calculated total contract costs across the contract term, including costs that will be

reimbursed to us, and costs incurred to date as a percentage of total contract costs. We multiplied this percentage by the consideration deemed highly probable of not having a significant reversal, calculating the cumulative revenue to be recognized. When variable consideration increases due to a further milestone becoming highly probable that a significant reversal of revenue will not occur, a catch-up in revenue is recorded to reflect efforts already expended by us up to that point.

Recognition of Clinical Trial Expenses

As part of the process of preparing our consolidated financial statements, we may be required to estimate accrued expenses related to our preclinical studies and clinical trials. To obtain reasonable estimates, we review open contracts and purchase orders. In addition, we communicate with applicable personnel in order to identify services that have been performed, but for which we have not yet been invoiced. In most cases, our vendors provide us with monthly invoices in arrears for services performed. We confirm our estimates with these vendors and make adjustments as needed. Examples of our accrued expenses include fees paid to CROs for services performed on preclinical studies and clinical trials and fees paid for professional services.

Recent Accounting Pronouncements

See note 2.1 to our consolidated financial statements for the year ended December 31, 2022 included elsewhere in this report for a discussion of new standards and interpretations recently and not yet adopted by us.

Jumpstart Our Business Startups Act of 2012

In April 2012, the U.S. Jumpstart Our Business Startups Act of 2012, or the JOBS Act, was enacted. Section 107(b) of the JOBS Act provides that an "emerging growth company," or EGC, can take advantage of an extended transition period for complying with new or revised accounting standards. Thus, an EGC can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. Given that we currently report and expect to continue to report under IFRS as issued by the IASB, we have irrevocably elected not to avail ourselves of this extended transition period, and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies in the United States.

We intend to rely on other exemptions and reduced reporting requirements under the JOBS Act. Subject to certain conditions, as an EGC, we may rely on certain of these exemptions, including exemptions from (1) providing an auditor's attestation report on our system of internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act and (2) complying with any requirement that may be adopted by the PCAOB regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, known as the auditor discussion and analysis.

We will remain an EGC until the earliest of (a) the last day of our fiscal year during which we have total annual gross revenue of at least $1.235 billion; (b) December 31, 2025; (c) the date on which we have, during the previous three-year period, issued more than $1.0 billion in non-convertible debt; or (d) the date on which we are deemed to be a "large accelerated filer" under the Securities Exchange Act of 1934, as amended, which would occur if the market value of our equity securities that are held by non-affiliates exceeds $700 million as of the last business day of our most recently completed second fiscal quarter. Once we cease to be an EGC, we will not be entitled to the exemptions provided in the JOBS Act.

We have taken advantage of reduced reporting requirements in this report. Accordingly, the information contained herein may be different than the information you receive from other public companies in which you hold equity securities.

B. Liquidity and Capital Resources

Overview

Since our inception, we have incurred significant operating losses and negative cash flows. We anticipate that we will continue to incur losses for the foreseeable future. We expect that our research and development and administrative expenses will increase in connection with conducting clinical trials and seeking marketing approval for our product candidates, as well as costs associated with operating as a public company in the United States.

As of December 31, 2022, we had cash, cash equivalents and U.S. Treasury Bills of £71.1 million ($86.0 million), which reflects the registered direct offering, or the Offering, of 5,950,000 ADSs, at a public offering price of $9.50 per ADS, in August 2022. Our aggregate gross proceeds from this offering were $56.5 million (approximately £46.4 million) before deducting $4.1 million (approximately £3.3 million) in underwriting discounts, commissions and estimated offering expenses. We believe that our current cash, cash equivalents and U.S. Treasury Bills will be only sufficient to fund our operating expenses and capital expenditure requirements through the first quarter of 2024. Based on the Company's evaluation as described in the consolidated financial statements, footnote 2.3 Going Concern, there is a material uncertainty which may cast significant doubt (or raise substantial doubt as contemplated by Public Company Accounting Oversight Board ("PCAOB") standards) on the Company's ability to continue as a going concern. As a result, we will need additional capital to fund our operations, which we may obtain from additional equity financings, debt financings, research funding, collaborations, contract and grant revenue or other sources. However, there is no assurance that we will be successful in obtaining sufficient funding on acceptable terms.

To date, we have financed our operations primarily through the issuances of our equity securities and from upfront, milestone and research payments under collaboration agreements with third parties.

We have no ongoing material financing commitments, such as lines of credit or guarantees, that are expected to affect our liquidity over the next five years, other than operating leases.

On October 15, 2021, we entered into an Open Market Sale Agreement, or the Sales Agreement, with Jefferies LLC, or Jefferies, under which Jefferies, as our exclusive agent, at our discretion and at such times that we may determine from time to time, may sell over a three-year period from the execution of the Sales Agreement up to a maximum of $100.0 million of ADSs. Under the terms of the Sales Agreement, Jefferies may sell the ADSs at market prices by any method that is deemed to be an "at the market offering" as defined in Rule 415 under the Securities Act of 1933, as amended. The ADSs offered under the Sales Agreement are being offered pursuant to a registration statement on Form F-3 that became effective on October 22, 2021. We may offer and sell up to $300.0 million of our shares, represented by ADSs, from time to time in one or more offerings. During the year ended December 31, 2022, no shares of our common stock were issued pursuant to the Sales Agreement.

We may also achieve further milestones from our current collaboration partners which will further extend our cash runway.

Cash Flows

The following table summarizes the results of our cash flows for the years ended December 31, 2022, 2021 and 2020.

	Year ended December 31,		
	2022	2021	2020
	£000s	£000s	£000s
Net cash inflow/(outflow) from operating activities	**(45,456)**	6,806	(10,776)
Net cash inflow/(outflow) from investing activities	**(16,542)**	8,676	9,618
Net cash inflow from financing activities	**43,049**	30,711	15,428
Increase/(decrease) in cash and cash equivalents	**(18,949)**	46,193	14,270

Operating activities

Net cash outflow from operating activities decreased to £45.5 million for the year ended December 31, 2022 from a net cash inflow of £6.8 million for the year ended December 31, 2021. This was primarily due to a decrease in upfront cash payments from collaborators in 2022 (£41.5 million in 2021). Further decreases were from additional cash spend of £10.5 million from research, development and administrative costs incurred as we continue to expand and advance our research and development portfolio.

Net cash inflow from operating activities increased by £17.5 million to £6.8 million for the year ended December 31, 2021 from a net cash outflow of £10.8 million for the year ended December 31, 2020. This was primarily due to increases in upfront cash payments from collaborators of £25.5 million (£41.5 million in 2021, less £16.0 million in 2020) and additional milestones £2.9 million. These increases in cash flow were offset by net cash expenses which increased £16.8 million from research, development and administrative costs incurred as we continue to expand and advance our research and development portfolio. The remainder of the increase was due to additional amounts received from R&D tax credits received.

Investing activities

Net cash outflow from investing activities was £16.5 million for the year ended December 31, 2022, compared to £8.7 million inflow for the year ended December 31, 2021. This change was primarily due to the purchase of U.S. Treasury Bills with maturities over three months of £16.3 million in 2022 while there was a redemption of term deposits of £10 million in 2021.

Net cash inflow in investing activities was £8.7 million for the year ended December 31, 2021, compared to £9.6 million outflow for the year ended December 31, 2020. This change was primarily due to a cash increase used for purchasing property, plant and equipment of £0.8 million.

Financing activities

The increase in net cash from financing activities to £43.0 million for the year ended December 31, 2022 from £30.7 million inflow for the year ended December 31, 2021 was due to the proceeds we received from the Offering. The aggregate gross proceeds of the Offering were $56.5 million (approximately £46.4 million) before deducting $4.1 million (approximately £3.3 million) in underwriting discounts, commissions and estimated offering expenses.

In 2021, we received aggregate gross proceeds of $45 million (approximately £33 million) before deducting approximately £2.4 million in placement agent fees and other expenses from an oversubscribed private placement of our ADSs.

The net cash from financing activities was £15.4 million for the year ended December 31, 2020 due to the $20.0 million investment in our ordinary shares made by AstraZeneca in the first half of 2020 (equivalent to £15.6 million based on the exchange rate at the payment date).

Operating and Capital Expenditure Requirements

We have not achieved profitability on an annual basis since our inception, and we expect to incur net losses in the future. We expect that our operating expenses will increase as we continue to invest to grow our product candidate pipeline, hire additional employees and increase research and development expenses.

Additionally, as a public company, we incur significant additional audit, legal and other expenses. We believe that our existing capital resources will be sufficient to fund our operations, including currently anticipated research and development activities and planned capital spending, through the first quarter of 2024.

Our future funding requirements will depend on many factors, including but not limited to:

- the scope, rate of progress and cost of our clinical trials, preclinical programs and other related activities;
- the extent of success in our early preclinical and clinical-stage research programs, which will determine the amount of funding required to further the development of our product candidates;
- the cost of manufacturing clinical supplies and establishing commercial supplies of our product candidates and any products that we may develop;
- the costs involved in filing and prosecuting patent applications and enforcing and defending potential patent claims;
- the outcome, timing and cost of regulatory approvals of our product candidates;
- the cost and timing of establishing sales, marketing and distribution capabilities; and
- the costs of hiring additional skilled employees to support our continued growth and the related costs of leasing additional office space.

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

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

D. Trends Information

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

E. Critical Accounting Estimates

Critical accounting estimates are discussed in note 2.18 to our consolidated financial statements.

ITEM 6: DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES

A. Executive Officers and Directors

The following table sets forth information regarding our executive officers and directors as of the date of this report, including their ages as of the date of this Annual Report.

Name	Age	Position(s)
Executive Officers:		
Craig Tooman	57	President, Chief Executive Officer and Executive Director
Giles Campion, M.D.	68	Head of R&D, Chief Medical Officer and Executive Director
Rhonda Hellums	51	Chief Financial Officer
Non-Executive Directors:		
Iain Ross	69	Non-Executive Chairman
James Ede-Golightly	43	Non-Executive Director
Alistair Gray	74	Senior Independent Non-Executive Director
Dave Lemus	60	Non-Executive Director
Steven Romano, M.D.	63	Non-Executive Director
Michael Davidson, M.D.	66	Non-Executive Director

Executive Officers

Craig Tooman has served as our President, Chief Executive Officer and as a member of our board of directors since February 2022 and previously served as our Chief Financial Officer from January 2021 until February 2022. Mr. Tooman has experience in the biopharmaceutical industry spanning more than 30 years, including 15 years of experience as a public company CEO and CFO. Prior to joining us, from September 2019 to January 2021, he served as CFO and COO at Vyome Therapeutics, Inc. and prior to his tenure at Vyome, from November 2013 to July 2019, Mr. Tooman served as CFO, and then subsequently as CEO and Board Director of Aratana Therapeutics, Inc., where he successfully negotiated a merger with Elanco. Before Aratana, from 2005 to 2010, Mr. Tooman served as the CFO of Enzon Pharmaceuticals, Inc. until its acquisition by Sigma Tau, and prior to that led the $1.1 billion M&A initiative and integration of ILEX Oncology, Inc. and Genzyme Corporation. Mr. Tooman has also held key positions at Pharmacia and Upjohn. Mr. Tooman currently serves on the Supervisory Board, and the Audit and Remuneration Committees of CureVac. He also serves on the Board of Directors of Ondine Biomedical Inc. and Verté Therapeutics. Mr. Tooman received a BA degree in Economics from Kalamazoo College and studied at Waseda University in Tokyo as part of that program. He earned his MBA in finance from the University of Chicago.

Giles Campion, M.D. has served as our EVP, Head of R&D and Chief Medical Officer since June 2019 and as a member of our board of directors since May 2020. Dr. Campion is an expert in translational medicine and a highly experienced biotech and pharmaceutical professional across many therapeutic areas, most recently in orphan neuromuscular disorders. He has held senior global research and development roles in several large pharmaceutical, diagnostics and biotech companies, including responsibilities at the board level. Dr. Campion served as Chief Medical Officer for Albumedix Ltd. from January 2017 to July 2018. He previously served Group Vice President, Neuromuscular Franchise at BioMarin Pharmaceutical Inc., or BioMarin, from February 2015 to March 2016, following BioMarin's acquisition of Prosensa Holding N.V., or Prosensa. Dr. Campion served as Chief Medical Officer and Senior Vice President of Research and Development at Prosensa from 2009 until its acquisition by BioMarin. Dr. Campion has also served as a medical advisor to MyoTherix, Inc. and a co-founder of PepGen Ltd. Dr. Campion holds bachelors and doctorate degrees in medicine from the University of Bristol, is listed on the General Medical Council (U.K.) Specialist Register (Rheumatology).

Rhonda Hellums has served as our Chief Financial Officer since February 2022 and has previously served as our Vice President, Finance since joining in April 2021. Ms. Hellums has over 25 years of corporate finance, accounting, strategic planning, M&A, treasury management, investor and public relations. Prior to joining Silence, from 2019 to 2021, she, she served as CFO of Deer Oaks Mental Health Associates and prior to that, from 2014 to 2019, Ms. Hellums served Vice President of Finance, and then subsequently as CFO of Aratana Therapeutics. Ms. Hellums has held management positions at several healthcare companies, including Kinetic Concepts, Inc. (now 3M+KCI), Enzon

Pharmaceutical, Inc. Genzyme Corporation, and ILEX Oncology, Inc. Ms. Hellums received her BBA degree in Accounting and Information Systems and MBA from the University of Texas at San Antonio.

Non-Executive Directors

Iain Ross has served as our Non-Executive Chairman since September 2020 after serving as Executive Chairman from December 2019 to September 2020. He previously served as our Non-Executive Chairman from April 2019 to December 2019 and as our Chairman from 2004 to 2010. Mr. Ross has experience in the international life sciences and technology sectors and has held significant roles in multi-national companies including Sandoz, Hoffman La Roche, Reed Business Publishing and Celltech Group plc. He has completed multiple financing transactions, and has over 30 years' experience in cross-border management as a chairman and CEO. He has led and participated in eight Initial Public Offerings (IPOs) and has direct experience of M&A transactions in Europe, the United States and the Pacific Rim. Currently he is Executive Chairman of ReNeuron Group plc (LSE) and Non-Executive Chairman of Kazia Therapeutics Limited (ASX & Nasdaq). In addition, he is a non-executive director of BiVictriX Therapeutics plc (LSE) and advises a number of private companies in the biotechnology sector. He is a qualified Chartered Director and Fellow of Royal Holloway, London University.

James Ede-Golightly has served as a member of our board of directors since April 2019. Mr. Ede-Golightly is currently chairman of Oxehealth Ltd, East Balkan Properties Plc and Oxford Advanced Surfaces Ltd. Among other directorships, Mr. Ede-Golightly is non-executive director of Sarossa plc, Serendipity Capital Ltd and Plant Health Care plc, and has extensive experience as a non-executive director of AIM-quoted companies with international business interests. Mr. Ede-Golightly was a founder of ORA Capital Partners in 2006, having previously worked as an analyst at Merrill Lynch Investment Managers and Commerzbank. Mr. Ede-Golightly is a CFA Charterholder and holds an M.A. degree in economics from Cambridge University. In 2012, he was awarded New Chartered Director of the Year by the Institute of Directors.

Alistair Gray has served as a member of our board of directors since November 2015 and was appointed as Senior Independent Director in December 2019. Mr. Gray currently serves as non-executive director/chair of the Edrington Group's Employee Benefit Trust, chair of the Scottish Enterprise's Pension Trustee Board and Life Assurance Scheme Trustee Board and as a non-executive director of Scottish Golf Ltd. Mr. Gray is also a founder and director of Renaissance & Company, a strategic management consultancy firm. Mr. Gray previously held senior management positions with Unilever and John Wood Group PLC, and he also chaired the Audit and Remuneration committees of AorTech International PLC and Highland Distillers PLC. Mr. Gray entered strategic management consulting at Arthur Young Management Consultants (now EY) and PA Consulting Group, where he served as a director for over ten years. Mr. Gray also served as a Fellow of the Institute of Directors and Institute of Consultants. He graduated from the University of Edinburgh in Mathematics and Economics, following this with a management accounting qualification. He is a member of the faculty of Strathclyde Business School and a Visiting Professor at the University's Design Manufacturing and Engineering Management department. He is also a Visiting Professor at Loughborough University London and the University of Stirling.

Dave Lemus has served as a member of our board of directors since June 2018. Previously, Mr. Lemus was the Chief Executive Officer of Ironshore Pharmaceuticals Inc. and prior to this, Mr. Lemus served as Chief Operating Officer and Chief Financial Officer of Medigene AG. From 2011 to 2015, he served as Chief Executive Officer of Sigma Tau Pharmaceuticals, Inc. Mr. Lemus was also Chief Financial Officer and Executive Vice President of MorphoSys AG from 1998 to 2011, during which time he took the company public on the Frankfurt Stock Exchange in Germany's first biotechnology initial public offering. In addition to his position on our board of directors, Mr. Lemus also currently serves as non-executive director of Sorrento Therapeutics Inc. (Nasdaq: SRNE), Scilex Holding Company (Nasdaq: SCLX) and BioHealthInnovation, Inc. Mr. Lemus received an M.S. from the Massachusetts Institute of Technology and received a B.S. in accounting from the University of Maryland College Park. Mr. Lemus is also a Certified Public Accountant in the United States.

Steven Romano, M.D. has served as a member of our board of directors since July 2019. Dr. Romano is a pharmaceutical executive and board-certified psychiatrist with over 28 years of drug development experience across a wide range of therapeutic and disease areas. Dr. Romano most recently served as executive vice president and chief scientific officer at Mallinckrodt plc, where he had responsibility for research and development, regulatory, safety sciences and medical affairs. Prior to joining Mallinckrodt, Dr. Romano spent 16 years at Pfizer, Inc. where he held a series of senior research and development and medical roles of increasing responsibility, culminating in his most recent position as SVP, Head, Global Medicines Development, Global Innovative Pharmaceuticals Business. He has

recently served as Chairman of the National Pharmaceuticals Council, a health policy research organization, and is a past president of the International Society for CNS Clinical Trials and Methodology, an independent organization focused on enhancing therapeutic development of central nervous system therapeutics. Dr. Romano graduated from Washington University in St. Louis with a bachelor's degree in biology and English literature, received his M.D. from the University of Missouri-Columbia School of Medicine and completed his psychiatry and fellowship at Weill Cornell Medical Center, where he held academic and clinical positions prior to entering the industry.

Michael H. Davidson, M.D. FACC, FNLA, has served as a member of our board of directors since January 2021. Dr. Davidson is Professor of Medicine and Director of the Lipid Clinic at the University of Chicago. He also serves as the Chief Executive Officer of New Amsterdam Pharma Company N.V. (Nasdaq: NAMS) which was listed on Nasdaq in November 2022. Dr. Davidson is a leading expert in the field of Lipidology. He has conducted over 1,000 clinical trials, published more than 350 medical journal articles and written three books on Lipidology. His research background encompasses both pharmaceutical and nutritional clinical trials including extensive research on statins, novel lipid-lowering drugs, and omega-3 fatty acids. Dr. Davidson is a serial biotech entrepreneur, founding three companies, the Chicago Center for Clinical Research, which became the largest investigator site in the United States and was acquired by Pharmaceutical Product Development in 1996, Omthera Pharmaceuticals in 2008, which was acquired by AstraZeneca in 2013 for $440 million, and most recently, he was the founding CEO/CSO of Corvidia Therapeutics, which was acquired by Novo Nordisk for up to $2.1 billion in 2020. He is also an independent director of Nasdaq-listed Tenax Therapeutics, Inc. (Nasdaq: TENX) and serves on the board of two private biotech companies, Sonothera and NanoPhoria Bioscience. Dr. Davidson is board-certified in internal medicine, cardiology, and clinical lipidology. He was President (2010-2011) of the National Lipid Association, named as one The Best Doctors in America for the past 20 years and "Father of the Year" by the American Diabetes Association, 2010.

Agreement to Appoint a Director

In July 2019, Mallinckrodt, through its affiliate, Cache Holdings Limited, or Cache, purchased $5 million worth of our ordinary shares. In addition to the cash payment for the shares, we also provide Cache the right to nominate one person as a director on our board. The first director nominated pursuant to this provision was Dr. Romano. The Cache nominated director must resign if (i) prior to the issuance of new ordinary shares, Cache's holding represent less than 5% of the voting rights of our shares outstanding, or (ii) following the issuance of new ordinary shares Cache's holding represent less than 5% of the voting rights of our shares outstanding and they've transferred at least 2,531,083 of our ordinary shares. Cache must consult with us prior to making any nomination.

B. Compensation

Executive Officer Remuneration

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

Name and Principal Position[1]	Salary £000s	Bonus(1) £000s	Option Awards(2) £000s	Pension/Post Retirement Benefits £000s	All Other Compensation £000s	Total £000s
Craig Tooman	461	162	5,290	14	13	5,940
President and Chief Executive Officer (3)						
Giles Campion, M.D.	350	129	1,017	35	9	1,540
Executive Vice President, Head of R&D						
Rhonda Hellums	334	57	1,901	15	32	2,339
Chief Financial Officer (4)						
Total	1,145	348	8,208	64	55	9,820

(1) Amount shown reflect bonuses awarded for achievement of performance goals paid in 2022.
(2) Amount shown represents the aggregate grant date fair value of option awards granted in 2022 measured using the Black Scholes model. For a description of the assumptions used in valuing these awards, see note 24 to our consolidated financial statements included elsewhere in this Annual Report. Total option award compensation expense for the year ended December 31, 2022 for all key management personnel including the former CEO and non-executive directors was £3.5 million.
(3) Mr. Tooman served as our Chief Financial Officer during 2021 and became our President and Chief Executive Officer on February 21, 2022.
(4) Ms. Hellums became our Chief Financial Officer on February 21, 2022.

Executive Service Agreements

Service Agreement of Craig Tooman

Craig Tooman, our President and Chief Executive Officer, entered into an amended and restated employment agreement with us on February 21, 2022. Mr. Tooman's employment with us (under a prior agreement) commenced on January 28, 2021.

Pursuant to the terms of the employment agreement, Mr. Tooman is entitled to an annual base salary, initially $575,000, which is subject to annual review. Under the terms of the employment agreement, Mr. Tooman is also entitled to: (i) participate in all employee benefit plans and other fringe benefits plans generally available to similarly situated employees, subject to customary conditions; (ii) 5 weeks' paid holiday per annum; (iii) payment of reasonable attorney's fees for the review of his employment agreement and all related documents up to a maximum of $10,000; and (iv) payment for the preparation of annual tax returns up to a maximum of $10,000 per year.

Mr. Tooman is eligible to participate in our discretionary bonus plan. Mr. Tooman's maximum annual bonus entitlement is 60% of his annual base salary. If Mr. Tooman's employment is terminated by us (other than for "Cause," as defined in the employment agreement, disability or death) or by Mr. Tooman for "Good Reason" (as defined in the employment agreement) and provided he is not in breach of the restrictive covenants (including post-termination) applicable to him (which we refer to herein as a Severance Good Leaver) prior to the end of any bonus year, he is eligible to be paid: (i) subject to Mr. Tooman executing a customary release of claims, such release becoming effective, or the Release Condition, any unpaid short-term bonus for any completed performance period and (ii) a pro rata bonus for the year in which the termination occurs based on the achievement of applicable performance goals.

In connection with Mr. Tooman's promotion to President and Chief Executive Officer, we granted him options representing the right to acquire 125,000 of our ADSs. The ADSs will vest in equal installments monthly over the next 48 months. The exercise price of the ADSs is $18.99.

Mr. Tooman's employment is "at will" and is terminable by either party on not less than 45 days' prior written notice (other than in the case of his death, disability or termination by us for Cause). If Mr. Tooman's employment is terminated and he is not a Severance Good Leaver, he will only be entitled to payments and benefits accrued at the termination date.

If Mr. Tooman is a Severance Good Leaver and subject to the Release Condition being met, in addition to payments and benefits accrued at the termination date, he is eligible to receive (i) continuation of his annual base salary for a period of 12 months, or the Tooman Separation Period, paid over the Tooman Separation Period in accordance with normal payroll practices and (ii) if elected by Mr. Tooman, continuation coverage under the Company's medical plan for no longer than the Tooman Separation Period, together with payment of the amount of COBRA premiums until the earliest of the expiration of the Severance Period, eligibility for healthcare coverage with a subsequent employer and ineligibility for COBRA benefits.

Any equity based awards held by Mr. Tooman will be treated on his termination in accordance with the relevant plan rules and award documentation save that, if Mr. Tooman becomes a Severance Good Leaver, such termination shall be deemed to be for a "Good Leaver Reason" for the purposes of the applicable share plan.

In the event of a "Change of Control" (as defined in the employment agreement), any equity awards held by Mr. Tooman will vest and become exercisable in full. In addition, if Mr. Tooman becomes a Severance Good Leaver within 12 months after the occurrence of a "Change of Control," Mr. Tooman will be entitled to the severance benefits described above save that the Separation Period shall be increased to 18 months and the amount due will be paid in a single sum payment.

If Mr. Tooman's employment is terminated by reason of his death or disability (in the circumstances described in the employment agreement), Mr. Tooman (or his estate) will be entitled to be receive: (i) payments and benefits accrued at the termination date; (ii) the annual bonus actually earned for the preceding bonus year to the extent unpaid on termination; and (iii) a pro-rata bonus in respect of the proportion of such year during which Mr. Tooman is employed by us. In addition, all vested equity awards will be treated in accordance with the relevant plan rules and award documentation as if Mr. Tooman was a "Good Leaver."

During the term of his employment, Mr. Tooman is restricted from accepting appointments with third parties save as agreed by us. He is permitted to continue his role on the board of directors of CureVac N.V, Odine Biomedical Inc. and a privately-held company as approved by the Non-Executive Chairman of the board of directors.

Compensation paid to Mr. Tooman is subject to repayment and/or claw-back obligations arising under applicable law or otherwise implemented under any Company clawback policy in effect from time to time.

The employment agreement contains customary provisions under Section 409A of the Code and standard assignment provisions relating to the ownership of intellectual property. Mr. Tooman is subject to confidentiality obligations which remain in place following termination of employment, and to non-solicitation, non-employment and non-inducement restrictive covenants for a period of 12 months post-termination of his employment.

Service Agreement of Rhonda Hellums

Rhonda Hellums, our Chief Financial Officer, entered into an amended and restated employment agreement with us on February 21, 2022. Ms. Hellums' employment with us (under a prior agreement) commenced in April 2021.

Pursuant to the terms of the employment agreement, Ms. Hellums is entitled to an annual base salary, initially $420,000, which is subject to annual review. Under the terms of the employment agreement, Ms. Hellums is also entitled to: (i) participate in all employee benefit plans and other fringe benefits plans generally available to similarly situated employees, subject to customary conditions and (ii) 5 weeks' paid holiday per annum.

Ms. Hellums is eligible to participate in our discretionary bonus plan. Ms. Hellums' maximum annual bonus entitlement is 40% of her annual base salary. If Ms. Hellums' employment is terminated by us (other than for "Cause," as defined in the employment agreement, disability or death) or by Ms. Hellums for "Good Reason" (as defined in the

employment agreement) and provided she is a Severance Good Leaver prior to the end of any bonus year, she is eligible to be paid: (i) subject to Ms. Hellums satisfying the Release Condition, any unpaid short-term bonus for any completed performance period and (ii) a pro rata bonus for the year in which the termination occurs based on the achievement of applicable performance goals.

In connection with Ms. Hellums' promotion to Chief Financial Officer, we granted her options representing the right to acquire 50,000 of our ADSs. The ADSs will vest in equal installments monthly over the next 48 months. The exercise price of the ADSs is $18.99.

Ms. Hellums' employment is "at will" and is terminable by either party on not less than 45 days' prior written notice (other than in the case of her death, disability or termination by us for Cause). If Ms. Hellums' employment is terminated and she is not a Severance Good Leaver, she will only be entitled to payments and benefits accrued at the termination date.

If Ms. Hellums is a Severance Good Leaver and subject to the Release Condition being met, in addition to payments and benefits accrued at the termination date, she is eligible to receive (i) continuation of her annual base salary for a period of 6 months, or the Hellums Separation Period, paid over the Hellums Separation Period in accordance with normal payroll practices and (ii) if elected by Ms. Hellums, continuation coverage under the Company's medical plan for no longer than the Hellums Separation Period, together with payment of the amount of COBRA premiums until the earliest of the expiration of the Severance Period, eligibility for healthcare coverage with a subsequent employer and ineligibility for COBRA benefits.

Any equity-based awards held by Ms. Hellums will be treated on her termination in accordance with the relevant plan rules and award documentation save that, if Ms. Hellums becomes a Severance Good Leaver, such termination shall be deemed to be for a "Good Leaver Reason" for the purposes of the applicable share plan.

In the event of a "Change of Control" (as defined in the employment agreement), any equity awards held by Ms. Hellums will vest and become exercisable in full. In addition, if Ms. Hellums becomes a Severance Good Leaver within 12 months after the occurrence of a "Change of Control," Ms. Hellums will be entitled to the severance benefits described above, save that the Separation Period shall be increased to 12 months and the amount due will be paid in a single sum payment.

If Ms. Hellums' employment is terminated by reason of her death or disability (in the circumstances described in the employment agreement), Ms. Hellums (or her estate) will be entitled to be receive: (i) payments and benefits accrued at the termination date; (ii) the annual bonus actually earned for the preceding bonus year to the extent unpaid on termination; and (iii) a pro-rata bonus in respect of the proportion of such year during which Ms. Hellums is employed by us. In addition, all vested equity awards will be treated in accordance with the relevant plan rules and award documentation as if Ms. Hellums was a "Good Leaver."

During the term of her employment, Ms. Hellums is restricted from accepting appointments with third parties save as agreed by us.

Compensation paid to Ms. Hellums is subject to repayment and/or claw-back obligations arising under applicable law or otherwise implemented under any Company clawback policy in effect from time to time.

The employment agreement contains customary provisions under Section 409A of the Code and standard assignment provisions relating to the ownership of intellectual property. Ms. Hellums is subject to confidentiality obligations which remain in place following termination of employment, and to non-solicitation, non-employment and non-inducement restrictive covenants for a period of 12 months post-termination of her employment.

Service Agreement of Giles Campion

Giles Campion, our executive director, Chief Medical Officer and Head of R&D, entered into an employment agreement with us on May 26, 2020 (with an effective date of June 1, 2020). This agreement also governs the terms of his appointment as a director. Dr. Campion's employment with us (under a prior agreement) commenced on June 1, 2019.

Pursuant to the terms of the employment agreement, Dr. Campion is entitled to an annual base salary, initially £306,000, which is subject to annual review. Under the terms of the employment agreement, Dr. Campion is also: (i) entitled to employer pension contributions at a rate of twice the contributions made by Dr. Campion, up to a maximum employer contribution of 10%, and no less than 5%, of Dr. Campion's annual base salary each year (or to receive an equivalent cash payment in lieu of such contributions if Dr. Campion opts out of our pension scheme provided Dr. Campion provides evidence that he already has pension savings at or in excess of the U.K. "Lifetime Allowance"); (ii) entitled to participate, at our expense, in our life and private medical insurance schemes; and (iii) entitled to 25 days' paid holiday per annum, plus holiday pay during the usual U.K. public holidays. Dr. Campion is eligible to participate in our discretionary bonus plan. Dr. Campion's maximum annual bonus entitlement is 50% of his annual base salary. If Dr. Campion's employment is terminated prior to the end of any bonus year, he is eligible to be paid a pro-rata bonus in respect of the proportion of such year worked by him.

Dr. Campion's employment is terminable by either party on not less than six months' prior written notice (increasing to twelve months' following a change of control of the Company). We may elect to terminate Dr. Campion's employment at any time by notifying him of such in writing and paying him his basic salary, benefits, bonus and holiday pay in lieu of the remaining period of notice. We may elect to make such payment in lieu of notice in equal monthly installments over the period of unworked notice and, if we so elect, Dr. Campion is obliged to seek alternative income during this period and to notify us of any payments, insurance or benefits so received. The remaining installments due to Dr. Campion will then be reduced by the amount of such net income. We may elect to put Dr. Campion on garden leave for all or part of any period of notice. We retained the right to terminate Dr. Campion with immediate effect without notice or payment in lieu of notice in certain limited circumstances as defined in the employment agreement.

The employment agreement contains standard assignment provisions relating to the ownership of intellectual property. Dr. Campion is subject to confidentiality obligations which remain in place following termination of employment, and to non-solicitation, non-deal and non-compete restrictive covenants for a period of 12 months post-termination of his employment (less any time spent by Dr. Campion on garden leave).

Service Agreement and Separation Agreement of Mark Rothera

Mark Rothera, our former President and Chief Executive Officer, entered into an employment agreement with us on September 11, 2020 pursuant to which his employment commenced on September 14, 2020 until he stepped down on February 21, 2022. This agreement also governed the terms of his appointment as a director during that period.

Pursuant to the terms of the employment agreement, Mr. Rothera was entitled to an annual base salary, initially $575,000, subject to annual review, and to: (i) a cash payment in lieu of pension contributions equal to 6% of Mr. Rothera's annual base salary from time to time; (ii) participate in all employee benefit plans and other fringe benefits plans generally available to similarly situated employees, subject to customary conditions; (iii) 5 weeks' paid holiday per annum; (iv) payment for the preparation and submission of Mr. Rothera's annual tax returns in the United Kingdom and the United States, including returns for the year in which his employment terminates; (v) payment of reasonable attorney's fees for the review of his employment agreement and all related documents up to a maximum of $10,000; and (vi) payment of a relocation allowance of up to $50,000 for expenses incurred in the first 12 months of the employment, and reimbursement of the cost of renting an apartment in New Jersey for a total of six months up until December 31, 2021 up to a maximum of $9,000 per month, on a tax grossed-up basis.

In connection with Mr. Rothera's departure, we entered into a separation agreement, or the Separation Agreement, governing the terms of his departure. Pursuant to the Separation Agreement, Mr. Rothera is entitled to: (i) a cash payment of $604,095 (less applicable taxes and withholdings), payable in equal installments according to our normal payroll practices; (ii) a pro-rated bonus for our 2022 fiscal year to be determined based on our financial performance

at the end of the year; (iii) if elected by Mr. Rothera, continuation coverage under the Company's medical plan for no longer than the Separation Period, together with an additional monthly payment equal to the excess of the premium charged for such continuation coverage over the amount charged to active employees for the same coverage; (iv) payment for the preparation of annual tax returns for 2021 and 2022, provided that we will not be required to pay more than $20,000 in the aggregate.

Under the Separation Agreement, Mr. Rothera's equity awards continued to vest until August 17, 2022 and vested options were exercisable until February 18, 2023, as provided for in the applicable share plan.

The employment agreement contained customary 409A provisions and standard assignment provisions relating to the ownership of intellectual property. Mr. Rothera is subject to confidentiality obligations which remain in place following termination of employment, and to non-solicitation, non-employment, non-inducement and non-compete restrictive covenants which were effective for a period of 12 months post-termination of his employment. The Separation Agreement also contains a general release of all claims Mr. Rothera may have brought against us, except for Mr. Rothera's right to enforce the terms of the Separation Agreement or bring a charge before the U.S. Equal Employment Opportunity Commission.

Remuneration paid to Mr. Rothera during the year ended December 31, 2022, included: £554 thousand in salary inclusive of severance payments, paid in installments from date his separation date for an additional 12 months in line with his severance agreement; a bonus payment of £228 thousand; option awards of £3,254 thousand in aggregate grant date fair value in 2022 measured using the Black Scholes model; and £63 thousand in other benefits.

Equity Incentive Plans

2018 Employee Long-Term Incentive Plan

On February 2, 2018, we adopted our 2018 Employee Long Term Incentive Plan, or the Employee LTIP. The Employee LTIP was subsequently amended on October 6, 2019 and on June 22, 2020 when the sub-plan for U.S. employees, or the Employee U.S. Sub-Plan, was adopted and the board of directors approved the restatement of the Employee LTIP to provide a new share reserve (subject to shareholder approval, which was obtained on July 23, 2020).

Eligibility and Administration

Our employees and the employees of our subsidiaries from time to time may be granted awards under the Employee LTIP at the discretion of the board of directors. No awards may be granted after the tenth anniversary of the adoption of the Employee LTIP.

The Employee LTIP is administered by our board of directors, which may delegate its duties and responsibilities to one or more committees of our directors and/or officers (together, referred to in this summary as the board of directors).

Limits

Pursuant to the terms of the Employee LTIP, as restated and approved by our shareholders on July 23, 2020, we are permitted to grant awards over 8,700,000 of our ordinary shares, which reserve shall automatically increase on January 1st of each year, until 2028, in an amount up to 5% of the total number of our outstanding ordinary shares on December 31st of the preceding calendar year. This cap covers awards granted under the Employee LTIP, the Employee U.S. Sub-Plan, the Non-Employee LTIP and the Non-Employee U.S. Sub-Plan (each as defined below), but excludes awards already satisfied by the issuance of shares prior to the date on which our shareholders approve such reserve. If an award expires, lapses or is terminated, exchanged for cash, surrendered, repurchased or cancelled without having been fully exercised, the unused shares in respect of such award return to the reserve.

As of December 31, 2022, awards of 11,571,487 which represents 3,857,162 ADSs at a 3:1 ratio were outstanding under the Employee LTIP (all granted in the form of options).

Awards under the Employee LTIP may generally not be granted to an individual on or after October 1, 2019 if, when taken with any other awards granted to that individual on or after that date, the market value of such awards normally vesting in a 12-month period would exceed 250% of that individual's annual base salary. If the board of directors determines that exceptional circumstances exist, awards in excess of this limit may be granted, subject to a higher limit of 300% of that individual's annual remuneration.

Awards

Awards under the Employee LTIP may be in the form of a conditional right to acquire ADS/shares, or a Conditional Share Award, an option (including a CSOP option, as described below) to acquire shares with an exercise price which will not normally be less than £0.05 (being the nominal value of a share), unless arrangements are in place for such nominal value to be paid up as at the date of issue of the relevant shares, or a right to acquire shares subject to forfeiture in certain circumstances, or Restricted Shares.

Awards in the form of CSOP options may be granted to our U.K. employees who meet the criteria under the Company Share Option Plan, or CSOP, regime. Employees who have a material interest in our company cannot be granted CSOP options. A material interest is either beneficial ownership of, or the ability to control directly or indirectly, more than 30% of our ordinary share capital. CSOP options can only be granted for so long as we continue to meet the criteria under the CSOP regime.

Awards granted as CSOP options are subject to the limits in respect of such awards under the CSOP regime.

Terms Generally Applicable to Awards

No payment is required to be made by the employee when an award is granted.

An award price, payable prior to vesting or exercise (as applicable) or an award may be specified. If such award price is lower than the nominal value of a share, there must be arrangements in place for such nominal value to be paid up as at the date of issue of the relevant shares. Awards granted in the form of CSOP options must be granted with a market value exercise price.

Awards may be granted subject to objective performance conditions or other conditions set on or before the date the award is granted. Any such conditions may be substituted, varied or waived if an event occurs such that we consider such conditions to no longer be appropriate. Such substitution, variation or waiver must be implemented in such a manner as is reasonable in the circumstances and, in the case of a substitution or variation, which produces a fairer measure of performance and is not materially less difficult to satisfy than if the event had not occurred. Awards have typically been granted in the form of options vesting according to performance conditions measured over at least three years.

Awards may be granted subject to a post-vesting holding period during which the shares acquired on vesting of such award may not be transferred, assigned or otherwise disposed of other than to fund participation in a rights issue or to cover any applicable withholding taxes. The award holder may be required to take certain steps, including depositing the shares with a third party, to aid the enforcement of any such holding period.

Awards are not capable of transfer other than on death to the employee's personal representative.

The number of shares subject to awards, the description thereof and/or any award price may be adjusted in the event of a variation in the share capital of the company. Any adjustment to awards granted in the form of CSOP options must be made in accordance with the CSOP regime.

Awards other than CSOP options may be granted on terms that include a right to receive an additional amount of shares or cash on or following vesting of the award equal in value to the dividends which would have been paid had the award holder held an equivalent number of shares to those vesting during the period from the date of grant to the date of vesting.

Awards other than CSOP options may, in the discretion of the board of directors, be settled in cash, or 'net' settled.

Awards in the form of options granted to U.S. taxpayers with an exercise price of less than 100% of the fair market value of a share on the date of grant, determined in accordance with Section 409A of the Code must, if required for compliance with such Section, be exercised within 2.5 calendar months after the end of the relevant U.S. tax year (or, if later, the tax year of the entity engaging the U.S. taxpayer) in which the option first becomes exercisable.

Leavers

Leaver provisions apply to awards depending on whether the award is granted before October 1, 2019, or an Old Award, or on or after October 1, 2019 or a New Award.

Old Awards generally continue to vest and may only be exercised while the award holder remains employed by us or one of our subsidiaries, and such awards generally lapse on cessation of such employment.

Where the holder of the Old Award is a Good Leaver (as defined below), awards generally continue to vest until the normal vesting date, to the extent any applicable performance conditions were met at the date of grant. The board of directors may determine that the Old Award will instead vest immediately to an extent determined by the board of directors taking into account such factors as it considers relevant. Any vested portion of the Old Award may be exercised within a period of 90 days following the later of the date of termination or the vesting date, or such other period as the board of directors may determine, and shall lapse thereafter.

"Good Leaver" is defined to include cessation of employment by reason of injury, ill health, disability, the employing company or undertaking in which the award holder works being sold out of our group or cessation of employment in any other circumstances if the board of directors so decides (other than summary dismissal).

Where the holder of an Old Award dies, a proportion of each Old Award will vest immediately, such proportion to be determined by the board. Alternatively, the board may decide that the Old Award will continue to vest according to the prescribed vesting schedule. The Old Awards may be exercised by the deceased employee's representative for 12 months following the death. In the case where a holder of an Old Award ceases to be an employee by reason of injury, illness, disability or transfer outside of the company, a proportion of each Old Award will vest immediately, such proportion to be determined by the board. Alternatively, the board may decide that the Old Award will continue to vest according to the prescribed vesting schedule. The holder may exercise the Old Award during the period ending 90 days following the cessation of employment.

New Awards generally continue to vest while the award holder remains employed by us or one of our subsidiaries. Where the New Award holder is a Good Leaver (as defined above), dies or is terminated by his or her employer for a reason other than other than summary dismissal or termination for "cause" (as defined in his or her employment agreement), New Awards may be exercised for a period of twelve months following such termination (or such shorter period not less than 90 days as the board of directors may specify) and shall lapse thereafter. In all other circumstances, New Awards lapse on cessation of employment.

If the holder of a CSOP option dies, his or her option must be exercised within 12 months thereafter, and lapses to the extent not so exercised.

The board of directors may also take steps to preserve the interests of an award holder who relocates to a new country.

Corporate Transactions

The board of directors may in its discretion determine that all or a proportion of unvested awards will vest in connection with a change of control (as defined in section 995 of the U.K. Income tax Act 2007) of the Company. An option that is already vested or which vests in these circumstances may be exercised within one month of the change of control or such longer period as determined by the board of directors and shall lapse at the end of such period. Vesting of awards may similarly be accelerated in the discretion of the board of directors in connection with (i) a person becoming entitled or bound to acquire shares in the Company under sections 979 to 982 of the Companies Act; (ii) a person obtaining control of the Company in pursuance of a compromise or arrangement sanctioned by the court under section 899 of the Companies Act; (iii) notice being given for the voluntary winding-up of the Company; or (iv) a demerger, distribution (which is not an ordinary dividend) or other transaction in respect of the Company. The board of directors may also determine that awards will vest in advance of the occurrence of the aforementioned corporate events.

Notwithstanding the above, the board of directors may determine that awards shall instead be exchanged for equivalent awards over shares in an acquiring company in connection with certain corporate events (and the vesting of such awards shall not be accelerated).

The treatment of awards granted in the form of CSOP options is subject to certain additional restrictions under the CSOP regime.

Clawback

Awards granted to applicable employees, including the Executive Officers, may be subject to clawback in the period of two years after vesting (or such longer period as may be specified by the board of directors and notified to the applicable employee). Clawback may be applied in certain circumstances including where there has been a material misstatement of our financial results, an error in assessing the performance conditions to which an award is subject or the determination of the number of shares subject to an award, a breach of confidentiality obligations, or certain acts of negligence, fraud or serious misconduct.

All awards are subject to adjustment (including a reduction in the number of shares under award to nil) prior to vesting in the same circumstances as in which clawback may be applied.

Amendment

The board of directors has the power to amend the Employee LTIP, including to adopt sub-plans for the benefit of employees located outside the United Kingdom. An amendment may not materially adversely affect the rights of existing award holders except to take account of legal or regulatory requirements or where all award holders affected by the amendment have been notified thereof and the majority of them have consented to it.

Employee U.S. Sub–Plan

On June 22, 2020, the board of directors adopted the Employee U.S. Sub-Plan under the Employee LTIP. Our shareholders approved the Employee U.S. Sub-Plan on July 23, 2020. The Employee U.S. Sub-Plan permits the grant of awards to eligible participants under the Employee LTIP who are U.S. residents and U.S. taxpayers, including potentially tax efficient incentive stock options. Unless options granted under the Employee U.S. Sub-Plan are structured to be compliant with Section 409A of the Code, the exercise price of options granted under the Employee U.S. Sub- Plan shall not be less than 100% of the fair market value of a share on the date of grant, determined in accordance with Section 409A of the Code. Conditional share awards granted under the Employee U.S. Sub-Plan are termed Restricted Stock Units, or RSUs. The maximum number of shares that may be issued under the Employee U.S. Sub-Plan upon the exercise of incentive stock options is 26,100,000.

2018 Non-Employee Long-Term Incentive Plan

On February 2, 2018, we adopted our 2018 Non-Employee Long Term Incentive Plan, or the Non-Employee LTIP. The Non-Employee LTIP was subsequently amended on October 6, 2019 and on June 22, 2020 when the sub-plan for United States non-employees, or the Non-Employee U.S. Sub-Plan, was adopted and the board of directors approved the restatement of the Non-Employee LTIP to provide a new share reserve (subject to shareholder approval, which was obtained on July 23, 2020).

The terms of the Non-Employee LTIP are similar to those of the Employee LTIP described above, except that only individuals, partnerships or companies who providing services to us or a subsidiary under a contract for the provision of services (including our non-executive directors) may participate. Awards have typically been granted to our non-executive directors as options to purchase our ordinary shares which vest subject to certain performance conditions being met.

As of December 31, 2022, awards over 839,997 shares were outstanding under the Non-Employee LTIP (all granted in the form of options).

Non-Employee U.S. Sub –Plan

In June 2020, the board of directors adopted the Non-Employee U.S. Sub-Plan under the Non-Employee LTIP. Our shareholders approved the Non-Employee U.S. Sub-Plan on July 23, 2020. The Non-Employee U.S. Sub-Plan permits the grant of awards to eligible participants under the Non-Employee LTIP who are U.S. residents and U.S. taxpayers. Unless options granted under the Employee U.S. Sub-Plan are structured to be compliant with Section 409A of the Code, the exercise price of options granted under the Non-Employee U.S. Sub- Plan shall not be less than 100% of the fair market value of a share on the date of grant, determined in accordance with Section 409A of the Code. Conditional share awards granted under the Non-Employee U.S. Sub-Plan are termed Restricted Stock Units, or RSUs.

2022 Grants

The following table summarizes the options that we granted to our directors and executive officers under the 2018 Long Term Incentive Plan in 2022:

Name	Ordinary Shares/Underlying Options	Exercise price per share	Exercise price per ADS	Grant Date	Expiration Date	Number of underlying shares	Number of underlying ADSs
Craig Tooman	Underlying Options	£ 6.51	$ 23.60	6-Jan-22	6-Jan-32	264,999	88,333
Craig Tooman	Underlying Options	£ 5.24	$ 18.99	21-Feb-22	21-Feb-32	375,000	125,000
Craig Tooman	Underlying Options	£ 3.20	$ 11.59	16-Sep-22	16-Sep-32	900,000	300,000
Rhonda Hellums	Underlying Options	£ 6.51	$ 23.60	6-Jan-22	6-Jan-32	55,998	18,666
Rhonda Hellums	Underlying Options	£ 5.24	$ 18.99	21-Feb-22	21-Feb-32	150,000	50,000
Rhonda Hellums	Underlying Options	£ 3.20	$ 11.59	16-Sep-22	16-Sep-32	375,000	125,000
Giles Campion M.D.	Underlying Options	£ 6.51	$ 23.60	6-Jan-22	6-Jan-32	199,998	66,666
Mark Rothera	Underlying Options	£ 6.51	$ 23.60	6-Jan-22	6-Jan-32	639,999	213,333
Iain Ross	Underlying Options	£ 6.51	$ 23.60	6-Jan-22	6-Jan-32	90,000	30,000
Alistair Gray	Underlying Options	£ 6.51	$ 23.60	6-Jan-22	6-Jan-32	48,000	16,000
Dave Lemus	Underlying Options	£ 6.51	$ 23.60	6-Jan-22	6-Jan-32	48,000	16,000
James Ede-Golightly	Underlying Options	£ 6.51	$ 23.60	6-Jan-22	6-Jan-32	48,000	16,000
Stephen Romano M.D.	Underlying Options	£ 6.51	$ 23.60	6-Jan-22	6-Jan-32	48,000	16,000
Michael Davidson M.D.	Underlying Options	£ 6.51	$ 23.60	6-Jan-22	6-Jan-32	48,000	16,000

Non-Executive Directors Remuneration

The following table sets forth the remuneration paid to our non-executive directors for service on our board of directors during the year ended December 31, 2022. The remuneration paid to our executive directors, Mr. Tooman (and Mr. Rothera until February 2022) and Dr. Campion, during the year ended December 31, 2022 is described in the section titled "*Executive Officer Remuneration.*"

	Base salary	Taxable benefits	Pension	Option Awards (1)	Total fixed remuneration
	£'000s	£'000s	£'000s	£'000s	£'000s
Non-Executive Directors:					
Iain Ross	90	-	-	458	548
Alistair Gray	54	-	-	244	298
Dave Lemus	46	-	-	244	290
James Ede-Golightly	44	-	-	244	288
Stephen Romano M.D.	37	-	-	244	281
Michael Davidson M.D.	40	-	-	244	284

(1) Amount shown represents the aggregate grant date fair value of option awards granted in 2022 measured using the Black Scholes model. For a description of the assumptions used in valuing these awards, see note 24 to our consolidated financial statements included elsewhere in this Annual Report.

Non-Executive Director Letters of Appointment

We have entered into letters of appointment with each of our non-executive directors. The appointment of our non-executive directors can be terminated by either us or the director upon three calendar months' written notice, or by us in our absolute discretion at any time with immediate effect on payment of money in lieu of notice.

Under the non-executive director appointment letters, we may also terminate each appointment with immediate effect if the non-executive director: (1) commits a material breach of his obligations under the letter of appointment; (2) commits a serious or repeated breach or non-observance of his obligations to us; (3) has been guilty of any fraud or dishonesty or acts in any manner which, in our opinion, brings or is likely to bring us into disrepute or is materially adverse to our interests; (4) is incompetent or guilty of gross misconduct and/or any serious or persistent negligence or misconduct in respect of his obligations under the letter of appointment; (5) failed or refused after a written warning to carry out the duties reasonably and properly required under the letter of appointment; (6) is convicted of an arrestable criminal offense other than a road traffic offense for which a fine or non-custodial penalty is imposed; (7) is declared bankrupt or makes an arrangement with or for the benefit of his creditors, or suffers comparable proceedings in another jurisdiction; (8) is disqualified from acting as a director in any jurisdiction; (9) accepts a position with another company, without our prior agreement, which in the reasonable opinion of the Board may give rise to a conflict of interest between his position as a director of our company and his interest in such other company; or (10) commits any offense under the U.K. Bribery Act 2010.

C. Board Practices

Composition of our Board of Directors

Our board of directors is currently composed of eight members. In 2022, our board consisted of two executive directors, consisting of Mr. Tooman (Mr. Rothera until February 2022) and Dr. Campion, and six non-executive directors. As a foreign private issuer, under the listing requirements and rules of Nasdaq, we are not required to have independent directors on our board of directors, except that our audit committee is required to consist fully of independent directors, subject to certain phase-in schedules. Our board of directors has determined that none of our directors, other than our executive directors, and Mr. Ross, who, having served as our Executive Chairman until September 14, 2020, was employed by us within the last three years, has a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of director and that each of these five directors is "independent" as that term is defined under Nasdaq rules. There are no family relationships among any of our executive officers or directors.

In accordance with our articles of association, any director who served as a director at each of the preceding two annual general meetings of shareholders and who was not appointed or re-appointed by the shareholders at a general meeting at, or since, either such meeting shall retire from office at the next annual general meeting of shareholders. Retiring directors are eligible for re-election. See "Description of Share Capital and Articles of Association—Articles

of Association— Directors" filed as Exhibit 2.3 to this report. Our executive directors are employed as officers on an "at will" basis and they will continue to serve unless terminated or unless they quit.

Committees of our Board of Directors

Our board of directors has four standing committees: an audit and risk committee, a remuneration committee, a nominations committee, and a science and technology committee.

Audit and Risk Committee of the Board

Our audit and risk committee, which consists of Messrs. Ede-Golightly, Gray, and Lemus and Dr. Davidson, assists the board of directors in overseeing our accounting and financial reporting processes and the audits of our financial statements. Mr. Lemus serves as chairman of the audit and risk committee. The audit and risk committee consists exclusively of members of our board who are financially literate, and Mr. Lemus is considered an "audit committee financial expert" as defined by applicable SEC rules and has the requisite financial sophistication as defined under applicable Nasdaq rules. 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 and the Nasdaq corporate governance rules. The audit and risk committee is governed by a charter that complies with the rules of Nasdaq.

The audit and risk committee's responsibilities include:

- monitoring the integrity of our financial and narrative reporting, preliminary announcements and any other formal announcements relating to our financial performance;
- reviewing the appropriateness and completeness of our internal controls;
- considering annually whether we should have an internal audit function;
- overseeing our relationship with the external auditors and assessing the effectiveness of the external audit process, including in relation to appointment and tendering, remuneration and other terms of engagement, appropriate planning ahead of each annual audit cycle, the independence of external auditors, and approving any non-audit services to be provided by the external auditors;
- maintaining regular, timely, open and honest communication with the external auditors, ensuring the external auditors report to the committee on all relevant matters to enable the committee to carry out its oversight responsibilities;
- monitoring risk;
- reviewing accounting policies and key estimates and judgments; and
- establishing procedures for compliance, whistleblowing and fraud.

Remuneration Committee of the Board

Our remuneration committee, which consists of Messrs. Ede-Golightly, Lemus and Dr. Romano and Dr. Davidson, assists the board of directors in determining executive director and officer compensation. Mr. Ede-Golightly serves as chairman of the remuneration committee.

The remuneration committee's responsibilities include:

- setting a remuneration policy that is designed to promote our long-term success and reviewing the on-going appropriateness of such policy;

- ensuring that the remuneration of executive directors and other senior executives reflects both their individual performance and their contribution to our overall results;
- determining the terms of employment and remuneration of executive directors and other senior executives, including recruitment and retention terms;
- approving the design and performance targets of any annual incentive schemes that include the executive directors and other senior executives;
- agreeing upon the design and performance targets, where applicable, of all share incentive plans requiring shareholder approval;
- rigorously assessing the appropriateness and subsequent achievement of the performance targets related to any share incentive plans;
- recommending to our board of directors the fees to be paid to our Chair, who is excluded from this process;
- gathering and analyzing appropriate data from comparator companies in the biotechnology sector; and
- the selection and appointment of external advisers to the remuneration committee, if any, to provide independent remuneration advice where necessary.

Nominations Committee of the Board

Our nominations committee, which consists of Messrs. Ross, and Gray and Dr. Romano, assists our board of directors in identifying individuals qualified to become members of our board and executive officers consistent with criteria established by our board in developing our corporate governance principles. Mr. Ross serves as chairman of the nominations committee.

The nominations committee's responsibilities include:

- regularly reviewing the structure, size and composition (including the skills, knowledge, experience and diversity) required of our board of directors compared to its current position and making recommendations to the board of directors with regard to any changes;
- determining the qualities and experience required of our executive and non-executive directors and identifying suitable candidates, assisted where appropriate by recruitment consultants;
- formulating plans for succession for both executive and non-executive directors, and in particular for the key roles of Chair and Chief Executive Officer;
- assessing the re-appointment of any non-executive director at the conclusion of his or her specified term of office, having given due regard to the director's performance and ability to continue to contribute to our board of directors in the light of the knowledge, skills and experience required; and
- assessing the re-election by shareholders of any director, having due regard to his or her performance and ability to continue to contribute to our board of directors in the light of the knowledge, skills and experience required and the need for progressive refreshing of the board of directors.

Science and Technology Committee of the Board

Our science and technology committee, which consists of Drs. Campion, Davidson and Romano, assists our board of directors in overseeing our scientific and research strategy. Dr. Romano serves as chairman of the science and technology committee. Our board of directors is responsible for appointing the members of the science and technology

committee and each member can be appointed for a term of up to three years and such term may be extended by no more than two additional three-year periods.

The science and technology committee's responsibilities include:

- reviewing, evaluating and providing strategic advice to the board of directors on the quality, direction and competitiveness of our research and development programs;
- reviewing, evaluating and providing strategic advice to the board of directors on our research and development strategy and plans, and the means for and progress in achieving its goals and objectives;
- at the request of the board of directors, performing a scientific and technical review of internal and external investments, including business development projects, potential acquisitions, and purchase of new technologies;
- conducting regular reviews of the pipeline; and
- monitoring, identifying and discussing significant emerging science and technology issues and trends, including their impact on any research and development programs, plans, or policies.

D. Employees

As of December 31, 2022, we had 122 employees. Of these employees, 93 employees are engaged in research and development activities and 29 employees are engaged in general and administrative activities. We have no collective bargaining agreements with our employees and we have not experienced any work stoppages.

E. Share Ownership

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

ITEM 7: MAJOR SHAREHOLDERS AND RELATED PARTY TRANSACTIONS

A. MAJOR SHAREHOLDERS

The following table sets forth information with respect to the beneficial ownership of our ordinary shares as of March 1, 2023 by:

- each person, or group of affiliated persons, that beneficially owns 5% or more of our outstanding ordinary shares;
- each of our directors and executive officers; and
- all of our directors and executive officers as a group.

Beneficial ownership is determined in accordance with the rules of the SEC. These rules generally attribute beneficial ownership of securities to persons who possess sole or shared voting power or investment power with respect to those securities and include ordinary shares that can be acquired within 60 days of March 1, 2023. Percentage ownership calculations are based on 107,864,673 ordinary shares issued and outstanding as of March 1, 2023, plus, consistent with SEC rules on disclosure of beneficial ownership, ordinary shares that each security holder has the ability to acquire within 60 days of March 1, 2023.

Except as otherwise indicated, all persons listed below have sole voting and investment power with respect to the ordinary shares beneficially owned by them, subject to applicable community property laws. The information is not

necessarily indicative of beneficial ownership for any other purpose. None of our shareholders have different voting rights from other shareholders. We are not aware of any arrangement that may, at a subsequent date, result in a change of control of our company.

Except as otherwise indicated in the table below, addresses of the directors, executive officers and named beneficial owners are care of Silence Therapeutics plc, 72 Hammersmith Road, London W14 8TH, United Kingdom.

Name of Beneficial Owner	Number of Ordinary Shares Beneficially Owned	Percentage Beneficially Owned
5% or Greater Shareholders:		
Richard Griffiths	27,373,392	25.4%
Compagnie Odier SCA [1]	21,281,802	19.7%
Robert Keith	12,291,528	11.4%
TCG Crossover Management, LLC	6,314,625	5.9%
Deep Track Capital LP	5,854,740	5.4%
Executive Officers and Directors:		
Craig Tooman [2]	786,678	0.7%
Rhonda Hellums [3]	181,497	0.2%
Giles Campion, M.D. [4]	1,082,541	1.0%
Mark Rothera [5]	-	*
Iain Ross [6]	1,080,768	1.0%
James Ede-Golightly [7]	33,903	*
Alistair Gray [8]	31,527	*
Dave Lemus [9]	31,527	*
Steven Romano, M.D. [10]	36,993	*
Michael Davidson, M.D. [11]	36,993	*
All current directors and executive officers as a group (10 persons)	3,302,427	3.1%

*Represents beneficial ownership of less than one percent

(1) Lombard Odier Asset Management (USA) Corp. is the investment adviser to this holder, and as such it and its portfolio managers Adam McConkey and Robert Giles have the power to vote or dispose of the ordinary shares held of record by this holder and may be deemed to beneficially own those securities. Each of Mr. McConkey and Mr. Giles disclaims beneficial ownership of such securities, except to the extent of his pecuniary interest therein. The address of Lombard Odier Asset Management (USA) Corp. is 452 Fifth Avenue, 25th Floor, New York, NY 10018.
(2) Consists of 31,986 ordinary shares held and 574,281 ordinary shares issuable upon the exercise of share options that will be vested and exercisable within 60 days of March 1, 2023.
(3) Consists of 1,500 ordinary shares held and 179,997 ordinary shares issuable upon the exercise of share options that will be vested and exercisable within 60 days of March 1, 2023.
(4) Consists of 23,943 ordinary shares held and 1,032,864 ordinary shares issuable upon the exercise of share options that will be vested and exercisable within 60 days of March 1, 2023.
(5) Consists of no ordinary shares held and no ordinary shares issuable upon the exercise of share options that will be vested and exercisable within 60 days of March 1, 2023.
(6) Consists of 64,941 ordinary shares held and 1,005,825 ordinary shares issuable upon the exercise of share options that will be vested and exercisable within 60 days of March 1, 2023.
(7) Consists of 9,903 ordinary shares held and 18,666 ordinary shares issuable upon the exercise of share options that will be vested and exercisable within 60 days of March 1, 2023.
(8) Consists of 9,903 ordinary shares held and 18,666 ordinary shares issuable upon the exercise of share options that will be vested and exercisable within 60 days of March 1, 2023.
(9) Consists of 7,527 ordinary shares held and 18,666 ordinary shares issuable upon the exercise of share options that will be vested and exercisable within 60 days of March 1, 2023.
(10) Consists of 12,993 ordinary shares held and 18,666 ordinary shares issuable upon the exercise of share options that will be vested and exercisable within 60 days of March 1, 2023.
(11) Consists of 12,993 ordinary shares held and 18,666 ordinary shares issuable upon the exercise of share options that will be vested and exercisable within 60 days of March 1, 2023.

We estimate that as of March 1, 2023, approximately 41% of our outstanding ordinary shares are held by 30 U.S. record holders.

B. Related Party Transactions.

Since January 1, 2022, we have engaged in the following transactions with our directors, executive officers or holders of more than 10% of our outstanding share capital and their affiliates, which we refer to as our related parties.

During the year ended December 31, 2022, we paid £60 thousand (2021: £nil) to Gladstone Consultancy Partnership, a company controlled by Director Iain Ross, for consulting and advisory services. The amounts payable were settled before the relevant period ends.

C. Interests of Experts and Counsel

Not applicable.

ITEM 8: FINANCIAL INFORMATION

A. Consolidated Statements and Other Financial Information.

Consolidated Financial Statements

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

Legal Proceedings

From time to time, we may become involved in litigation or other legal proceedings relating to claims arising from the ordinary course of business. We are currently not party to any legal proceedings that are likely to have a material adverse effect on our results of operations, financial condition or cash flows.

Dividend Distribution Policy

We have never declared or paid any dividends on any class of our issued share capital. We intend to retain any earnings for use in our business and do not currently intend to pay dividends on our ordinary shares. The declaration and payment of any future dividends will be at the discretion of our board of directors and will depend upon our results of operations, cash requirements, financial condition, contractual restrictions, any future debt agreements or applicable laws and other factors that our board of directors may deem relevant.

Under the laws of England and Wales, among other things, we may only pay dividends if we have sufficient distributable reserves (on a non-consolidated basis), which are our accumulated realized profits that have not been previously distributed or capitalized less our accumulated realized losses, so far as such losses have not been previously written off in a reduction or reorganization of capital. See “Description of Share Capital and Articles of Association” filed as Exhibit 2.3 to this report for additional information.

B. Significant Changes.

None.

ITEM 9: THE OFFER AND THE LISTING

A. Offer and Listing Details.

Our ADSs are listed on the Nasdaq Global Market under the symbol “SLN”.

B. Plan of Distribution.

Not applicable.

C. Markets.

Our ADSs are listed on The Nasdaq Global Market under the symbol “SLN”.

D. Selling Shareholders.

Not applicable.

E. Dilution.

Not applicable.

F. Expenses of the Issue.

Not applicable.

ITEM 10: ADDITIONAL INFORMATION

A. Share Capital.

Not applicable.

B. Memorandum and Articles of Association.

A copy of our Articles of Association is attached as Exhibit 1.1 to this Annual Report. The information called for by this Item is set forth in Exhibit 2.3 to this Annual Report and is incorporated by reference into this Annual Report.

C. Material Contracts.

Mallinckrodt License and Collaboration Agreement

In July 2019, we announced a strategic collaboration with Mallinckrodt to develop and commercialize RNAi drug targets designed to silence the complement cascade in complement-mediated disorders. Under the agreement, we granted Mallinckrodt an exclusive worldwide license to our C3 targeting program, SLN501, with options to license additional complement-mediated disease targets from us, with Mallinckrodt exercising two such targets in July 2020. We are responsible for preclinical activities, and for conducting the development program for each product until the end of phase 1 clinical trials, after which Mallinckrodt will assume clinical development and responsibility for global commercialization. In connection with the execution of the agreement, Mallinckrodt made an upfront cash payment to us of $20 million and purchased $5 million of our ordinary shares. We are eligible to receive up to $10 million in research milestone payments for each program, in addition to funding for phase 1 clinical development including GMP manufacturing. We will fund all other preclinical activities. We received a research milestone payment of $2 million in October 2019 upon the initiation of work under our work plan for a particular C3 target. In September 2020, we received another $2 million research milestone payment following the initiation of work on a second complement target. In March 2021, we initiated work on the third complement target which triggered another $2 million research milestone payment. In April 2021, we received another $2.0 million research milestone for the initiation of the toxicology study for the first identified target. The collaboration provides for potential additional development and regulatory milestone payments in aggregate of up to $100 million for the initial C3 target and up to $140 million for each of the two optioned complement-mediated disease targets, with such milestones relating to the initiation of specified clinical trials in specified jurisdictions, and upon the receipt of regulatory approvals by specified authorities, in each case for multiple indications. We are also eligible to receive potential commercial milestone payments of up to $562.5 million upon the achievement of specified levels of annual net sales of licensed products for each program. We are also eligible to receive tiered, low double-digit to high-teen percentage royalties on net sales for licensed products for each program.

The agreement will terminate on the last to expire royalty term, which is determined on a licensed product-by-licensed product and country-by-country basis, and is the later of (1) 10 years from the first commercial sale of the licensed product in the country, (2) the last to expire valid claim within the licensed patent in the country or (3) expiration of regulatory exclusivity granted by the prevailing governmental authority for the licensed product in the country. Mallinckrodt has the right to terminate the agreement in its entirety or on a target-by-target basis, for any reason upon specified prior written notice to us. We may terminate the agreement in the event that Mallinckrodt begins a legal or administrative proceeding challenging the validity, ownership or enforceability of our patents. Either party may terminate the agreement upon a material breach by the other party that is not cured within a specified period after receiving written notice, or upon giving written notice following the other party's bankruptcy, insolvency or similar instance. If Mallinckrodt terminates the agreement with respect to a target after we have commenced a phase 1 trial of a product candidate directed to that target, then we would have the right to either complete or wind down the phase 1 trial, and Mallinckrodt would be responsible for our costs incurred through the date of termination.

AstraZeneca Research Collaboration, Option and License Agreement

We have also out-licensed the rights to some of our intellectual property associated with our siRNA stabilization chemistry technology to AstraZeneca in the context of a Research Collaboration, Option and License Agreement dated March 24, 2020, under which we and AstraZeneca will collaborate to discover, develop and commercialize siRNA therapeutics for the treatment of cardiovascular, renal, metabolic and respiratory diseases.

AstraZeneca agreed to make an upfront cash payment of $60 million, of which $20 million was paid in May 2020 and the remaining $40 million was paid in May 2021. AstraZeneca also made an equity investment of $20 million in us in March 2020. We anticipate initiating work on up to five targets in the early stages of the collaboration, with AstraZeneca having the option to extend the collaboration to a further five targets. AstraZeneca has agreed to pay us $10 million for each selected target at the point of candidate nomination.

Under the collaboration, we are responsible for designing siRNA molecules against gene targets selected by AstraZeneca, and for manufacturing of material to support GLP toxicology studies and phase 1 clinical trials. We and AstraZeneca will collaborate during the discovery phase, and AstraZeneca will lead clinical development and commercialization of molecules arising from the collaboration. We will have the option to negotiate for co-development of two programs beginning with phase 2 clinical trials.

For each target selected under the collaboration, we will be eligible to receive up to $140 million in milestone payments upon the achievement of milestones relating to initiation of specified clinical trials, the acceptance of specified regulatory filings and the first commercial sale in specified jurisdictions. For each target selected, we are also eligible to receive up to $250 million in sales-based milestone payments upon the achievement of specified annual net sales levels, as well as tiered royalties as a percentage of net sales ranging from the high single digits to the low double digits.

The agreement with AstraZeneca will expire on the last to expire royalty term, which is determined on a licensed product-by-licensed product and country-by-country basis, and is the later of (1) 10 years from the first commercial sale of the licensed product in the country, (2) the last to expire valid claim within the patent covering the composition of matter of the licensed compound contained in the licensed product in the country or (3) expiration of regulatory exclusivity granted by the prevailing governmental authority for the licensed product in the country. AstraZeneca has the right to terminate the agreement in its entirety or on a target-by-target basis, for any reason upon specified prior written notice to us. We may terminate the agreement on a target-by-target basis in the event that AstraZeneca begins a legal or administrative proceeding challenging the patentability, validity, ownership or enforceability of our patents. Either party may terminate the agreement on a target-by-target basis upon a material breach by the other party that is not cured within a specified period after receiving written notice, or in its entirety upon giving written notice following the other party's bankruptcy, insolvency or similar instance.

Hansoh Research Collaboration, Option and License Agreement

On October 15, 2021, we entered into a collaboration agreement with Hansoh, one of the leading biopharmaceutical companies in China, to develop siRNAs for three undisclosed targets leveraging Silence's proprietary mRNAi GOLD™ platform.

Under the terms of the agreement, Hansoh has the exclusive option to license exclusive rights to the first two targets in Greater China, Hong Kong, Macau and Taiwan following the completion of phase 1 trials. We will retain exclusive rights for those two targets in all other territories. We are responsible for all activities up until Hansoh exercises its option and we will retain responsibility for development outside the China region post phase 1 trials. Hansoh also has the exclusive option to license exclusive global rights to a third target at the point of IND filing. Hansoh will be responsible for all development activities post option exercise for the third target.

Both parties agreed to not exploit any other RNAi molecule designed to inhibit a relevant licensed target for the duration of the agreement with Hansoh. In addition, both parties agreed to not sell, license or otherwise transfer, or permit to exist or grant a lien, encumbrance, mortgage on the licensed target related intellectual property if such transfer or encumbrance would conflict with the rights granted to Hansoh.

Pursuant to the agreement, Hansoh made a $16 million upfront payment to us in December 2021. For first two targets in Greater China, Hong Kong, Macau and Taiwan under the collaboration, we will be eligible to receive up to $37 million in milestone payments upon the achievement of milestones relating to initiation of specified clinical trials, the acceptance of specified regulatory filings and approval for sale in specified jurisdictions. For the global target, we are eligible to receive up to $81 million in milestone payments upon the achievement of milestones relating to initiation of specified clinical trials, the acceptance of specified regulatory filings and regulatory approval in multiple geographies. For each target selected, we are also eligible to receive up to $367.5 million in sales-based milestone payments upon the achievement of specified annual net sales levels, as well as tiered low double-digit royalties as a percentage of net sales.

The agreement with Hansoh will expire on the last to expire royalty term, which is determined on a licensed product-by-licensed product and country-by-country basis, and is the later of (1) a certain number of years from the first commercial sale of the licensed product in the country, (2) the last to expire valid claim within the patent covering the composition of matter of the licensed compound contained in the licensed product in the country or (3) expiration of regulatory exclusivity granted by the prevailing governmental authority for the licensed product in the country. Hansoh has the right to terminate the agreement in its entirety after the option exercise date with respect to any licensed target in its entirety or on a country-by-country basis, for any or no reason, upon prior written notice to us. Hansoh also has the right to terminate the agreement with respect to any licensed target in its entirety or on a country-by-country basis prior to the option exercise date with respect to such licensed target, together with the associated research plan, or, in the case of termination of a licensed target in one or more, but not all, countries, the components of the associated research plan applicable solely to such terminated countries, for any or no reason, upon a shorter period of prior written notice to us if no IND has been filed in respect of a licensed product directed to the relevant licensed target and on a longer period of prior written notice to us if an IND has been filed. or on a target-by-target basis, for any reason upon specified prior written notice to us. We may terminate the agreement on a target-by-target basis in the event that Hansoh begins a legal or administrative proceeding challenging the patentability, validity, ownership or enforceability of our patents. Either party may terminate the agreement on a target-by-target basis upon a material breach by the other party that is not cured within a specified period after receiving written notice, or in its entirety upon giving written notice following the other party's bankruptcy, insolvency or similar instance.

Lease

We lease office space in London, England for our corporate headquarters and general and administrative functions under a lease with a term through September 2025. We also lease regional offices and laboratory space in Berlin, Germany and Hoboken, New Jersey.

We believe that our current facilities are adequate to meet our needs for the near future and that suitable additional or alternative space will be available on commercially reasonable terms to accommodate our foreseeable future operations.

D. Exchange Controls.

There are no governmental laws, decrees, regulations or other legislation in the United Kingdom that may affect the import or export of capital, including the availability of cash and cash equivalents for use by us, or that may affect the remittance of dividends, interest, or other payments by us to non-resident holders of our ordinary shares or ADSs

representing our ordinary shares, other than withholding tax requirements. There is no limitation imposed by the laws of England and Wales or in the Articles on the right of non-residents to hold or vote our shares.

E. Taxation

The following summary contains a description of material U.K. and U.S. federal income tax consequences of the acquisition, ownership and disposition of our ordinary shares or ADSs. This summary should not be considered a comprehensive description of all the tax considerations that may be relevant to the decision to acquire ADSs representing our ordinary shares.

Material U.S. Federal Income Tax Considerations for U.S. Holders

The following is a description of the material U.S. federal income tax consequences to the U.S. Holders described below of owning and disposing of our ordinary shares or ADSs. It is not a comprehensive description of all tax considerations that may be relevant to a particular person's decision to acquire securities. This discussion applies only to a U.S. Holder that holds our ordinary shares or ADSs as a capital asset for tax purposes (generally, property held for investment). In addition, it does not describe all of the tax consequences that may be relevant in light of a U.S. Holder's particular circumstances, including state and local tax consequences, estate tax consequences, alternative minimum tax consequences, the potential application of the Medicare contribution tax, the special tax accounting rules in Section 451(b) of the Code, and tax consequences applicable to U.S. Holders subject to special rules, such as:

- banks, insurance companies, and certain other financial institutions;
- U.S. expatriates and certain former citizens or long-term residents of the United States;
- dealers or traders in securities who use a mark-to-market method of tax accounting;
- persons holding ordinary shares or ADSs as part of a hedging transaction, "straddle," wash sale, conversion transaction or integrated transaction or persons entering into a constructive sale with respect to ordinary shares or ADSs;
- persons whose "functional currency" for U.S. federal income tax purposes is not the U.S. dollar;
- brokers, dealers or traders in securities, commodities or currencies;
- tax-exempt entities or government organizations;
- S corporations, partnerships, or other entities or arrangements classified as partnerships for U.S. federal income tax purposes (and investors therein);
- regulated investment companies or real estate investment trusts;
- persons who acquired our ordinary shares or ADSs pursuant to the exercise of any employee stock option or otherwise as compensation;
- corporations that accumulate earnings to avoid U.S. federal income tax;
- persons that own or are deemed to own ten percent or more of our shares (by vote or value); and
- persons holding our ordinary shares or ADSs in connection with a trade or business, permanent establishment, or fixed base outside the United States.

If an entity or arrangement that is classified as a partnership for U.S. federal income tax purposes holds ordinary shares or ADSs, the U.S. federal income tax treatment of a partner will generally depend on the status of the partner

and the activities of the partnership. Partnerships (including any entity or arrangement treated as a partnership for United States federal income tax purposes) holding ordinary shares or ADSs and partners in such partnerships are encouraged to consult their tax advisers as to the particular U.S. federal income tax consequences of holding and disposing of ordinary shares or ADSs.

The discussion is based on the Code, administrative pronouncements, judicial decisions, final, temporary and proposed Treasury Regulations, and the income tax treaty between the United Kingdom and the United States, or the Treaty, all as of the date hereof, changes to any of which may affect the tax consequences described herein — possibly with retroactive effect.

A "U.S. Holder" is a holder who, for U.S. federal income tax purposes, is a beneficial owner of ordinary shares or ADSs who is eligible for the benefits of the Treaty and is:

(1) a citizen or individual resident of the United States;

(2) a corporation, or other entity taxable as a corporation, created or organized in or under the laws of the United States, any state therein or the District of Columbia;

(3) an estate the income of which is subject to U.S. federal income taxation regardless of its source; or

(4) a trust if (a) a U.S. court is able to exercise primary supervision over the administration of the trust and one or more U.S. persons have authority to control all substantial decisions of the trust or (b) the trust has a valid election to be treated as a U.S. person under applicable U.S. Treasury Regulations.

U.S. Holders are encouraged to consult their tax advisers concerning the U.S. federal, state, local and non-U.S. tax consequences of owning and disposing of our ordinary shares or ADSs in their particular circumstances.

The discussion below assumes that the representations contained in the deposit agreement are true and that the obligations in the deposit agreement and any related agreement will be complied with in accordance with their terms. Generally, a holder of an ADS should be treated for U.S. federal income tax purposes as holding the ordinary shares represented by the ADS. Accordingly, generally no gain or loss will be recognized upon an exchange of ADSs for ordinary shares.

Passive Foreign Investment Company Rules

A non-U.S. corporation will be classified as a PFIC for any taxable year in which, after applying certain look-through rules, either:

- at least 75% of its gross income is passive income (such as interest income); or
- at least 50% of its gross assets (determined on the basis of a quarterly average) is attributable to assets that produce passive income or are held for the production of passive income (including cash).

For purposes of this test, we will be treated as owning our proportionate share of the assets and earning our proportionate share of the income of any other corporation, the equity of which we own, directly or indirectly, 25% or more (by value).

We do not believe we were a PFIC for our taxable year ended December 31, 2022 or for the year ended December 31, 2021. Regardless, no assurances regarding our PFIC status can be provided for any past, current or future taxable year. The determination of whether we are a PFIC is a fact-intensive determination made on an annual basis and the applicable law is subject to varying interpretation. In particular, the characterization of our assets as active or passive may depend in part on our current and intended future business plans, which are subject to change. In addition, the total value of our assets for PFIC testing purposes may be determined in part by reference to the market price of our ordinary shares or ADSs from time to time, which may fluctuate considerably. Under the income test, our status as a PFIC depends on the composition of our income which will depend on a variety of factors that are subject to

uncertainty, including the characterization of certain intercompany payments and payments from tax authorities, transactions we enter into in the future and our corporate structure. Even if we determine that we are not a PFIC for a taxable year, there can be no assurance that the IRS would not successfully challenge our position. Accordingly, our U.S. counsel expresses no opinion with respect to our PFIC status for any prior, current or future taxable year.

If we are classified as a PFIC in any year with respect to which a U.S. Holder owns the ordinary shares or ADSs, we will continue to be treated as a PFIC with respect to such U.S. Holder in all succeeding years during which the U.S. Holder owns the ordinary shares or ADSs, regardless of whether we continue to meet the tests described above unless we cease to be a PFIC and the U.S. Holder has made a "deemed sale" election under the PFIC rules. If such a deemed sale is made, a U.S. Holder will be deemed to have sold the ordinary shares or ADSs the U.S. Holder holds at their fair market value on the last day of the last taxable year for which we are a PFIC, and any gain from such deemed sale would be subject to the excess distribution rules described below. After the deemed sale election, so long as we do not become a PFIC in a subsequent taxable year, the U.S. Holder's ordinary shares or ADSs with respect to which such election was made will not be treated as shares in a PFIC and the U.S. Holder will not be subject to the rules described below with respect to any "excess distribution" the U.S. Holder receives from us or any gain from an actual sale or other disposition of the ordinary shares or ADSs. U.S. Holders should consult their tax advisers as to the possibility and consequences of making a deemed sale election if we cease to be a PFIC and such election becomes available.

For each taxable year we are treated as a PFIC with respect to U.S. Holders, U.S. Holders will be subject to special tax rules with respect to any "excess distribution" such U.S. Holder receives and any gain such U.S. Holder recognizes from a sale or other disposition (including a pledge) of ordinary shares or ADSs, unless (1) such U.S. Holder makes a "qualified electing fund" election, or QEF Election, with respect to all taxable years during such U.S. Holder's holding period in which we are a PFIC, or (2) our ordinary shares or ADSs constitute "marketable stock" and such U.S. Holder makes a mark-to-market election (as discussed below). Distributions a U.S. Holder receives in a taxable year that are greater than 125% of the average annual distributions a U.S. Holder received during the shorter of the three preceding taxable years or the U.S. Holder's holding period for the ordinary shares or ADSs will be treated as an excess distribution. Under these special tax rules:

- the excess distribution or gain will be allocated ratably over a U.S. Holder's holding period for the ordinary shares or ADSs;
- the amount allocated to the current taxable year, and any taxable year prior to the first taxable year in which we became a PFIC, will be treated as ordinary income; and
- the amount allocated to each other year will be subject to the highest tax rate in effect for that year and the interest charge generally applicable to underpayments of tax will be imposed on the resulting tax attributable to each such year.

The tax liability for amounts allocated to years prior to the year of disposition or "excess distribution" cannot be offset by any net operating losses for such years, and gains (but not losses) realized on the sale of the ordinary shares or ADSs cannot be treated as capital gains, even if a U.S. Holder holds the ordinary shares or ADSs as capital assets.

If we are a PFIC, a U.S. Holder will generally be subject to similar rules with respect to distributions we receive from, and our dispositions of the stock of, any of our direct or indirect subsidiaries that also are PFICs, as if such distributions were indirectly received by, and/or dispositions were indirectly carried out by, such U.S. Holder. U.S. Holders should consult their tax advisers regarding the application of the PFIC rules to our subsidiaries.

If a U.S. Holder makes an effective QEF Election, the U.S. Holder will be required to include in gross income each year, whether or not we make distributions, as capital gains, such U.S. Holder's pro rata share of our net capital gains and, as ordinary income, such U.S. Holder's pro rata share of our earnings in excess of our net capital gains. However, a U.S. Holder can only make a QEF Election with respect to ordinary shares or ADSs in a PFIC if such company agrees to furnish such U.S. Holder with certain tax information annually. We do not currently expect to provide such information in the event that we are classified as a PFIC.

U.S. Holders can avoid the interest charge on excess distributions or gain relating to our ordinary shares or ADSs by making a mark-to-market election with respect to the ordinary shares or ADSs, provided that the ordinary shares or ADSs are "marketable stock." Ordinary shares or ADSs will be marketable stock if they are "regularly traded" on certain U.S. stock exchanges or on a non-U.S. stock exchange that meets certain conditions. For these purposes, the ordinary shares or ADSs will be considered regularly traded during any calendar year during which they are traded, other than in de minimis quantities, on at least 15 days during each calendar quarter. Any trades that have as their principal purpose meeting this requirement will be disregarded. Our ADSs are listed on Nasdaq, which is a qualified exchange for these purposes. Consequently, if our ADSs are listed on Nasdaq and are regularly traded, and you are a holder of ADSs, we expect the mark-to-market election would be available to U.S. Holders if we are a PFIC. Each U.S. Holder should consult its tax advisor as to the whether a mark-to-market election is available or advisable with respect to the ordinary shares or ADSs.

A U.S. Holder that makes a mark-to-market election must include in ordinary income for each year an amount equal to the excess, if any, of the fair market value of our ordinary shares or ADSs at the close of the taxable year over the U.S. Holder's adjusted tax basis in the ordinary shares or ADSs. An electing holder may also claim an ordinary loss deduction for the excess, if any, of the U.S. Holder's adjusted basis in the ordinary shares or ADSs over the fair market value of the ordinary shares or ADSs at the close of the taxable year, but this deduction is allowable only to the extent of any net mark-to-market gains for prior years. Gains from an actual sale or other disposition of the ordinary shares or ADSs will be treated as ordinary income, and any losses incurred on a sale or other disposition of the shares will be treated as an ordinary loss to the extent of any net mark-to-market gains for prior years. Once made, the election cannot be revoked without the consent of the IRS unless the ordinary shares or ADSs cease to be marketable stock.

However, a mark-to-market election generally cannot be made for equity interests in any lower-tier PFICs that we own, unless shares of such lower-tier PFIC are themselves "marketable stock." As a result, even if a U.S. Holder validly makes a mark-to-market election with respect to our ordinary shares or ADSs, the U.S. Holder may continue to be subject to the PFIC rules (described above) with respect to its indirect interest in any of our investments that are treated as an equity interest in a PFIC for U.S. federal income tax purposes. U.S. Holders should consult their tax advisers as to the availability and desirability of a mark-to-market election, as well as the impact of such election on interests in any lower-tier PFICs.

Unless otherwise provided by the U.S. Treasury, each U.S. shareholder of a PFIC is required to file an annual report containing such information as the U.S. Treasury may require. A U.S. Holder's failure to file the annual report will cause the statute of limitations for such U.S. Holder's U.S. federal income tax return to remain open with regard to the items required to be included in such report until three years after the U.S. Holder files the annual report, and, unless such failure is due to reasonable cause and not willful neglect, the statute of limitations for the U.S. Holder's entire U.S. federal income tax return will remain open during such period. U.S. Holders should consult their tax advisers regarding the requirements of filing such information returns under these rules.

Taxation of Distributions

Subject to the discussion above under "Passive Foreign Investment Company Rules," distributions paid on ordinary shares or ADSs, other than certain pro rata distributions of ordinary shares or ADSs, will generally be treated as dividends to the extent paid out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles). Because we may not calculate our earnings and profits under U.S. federal income tax principles, we expect that distributions generally will be reported to U.S. Holders as dividends. Subject to applicable limitations, dividends paid to certain non-corporate U.S. Holders may be taxable at preferential rates applicable to "qualified dividend income." However, the qualified dividend income treatment may not apply if we are treated as a PFIC with respect to the U.S. Holder. The amount of the dividend will not be eligible for the dividends-received deduction generally available to U.S. corporations under the Code. Dividends will generally be included in a U.S. Holder's income on the date of the U.S. Holder's receipt of the dividend. The amount of any dividend income paid in foreign currency will be the U.S. dollar amount calculated by reference to the exchange rate in effect on the date of actual or constructive receipt, regardless of whether the payment is in fact converted into U.S. dollars. If the dividend is converted into U.S. dollars on the date of receipt, a U.S. Holder should not be required to recognize foreign currency gain or loss in respect of the dividend income. A U.S. Holder may have foreign currency gain or loss if the dividend is converted into U.S. dollars after the date of receipt. Such gain or loss would generally be treated as U.S.-source ordinary income or loss. The amount of any distribution of property other than cash (and other than certain pro rata

distributions of ordinary shares or ADSs or rights to acquire ordinary shares or ADSs) will be the fair market value of such property on the date of distribution. For foreign tax credit purposes, our dividends will generally be treated as passive category income.

Sale or Other Taxable Disposition of Ordinary Shares and ADSs

Subject to the discussion above under "Passive Foreign Investment Company Rules," gain or loss realized on the sale or other taxable disposition of ordinary shares or ADSs will be capital gain or loss, and will be long-term capital gain or loss if the U.S. Holder held the ordinary shares or ADSs for more than one year. The amount of the gain or loss will equal the difference between the U.S. Holder's tax basis in the ordinary shares or ADSs disposed of and the amount realized on the disposition, in each case as determined in U.S. dollars. This gain or loss will generally be U.S.-source gain or loss for foreign tax credit purposes. The deductibility of capital losses is subject to limitations.

If the consideration received by a U.S. Holder is not paid in U.S. dollars, the amount realized will be the U.S. dollar value of the payment received determined by reference to the spot rate of exchange on the date of the sale or other disposition. However, if the ordinary shares or ADSs are treated as traded on an "established securities market" and you are either a cash basis taxpayer or an accrual basis taxpayer that has made a special election (which must be applied consistently from year to year and cannot be changed without the consent of the IRS), you will determine the U.S. dollar value of the amount realized in a non-U.S. dollar currency by translating the amount received at the spot rate of exchange on the settlement date of the sale. If you are an accrual basis taxpayer that is not eligible to or does not elect to determine the amount realized using the spot rate on the settlement date, you will recognize foreign currency gain or loss to the extent of any difference between the U.S. dollar amount realized on the date of sale or disposition and the U.S. dollar value of the currency received at the spot rate on the settlement date.

WE STRONGLY URGE YOU TO CONSULT YOUR TAX ADVISOR REGARDING THE IMPACT OF OUR PFIC STATUS ON YOUR INVESTMENT IN THE ORDINARY SHARES OR ADSs AS WELL AS THE APPLICATION OF THE PFIC RULES TO YOUR INVESTMENT IN THE ORDINARY SHARES OR ADSs.

Information Reporting and Backup Withholding

Payments of dividends and sales proceeds that are made within the United States or through certain U.S.-related financial intermediaries generally are subject to information reporting, and may be subject to backup withholding, unless (i) the U.S. Holder is a corporation or other exempt recipient or (ii) in the case of backup withholding, the U.S. Holder provides a correct taxpayer identification number and certifies that it is not subject to backup withholding.

Backup withholding is not an additional tax. The amount of any backup withholding from a payment to a U.S. Holder will be allowed as a credit against the holder's U.S. federal income tax liability and may entitle it to a refund, provided that the required information is timely furnished to the IRS.

Information with Respect to Foreign Financial Assets

Certain U.S. Holders who are individuals (and, under proposed regulations, certain entities) may be required to report information relating to the ordinary shares or ADSs, subject to certain exceptions (including an exception for ordinary shares or ADSs held in accounts maintained by certain U.S. financial institutions). U.S. Holders should consult their tax advisers regarding their reporting obligations with respect to their ownership and disposition of the ordinary shares or ADSs.

F. Dividends and Paying Agents.

Not applicable.

G. Statement by Experts.

Not applicable.

H. Documents on Display.

We maintain a corporate website at *www.silence-therapeutics.com*. Information contained in, or that can be accessed through, our website is not a part of, and shall not be incorporated by reference into, this Annual Report. We have included our website address in this report solely as an inactive textual reference. We make available free of charge on our website our Reports on Form 6-K, our Annual Reports on Form 20-F, and any other reports that we file or furnish with the SEC.

The SEC also maintains a website at *www.sec.gov* that contains reports, proxy and information statements and other information regarding issuers that file electronically, such as us, with the SEC.

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

I. Subsidiary Information.

Not applicable.

ITEM 11: QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Market risk arises from our exposure to fluctuation in interest rates and currency exchange rates. These risks are managed by maintaining an appropriate mix of cash deposits in the two main currencies we operate in, placed with a variety of financial institutions for varying periods according to expected liquidity requirements.

Credit and Liquidity Risk

Our cash, cash equivalents and U.S. Treasury Bills are on deposit with two financial institutions, one in the US and one in the UK, which management believes are of high credit quality. Such deposits may, at times, exceed federally insured limits. We invest our liquid resources based on the expected timing of expenditures to be made in the ordinary course of our activities. All financial liabilities are payable in the short term, meaning no more than three months, and we maintain adequate bank balances in either instant access or short-term deposits to meet those liabilities as they fall due. We do not believe we had any credit risk relating to our trade receivables as of December 31, 2022, 2021 and 2020, which consisted solely of amounts due from AstraZeneca, Mallinckrodt and Alnylam.

Currency Risk

Our functional currency is U.K. pounds sterling, and our transactions are commonly denominated in that currency. However, we receive payments under our collaboration agreements in U.S. dollars and we incur a portion of our expenses in other currencies, primarily Euros, and are exposed to the effects of these exchange rates. We seek to minimize this exposure by maintaining currency cash balances at levels appropriate to meet foreseeable short to mid-term expenses in these other currencies. Where significant foreign currency cash receipts are expected, we consider the use of forward exchange contracts to manage our exchange rate exposure.

Interest Rate Risk

As of December 31, 2022, we had cash, cash equivalents and U.S. Treasury Bills of £71.1 million. Our exposure to interest rate sensitivity is impacted primarily by changes in the underlying U.K. and U.S. bank interest rates. Our surplus cash and cash equivalents are invested in interest-bearing savings accounts and certificates of deposit from time to time. During the years ended December 31, 2022, 2021 and 2020, we have not entered into investments for trading or speculative purposes. Due to the conservative nature of our investment portfolio, which is predicated on capital preservation of investments with short-term maturities, we do not expect our operating results or cash flows to be significantly affected by changes in market interest rates.

See note 29 to our consolidated financial statements for quantitative disclosures about market risk.

ITEM 12: DESCRIPTION OF SECURITIES OTHER THAN EQUITY SECURITIES

A. Debt Securities.

Not applicable.

B. Warrants and Rights.

Not applicable.

C. Other Securities.

Not applicable.

D. American Depositary Shares.

Fees and Expenses

Persons depositing or withdrawing ordinary shares or ADS holders must pay:	For:
$5.00 (or less) per 100 ADSs (or portion of 100 ADSs)	Issuance of ADSs, including issuances resulting from a distribution of ordinary shares or rights or other property
	Cancellation of ADSs for the purpose of withdrawal, including if the deposit agreement terminates
$.05 (or less) per ADS	Any cash distribution to ADS holders
A fee equivalent to the fee that would be payable if securities distributed to you had been ordinary shares and the ordinary shares had been deposited for issuance of ADSs	Distribution of securities distributed to holders of deposited securities (including rights) that are distributed by the depositary to ADS holders
$.05 (or less) per ADS per calendar year	Depositary services
Registration or transfer fees	Transfer and registration of ordinary shares on our share register to or from the name of the depositary or its agent when you deposit or withdraw ordinary shares
Expenses of the depositary	Cable (including SWIFT) and facsimile transmissions (when expressly provided in the deposit agreement)
	Converting foreign currency to U.S. dollars
Taxes and other governmental charges the depositary or the custodian has to pay on any ADSs or ordinary shares underlying ADSs, such as stock transfer taxes, stamp duty or withholding taxes	As necessary
Any charges incurred by the depositary or its agents for servicing the deposited securities	As necessary

The depositary collects its fees for delivery and surrender of ADSs directly from investors depositing ordinary shares or surrendering ADSs for the purpose of withdrawal or from intermediaries acting for them. The depositary collects fees for making distributions to investors by deducting those fees from the amounts distributed or by selling a portion of distributable property to pay the fees. The depositary may collect its annual fee for depositary services by deduction from cash distributions or by directly billing investors or by charging the book-entry system accounts of participants acting for them. The depositary may collect any of its fees by deduction from any cash distribution payable (or by selling a portion of securities or other property distributable) to ADS holders that are obligated to pay those fees. The depositary may generally refuse to provide fee-attracting services until its fees for those services are paid.

From time to time, the depositary may make payments to us to reimburse us for costs and expenses generally arising out of establishment and maintenance of the ADS program, waive fees and expenses for services provided to us by the depositary or share revenue from the fees collected from ADS holders. In performing its duties under the deposit agreement, the depositary may use brokers, dealers, foreign currency dealers or other service providers that are owned by or affiliated with the depositary and that may earn or share fees, spreads or commissions.

The depositary may convert currency itself or through any of its affiliates, or the custodian or we may convert currency and pay U.S. dollars to the depositary. Where the depositary converts currency itself or through any of its affiliates, the depositary acts as principal for its own account and not as agent, advisor, broker or fiduciary on behalf of any other person and earns revenue, including, without limitation, transaction spreads, that it will retain for its own account. The revenue is based on, among other things, the difference between the exchange rate assigned to the currency conversion made under the deposit agreement and the rate that the depositary or its affiliate receives when buying or selling foreign currency for its own account. The depositary makes no representation that the exchange rate used or obtained by it or its affiliate in any currency conversion under the deposit agreement will be the most favorable rate that could be obtained at the time or that the method by which that rate will be determined will be the most favorable to ADS holders, subject to the depositary's obligation to act without negligence or bad faith. The methodology used to determine exchange rates used in currency conversions made by the depositary is available upon request.

Where the custodian converts currency, the custodian has no obligation to obtain the most favorable rate that could be obtained at the time or to ensure that the method by which that rate will be determined will be the most favorable to ADS holders, and the depositary makes no representation that the rate is the most favorable rate and will not be liable for any direct or indirect losses associated with the rate. In certain instances, the depositary may receive dividends or other distributions from the us in U.S. dollars that represent the proceeds of a conversion of foreign currency or translation from foreign currency at a rate that was obtained or determined by us and, in such cases, the depositary will not engage in, or be responsible for, any foreign currency transactions and neither it nor we make any representation that the rate obtained or determined by us is the most favorable rate and neither it nor we will be liable for any direct or indirect losses associated with the rate.

Payment of Taxes

You will be responsible for any taxes or other governmental charges payable on your ADSs or on the deposited securities represented by any of your ADSs. The depositary may refuse to register any transfer of your ADSs or allow you to withdraw the deposited securities represented by your ADSs until those taxes or other charges are paid. It may apply payments owed to you or sell deposited securities represented by your ADSs to pay any taxes owed and you will remain liable for any deficiency. If the depositary sells deposited securities, it will, if appropriate, reduce the number of ADSs to reflect the sale and pay to ADS holders any proceeds, or send to ADS holders any property, remaining after it has paid the taxes.

Description of ADSs

See Exhibit 2.4 for a description of the terms of our ADSs.

PART II

ITEM 13: DEFAULTS, DIVIDEND ARREARAGES AND DELINQUENCIES

None.

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

A. None

B. None

C. None

D. None

E. None.

ITEM 15: CONTROLS AND PROCEDURES

Limitations on Effectiveness of Controls and Procedures

In designing and evaluating our disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management is required to apply judgment in evaluating the benefits of possible controls and procedures relative to their costs.

Disclosure Controls and Procedures.

Our management, with the participation of our principal executive officer and principal financial officer, has evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a- 15(e) and 15d- 15(e) under the Exchange Act), as of the end of the period covered by this Annual Report. Based on such evaluation, our principal executive officer and principal financial officer have concluded that as of December 31, 2022, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over our financial reporting, as such term is defined in Rule 13a-15(f) and 15d-15(f) under the Exchange Act.

Our management, including the chief executive officer and chief financial officer, 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, including the chief executive officer and chief financial officer as of December 31, 2022, our internal control over financial reporting was effective.

Attestation Report of the Registered Public Accounting Firm

None.

Management's report was not subject to attestation by the Company's registered public accounting firm pursuant to rules of the SEC that permit the Company to provide only management's report in this annual report.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting (as defined in Rule 13a-15(f) under the Exchange Act) during the period covered by this Annual Report that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

ITEM 16A: AUDIT COMMITTEE FINANCIAL EXPERT

Our board of directors has determined that Dave Lemus qualifies as an audit committee financial expert as defined by the rules of the SEC and has the requisite financial sophistication under the applicable rules and regulations of Nasdaq. Mr. Lemus is independent as such term is defined in Rule 10A-3 under the Exchange Act and under the listing standards of Nasdaq.

ITEM 16B: CODE OF ETHICS

Code of Business Conduct and Ethics

We have adopted a Code of Business Conduct and Ethics that is applicable to all of our employees, executive officers, including our principal executive, principal financial and principal accounting officers, members of our board of directors, and consultants. The Code of Business Conduct and Ethics is available on our website at www.silence-therapeutics.com. The information and other content on our website are not part of this Annual Report and our website address is included in this Annual Report as an inactive textual reference only.

We intend to satisfy the disclosure requirement under Item 16B(d) and (e) of Form 20-F regarding amendment to, or waiver from, a provision of our Code of Business Conduct and Ethics, as well as Nasdaq's requirement to disclose waivers with respect to directors and executive officers, by posting such information in the "Investors" section of our website at www.silence-therapeutics.com. Our executive officers are responsible for administering the Code of Business Conduct and Ethics. Amendment, alteration or termination of the Code of Business Conduct and Ethics requires the approval of our board of directors.

ITEM 16C: PRINCIPAL ACCOUNTANT FEES AND SERVICES

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

Fee Category	**2022** **£'000s**	2021 £'000s
Audit Fees	463	403
Audit Related Fees	150	180
Tax	-	-
Other Services	-	-
Total Fees	613	583

Audit Fees

For the years ended December 31, 2022 and 2021, audit services includes fees for the year end, half-year as well as quarterly interim reviews in 2022.

Audit Related Fees

For the years ended December 31, 2022 and 2021, audit related services are associated with registration statements and offerings.

Tax Fees

We did not incur any tax fees for services from PricewaterhouseCoopers LLP in 2022 and 2021.

All Other Fees

We did not incur any other fees for services from PricewaterhouseCoopers LLP in 2022 and 2021.

Audit Committee Pre-Approval Policy and Procedures

All of the fees described above were pre-approved by the Audit and Risk Committee.

Our Audit and Risk Committee's specific responsibilities in carrying out its oversight of the quality and integrity of the accounting, auditing and reporting practices of the Company include the approval of audit and non-audit services to be provided by the external auditor. The Audit and Risk Committee approves in advance the particular services or categories of services to be provided to the Company during the following yearly period and also sets forth a specific budget for such audit services. All non-audit services are pre-approved by the audit committee.

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

None

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

None.

ITEMS 16F: CHANGE IN REGISTRANT'S CERTIFYING ACCOUNTANT

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

ITEM 16G: CORPORATE GOVERNANCE

We are a "foreign private issuer," as defined by the SEC. As a result, in accordance with Nasdaq rules, we comply with certain home country governance requirements and certain exemptions thereunder rather than complying with Nasdaq corporate governance standards, and we comply with periodic report filing requirements under the Exchange Act applicable to foreign private issuers rather than domestic issuers. We currently avail ourselves of the following limited exemptions under such rules pertaining to foreign private issuers:

- Exemption from filing quarterly reports on Form 10-Q containing unaudited financial and other specified information or current reports on Form 8-K upon the occurrence of specified significant events;
- Exemption from Section 16 under the Exchange Act, which requires insiders to file public reports of their securities ownership and trading activities and provides for liability for insiders who profit from trades in a short period of time;
- Exemption from the Nasdaq rules applicable to domestic issuers requiring disclosure within four business days of any determination to grant a waiver of the code of business conduct and ethics to directors and officers;
- Exemption from the requirement to obtain shareholder approval for certain issuances of securities, including shareholder approval of share option plans;
- Exemption from the requirement that our audit committee have review and oversight responsibilities over all "related party transactions," as defined in Item 7.B of Form 20-F;

- Exemption from the requirement that our board have a compensation committee that is composed entirely of independent directors with a written charter addressing the committee's purpose and responsibilities; and

- Exemption from the requirements that director nominees are selected, or recommended for selection by our board, either by (1) independent directors constituting a majority of our board's independent directors in a vote in which only independent directors participate, or (2) a committee comprised solely of independent directors, and that a formal written charter or board resolution, as applicable, addressing the nominations process is adopted.

Furthermore, Nasdaq Rule 5615(a)(3) provides that a foreign private issuer, such as us, may rely on home country corporate governance practices in lieu of certain of the rules in the Nasdaq Rule 5600 Series and Rule 5250(d), provided that we nevertheless comply with Nasdaq's Notification of Noncompliance requirement (Rule 5625), the Voting Rights requirement (Rule 5640) and that we have an audit committee that satisfies Rule 5605(c)(3), consisting of committee members that meet the independence requirements of Rule 5605(c)(2)(A)(ii).

Nasdaq Diversity Disclosure

Board Diversity Matrix (As of March 1, 2022)

Country of Principal Executive Offices:	United Kingdom
Foreign Private Issuer:	Yes
Disclosure Prohibited under Home Country Law:	No
Total Number of Directors:	8

Part I: Gender Identity	Female	Male	Non-Binary	Did Not Disclose Gender
Directors	-	8	-	-
Part II: Demographic Background				
Underrepresented Individual in Home Country Jurisdiction	-	1	-	-
LGBTQ+	-	1	-	-
Did Not Disclose Demographic Background	-	-	-	-

ITEM 16H: MINE SAFETY DISCLOSURE

None

ITEM 16I: DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS

Not applicable

PART III

ITEM 17: FINANCIAL STATEMENTS

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

ITEM 18: FINANCIAL STATEMENTS

The financial statements required under this Item 18 are filed as part of this Annual Report beginning on page F-1. The audit report of PricewaterhouseCoopers LLP, independent registered public accounting firm, is included herein preceding the financial statements.

ITEM 19: EXHIBITS

		Incorporated by Reference to Filings Indicated				
Exhibit Number	**Exhibit Description**	**Form**	**File No.**	**Exhibit No.**	**Filing date**	**Filed / Furnished Herewith**
1.1	Amended and Restated Articles of Association	F-1	333-248203	3.1	8/20/2020	
2.1*	Deposit Agreement, by and among the registrant and The Bank of New York Mellon and the Owners and Holders of American Depositary Shares, dated September 4, 2020	F-1	333-254021	4.1	3/8/2021	
2.2	Form of American Depositary Receipt	424B3	333-248217		9/4/2020	
2.3	Description of Share Capital and Articles of Association					X
2.4	Description of American Depositary Shares					X
4.1#	Silence Therapeutics plc 2018 Long-Term Incentive Plan	F-1	333-248203	10.1	8/20/2020	
4.2#	Silence Therapeutics plc 2018 Non-Employee Long-Term Incentive Plan	F-1	333-248203	10.2	8/20/2020	
4.3#	Employee U.S. Sub-Plan under the 2018 Employee Long-Term Incentive Plan	F-1	333-248203	10.3	8/20/2020	
4.4#	Non-Employee U.S. Sub-Plan under the 2018 Non-Employee Long-Term Incentive Plan	F-1	333-248203	10.4	8/20/2020	
4.5†+	License and Collaboration Agreement, by and between the registrant and Mallinckrodt Pharma IP Trading DAC, dated July 18, 2019	F-1	333-248203	10.5	8/20/2020	
4.6†+	Research Collaboration, Option and License Agreement, by and between the registrant and AstraZeneca AB, dated March 24, 2020	F-1	333-248203	10.6	8/20/2020	
4.7†+	Exclusive Research Collaboration, Option and License Agreement by and between the registrant and Hansoh (Shanghai) Healthtech Co., Ltd. and Jiangsu Hansoh Pharmaceutical Group Company Limited, dated October 14, 2021					X
4.8	Form of Deed of Indemnity between the registrant and its directors	F-1	333-248203	10.7	8/20/2020	
4.9	Form of Deed of Indemnity between the registrant and its executive officers	F-1	333-248203	10.8	8/20/2020	
8.1	Subsidiaries of the Registrant	F-1	333-248203	21.1	8/20/2020	
12.1	Rule 13a-14(a)/15d-14(a) Certification of Chief Executive Officer					X
12.2	Rule 13a-14(a)/15d-14(a) Certification of Chief Financial Officer					X
13.1	Section 1350 Certification of Chief Executive Officer					X

13.2	Section 1350 Certification of Chief Financial Officer	X
15.1	Consent of PricewaterhouseCoopers LLP	X
101.INS	Inline XBRL Instance Document	X
101.SCH	Inline XBRL Taxonomy Extension Schema Document	X
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document	X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document	X
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document	X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document	X
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)	X

* Exhibit 2.1 excludes Exhibit A thereto which was revised as set forth in Exhibit 2.2 listed above.
# Indicates management contract or compensatory plan.
† Portions of this exhibit (indicated by asterisks) have been omitted because the registrant has determined they are not material and would likely cause competitive harm to the registrant if publicly disclosed.
+ Certain schedules have been omitted pursuant to Item 601(a)(5) of Regulation S-K. The registrant hereby undertakes to furnish supplementally a copy of any omitted exhibit or schedule upon request by the SEC.

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.

		SILENCE THERAPEUTICS PLC
	By:	/s/ Craig Tooman
	Name:	Craig Tooman
Date: March 15, 2023	Title:	Chief Executive Officer

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Audited Consolidated Financial Statements

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PCAOB ID: 876 Auditor Name: PricewaterhouseCoopers LLP Auditor Location: Reading, United Kingdom

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Shareholders of Silence Therapeutics plc

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Silence Therapeutics plc and its subsidiaries (the "Group") as of December 31, 2022 and 2021, and the related consolidated income statements, statements of comprehensive income, statements of changes in equity and cash flow statements for each of the three years in the period ended December 31, 2022, including the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Group as of December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2022 in conformity with International Financial Reporting Standards as issued by the International Accounting Standards Board.

Substantial Doubt about the Group's Ability to Continue as a Going Concern

The accompanying consolidated financial statements have been prepared assuming that the Group will continue as a going concern. As discussed in Note 2.3 to the consolidated financial statements, the Group has incurred recurring losses since inception and cash outflows from operating activities and has stated that these events or conditions indicate that a material uncertainty exists that may cast significant doubt (or raise substantial doubt as contemplated by PCAOB standards) on the Group's ability to continue as a going concern. Management's plans in regard to these matters are also described in Note 2.3. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

These consolidated financial statements are the responsibility of the Group's management. Our responsibility is to express an opinion on the Group'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 Group in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits of these consolidated financial statements in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. The Group 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 Group's internal control over financial reporting. Accordingly, we express no such

opinion.

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

/s/PricewaterhouseCoopers LLP
Reading, United Kingdom
March 15, 2023

We have served as the Group's auditor since 2014.

SILENCE THERAPEUTICS PLC
CONSOLIDATED INCOME STATEMENTS
(in thousands, except for loss per share)

	Note	**2022**	2021	2020
		£000s	£000s	£000s
Revenue	3	**17,501**	12,415	5,479
Cost of sales		**(10,880)**	(7,456)	(3,762)
Gross profit		**6,621**	4,959	1,717
Research and development costs		**(35,605)**	(30,765)	(20,209)
General and administrative expenses		**(19,609)**	(20,008)	(13,983)
Other losses - net	7	**-**	-	(3,372)
Operating loss	5	**(48,593)**	(45,814)	(35,847)
Finance and other expenses	8	**(47)**	(52)	(323)
Finance and other income	9	**1,272**	10	129
Loss for the year before taxation		**(47,368)**	(45,856)	(36,041)
Taxation	10	**6,879**	6,446	3,494
Loss for the year after taxation		**(40,489)**	(39,410)	(32,547)
Loss per ordinary equity share (basic and diluted)	11	**(41.9) pence**	(44.3) pence	(39.8) pence

The accompanying accounting policies and notes form an integral part of these financial statements.

SILENCE THERAPEUTICS PLC
CONSOLIDATED STATEMENTS OF COMPREHENSIVE INCOME
(in thousands)

	2022	2021	2020
	£000s	£000s	£000s
Loss for the year after taxation	**(40,489)**	(39,410)	(32,547)
Other comprehensive expense, net of tax:			
Items that may subsequently be reclassified to profit or loss:			
Foreign exchange differences arising on consolidation of foreign operations	**544**	(677)	472
Total other comprehensive income/(expense) for the year	**544**	(677)	472
Total comprehensive expense for the year	**(39,945)**	(40,087)	(32,075)

The accompanying accounting policies and notes form an integral part of these financial statements.

SILENCE THERAPEUTICS PLC
CONSOLIDATED BALANCE SHEETS
(in thousands)

	Note	December 31, 2022	2021
		£000s	£000s
Non-current assets			
Property, plant and equipment	12	**2,201**	1,944
Goodwill	13	**8,009**	7,592
Other intangible assets	14	**320**	24
Financial assets at amortized cost	17	**284**	301
		10,814	9,861
Current assets			
Cash and cash equivalents	15	**54,816**	73,537
Financial assets at amortized cost	17	**16,328**	-
R&D tax credit receivable	10	**14,882**	6,945
Other current assets	18	**9,745**	5,520
Trade receivables	19	**915**	331
		96,686	86,333
Non-current liabilities			
Contract liabilities	22	**(63,485)**	(72,501)
		(63,485)	(72,501)
Current liabilities			
Contract liabilities	22	**(8,864)**	(4,247)
Trade and other payables	20	**(12,633)**	(10,783)
Lease liability	21	**(446)**	(137)
		(21,943)	(15,167)
Net assets		**22,072**	8,526
Capital and reserves attributable to the owners of the parent			
Share capital	24	**5,390**	4,489
Capital reserves	26	**277,860**	225,462
Translation reserve		**2,085**	1,541
Accumulated losses		**(263,263)**	(222,966)
Total shareholders equity		**22,072**	8,526

The financial statements on pages F1 to F33 were approved by the Board on March 14, 2023 and signed on its behalf.

Craig Tooman
Chief Executive Officer
Company number: 02992058

The accompanying accounting policies and notes form an integral part of these financial statements.

SILENCE THERAPEUTICS PLC
CONSOLIDATED STATEMENTS OF CHANGES IN EQUITY
(in thousands)

	Note	Share capital	Capital reserves	Translation reserve	Accumulated losses	Total equity
		£000s	£000s	£000s	£000s	£000s
At January 1, 2020		3,919	167,243	1,746	(151,999)	20,909
Recognition of share-based payments		-	4,395	-	-	4,395
Options exercised in the year		-	(331)	-	331	-
Proceeds from shares issued		246	15,584	-	-	15,830
Transactions with owners recognized directly in equity		246	19,648	-	331	20,225
Loss for year		-	-	-	(32,547)	(32,547)
Other comprehensive expense						
Foreign exchange differences arising on consolidation of foreign operations		-	-	472	-	472
Total comprehensive expense for the year		-	-	472	(32,547)	(32,075)
At December 31, 2020		4,165	186,891	2,218	(184,215)	9,059
Recognition of share-based payments	26	-	8,632	-	-	8,632
Options exercised in the year	26	-	(659)	-	659	-
Proceeds from shares issued	24 / 26	324	30,598	-	-	30,922
Transactions with owners recognized directly in equity		324	38,571	-	659	39,554
Loss for year		-	-	-	(39,410)	(39,410)
Other comprehensive income						-
Foreign exchange differences arising on consolidation of foreign operations		-	-	(677)	-	(677)
Total comprehensive expense for the year		-	-	(677)	(39,410)	(40,087)
At December 31, 2021		4,489	225,462	1,541	(222,966)	8,526
Recognition of share-based payments	26	-	10,252	-	-	10,252
Options exercised in the year	26	-	(192)	-	192	-
Proceeds from shares issued	24 / 26	901	42,338	-	-	43,239
Transactions with owners recognized directly in equity		901	52,398	-	192	53,491
Loss for year		-	-	-	(40,489)	(40,489)
Other comprehensive income						-
Foreign exchange differences arising on consolidation of foreign operations		-	-	544	-	544
Total comprehensive expense for the year		-	-	544	(40,489)	(39,945)
At December 31, 2022		5,390	277,860	2,085	(263,263)	22,072

The accompanying accounting policies and notes form an integral part of these financial statements.

SILENCE THERAPEUTICS PLC
CONSOLIDATED CASH FLOW STATEMENTS
(in thousands)

	Year ended December 31,		
	2022	2021	2020
	£000s	£000s	£000s
Cash flow from operating activities			
Loss before tax	**(47,368)**	(45,856)	(36,041)
Depreciation charges	**478**	411	476
Amortization charges	**4**	16	20
Charge for the year in respect of share-based payments	**10,252**	8,632	4,395
Net foreign exchange (gain)/loss	**713**	305	4,864
(Gain) on derivative financial instrument	**-**	-	(1,492)
Finance and other expenses	**-**	52	323
Finance and other income	**(1,272)**	(10)	(128)
(Gain) on disposal of property, plant and equipment	**-**	-	(3)
Revaluation of trade and other receivables related to contract liabilities	**-**	-	(4,864)
(Increase)/decrease in trade and other receivables	**(584)**	27,483	(29,302)
Increase in other current assets	**(4,225)**	(904)	(3,731)
(Increase) in R&D tax credit receivable	**(502)**	-	-
Decrease in derivative financial instrument	**-**	1,492	-
Increase in trade and other payables	**1,447**	2,405	1,303
(Decrease)/increase in contract liabilities	**(4,399)**	8,369	50,386
Cash generated/(spent) on operations	**(45,456)**	2,395	(13,794)
R&D tax credits received	**-**	4,411	3,018
Net cash (outflow)/inflow from operating activities	**(45,456)**	6,806	(10,776)
Cash flow from investing activities			
Redemption of financial assets at amortized cost – term deposits	**-**	10,000	10,000
Purchase of financial assets at amortized cost	**(16,125)**	-	-
Interest received	**23**	10	129
Purchase of property, plant and equipment	**(140)**	(1,311)	(511)
Purchase of intangible assets	**(300)**	(23)	(3)
Proceeds from sale of property, plant and equipment	**-**	-	3
Net cash (outflow)/inflow from investing activities	**(16,542)**	8,676	9,618
Cash flow from financing activities			
Repayment of lease liabilities	**(190)**	(211)	(402)
Proceeds from issue of share capital	**43,239**	30,922	15,830
Net cash inflow from financing activities	**43,049**	30,711	15,428
(Decrease)/increase in cash and cash equivalents	**(18,949)**	46,193	14,270
Cash and cash equivalents at start of year	**73,537**	27,449	13,515
Effect of exchange rate fluctuations on cash and cash equivalents held	**228**	(105)	(336)
Cash and cash equivalents at end of year	**54,816**	73,537	27,449

The accompanying accounting policies and notes form an integral part of these financial statements.

1. General information

1.1. Group

Silence Therapeutics plc and its subsidiaries (together the 'Group') are primarily involved in the discovery, delivery and development of RNA therapeutics. Silence Therapeutics plc, a public Company limited by shares registered in England and Wales, with company number 02992058, is the Group's ultimate parent Company. The Company's registered office is 27 Eastcastle Street, London, W1W 8DH and the principal place of business is 72 Hammersmith Road, London, W14 8TH.

2. Principal accounting policies

2.1. Basis of preparation

The consolidated financial statements have been prepared in accordance with IFRS (International Financial Reporting Standards) as issued by the IASB (International Accounting Standards Board). The consolidated financial statements have been prepared under the historical cost convention as modified by revaluation to fair value of the derivative financial instrument. The accounting policies set out below have, unless otherwise stated, been prepared consistently for all periods presented in these consolidated financial statements. The financial statements are prepared in sterling and presented to the nearest thousand pounds.

New standards and interpretations not yet adopted
Certain new accounting standards and interpretations have been published that are not mandatory for December 31, 2022 reporting periods and have not been early adopted by the Group. These include amendments to IAS1 'Presentation of financial statements' on classification of liabilities. These standards are not expected to have a material impact on the entity in the current or future reporting periods and on foreseeable future transactions.

2.2. Basis of consolidation

The Consolidated financial statements consolidate those of the Company and its controlled subsidiary undertakings drawn up to December 31, 2022. The Group controls an entity when the Group is expected 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. Where necessary, adjustments are made to the financial statements of subsidiaries to bring accounting policies into line with those used for reporting the operations of the Group. All intra Group transactions, balances, income and expenses are eliminated on consolidation.

2.3. Going concern

The Group has incurred recurring losses since inception, including net losses of £40.5 million for the year ended December 31, 2022. As of December 31, 2022, the Group had accumulated losses of £263.3 million and cash outflows from operating activities for the year ended 31 December 2022 of £45.5 million.

The Group expects to incur 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 Group may develop.

To-date, the Group has funded its operations through upfront payments and milestones from collaboration agreements, equity offerings and proceeds from private placements, as well as management of expenses and other financing options to support its continued operations. During 2021, the Group received $40.0 million (£30.8 million) of the upfront payments in respect of the AstraZeneca collaboration, $45 million from a private placement of ADSs (approximately $42.0 million / £30.8 million, net of expenses) and approximately $16.0 million (£10.7 million) of the upfront payment (net of taxes withheld, based on the exchange rate at the payment date), related to the Hansoh Pharmaceutical Group Company Limited or Hansoh, collaboration executed on October 14, 2021. In August 2022 the Group raised additional funds through a registered direct offering with aggregate gross proceeds of $56.5 million (approximately £46.4 million) before deducting $4.1 million (approximately £3.3 million) in underwriting discounts, commissions and estimated offering expenses. As of December 31, 2022, the Group had cash and cash equivalents and U.S. Treasury Bills of £71.1 million ($86.0 million).

The Group has the responsibility to evaluate whether conditions and/or events raise material uncertainty about its ability to meet its future financial obligations as they become due within one year after the date that the financial statements are issued. The forecast for evaluating the going concern basis of the Group includes continued investment in our technology platform and product pipeline. The forecast does not include collaboration milestones which have not been fully achieved or other assumptions for potential future non-dilutive or dilutive funding sources. Based on this evaluation, the Group believes that its current cash and cash equivalents are only sufficient to fund its operating

expenses through the first quarter of 2024. This indicates that a material uncertainty exists that may cast significant doubt (or raise substantial doubt as contemplated by Public Company Accounting Oversight Board ("PCAOB") standards) on the Group's ability to continue as a going concern and therefore the Group may be unable to realize assets and discharge liabilities in the normal course of business.

The Group will need to raise additional funding to fund its operation expenses and capital expenditure requirements in relation to its clinical development activities. The Group may seek additional funding through public or private financings, debt financing or collaboration agreements. Specifically, the Group may receive future milestone payments of up to $14 million from existing collaboration agreements in the next 12 months which will extend the ability to fund operations beyond the first quarter of 2024. However, these future milestone payments are dependent on achievement of certain development or regulatory objectives that may not occur. The Group has an authorized open market sale agreement and can potentially raise funds through the sale of ADSs. However, there is no assurance that we will be successful in obtaining sufficient funding on terms acceptable to us, or if at all. The inability to obtain future funding could impact; the Group's financial condition and ability to pursue its business strategies, including being required to delay, reduce or eliminate some of its research and development programs, or being unable to continue operations or unable to continue as a going concern.

These consolidated financial statements have been prepared assuming that the Group will continue as a going concern which contemplates the continuity of operations, realization of assets and the satisfaction of liabilities in the ordinary course of business and do not include adjustments that would result if the Group were unable to continue as a going concern.

2.4. Research and development

The Group recognize expenditure incurred in carrying out its research and development activities in line with management's best estimation of the costs incurred to date for each separately contracted study or activity. This includes the calculation of research and development accruals at each period to account for expenditure that has been incurred. This requires estimations of the full costs to complete each study or activity and also estimation of the current stage of completion. In all cases, the full cost of each study or activity is expensed by the time the final report or, where applicable, product, has been received. Further details on research and development can be found in note 2.11.

2.5. Revenue recognition

The Group's revenue for the year ended December 31, 2022 consists of royalty income and revenue from collaboration agreements.

Royalty income

The Group's royalty income is generated by a settlement and license agreement with Alnylam. Under this 15.contract, Alnylam is obliged to pay royalties to the Group on the net sales of ONPATTRO™ in the EU in a manner commensurate with the contractual terms. Invoices are raised in arrears on a quarterly basis based on sales information provided by Alnylam no later than 75 days after the quarter end.

The royalty exemption under IFRS 15 requires sales-based data. Royalty revenue is recognized when sales data is received, based on the level of sales when the related sales occur.

Revenue from collaboration agreements

We have considered the Mallinckrodt, AstraZeneca, and Hansoh contracts and assessed whether the research and development services and license of the IP in respect of each target are distinct.

For all contracts we have concluded the license of the intellectual property and the R&D services are not distinct, as Mallinckrodt, AstraZeneca, and Hansoh cannot benefit from the intellectual property absent the R&D services, as those R&D services are used to discover and develop a drug candidate and to enhance the value in the underlying intellectual property, and these services could not be performed by another party, indicating that the two are highly

interrelated. On this basis, we have concluded that there is a single performance obligation covering both the R&D services and the license of the intellectual property in respect of each target. We recognize revenue over the duration of the contract based on an input method based on cost to cost.

The contracts have multiple elements of consideration (some or all of the following), namely:

- Upfront payments (fixed);
- Subsequent milestone payments (variable);
- FTE costs rechargeable (variable);
- Recharges of direct costs for certain research activities (variable).

The Group's effort under the contracts continues throughout their entire duration. On this basis revenue is recognized over the contract period based on costs to completion.

Revenue has been calculated on the following ongoing basis for the year ended December 31, 2022:

- Total contract costs which includes actual FTE and direct costs incurred up to December 31, 2022 and forecast FTE and direct costs for the remainder of the contract
- Actual costs incurred up until December 31, 2022 are calculated as a percentage of total contract costs (actual and forecast)
- This percentage is then multiplied by the transaction price allocated to the performance obligation in question, thus calculating the cumulative revenue which is then used to calculate the revenue to be recognized in that period. In the case of the upfront and milestones, the consideration that is multiplied is in relation to the upfront and completed milestones only. Consideration in relation to milestones not yet been achieved is excluded from the calculation.

Forecast costs are monitored each period, with revenue recognized reflecting any changes in forecast or over/under spend in actuals.

Further details of the revenue amounts recognized in the year ended December 31, 2022 can be found in note 3.

2.6. Foreign currency translation

The consolidated financial statements are presented in sterling. The individual financial statements of each Group entity are prepared in the currency of the primary economic environment in which the entity operates (its functional currency).

In preparing the financial statements of the individual entities, transactions in currencies other than the entity's functional currency (foreign currencies) are recorded at the rates of exchange prevailing on the dates of the transactions. At each balance sheet date, monetary items denominated in foreign currencies are retranslated at the rates prevailing on the balance sheet date.

Exchange differences arising on the settlement of monetary items, and on the retranslation of monetary items, are included in the income statement for the year.

For the purpose of presenting consolidated financial statements, the assets and liabilities of the Group's foreign operations (including comparatives) are translated into sterling using exchange rates prevailing on the balance sheet date. Income and expense items (including comparatives) are translated at the average exchange rates for the year unless individually significant to the Group at which point they are translated at spot rate. Exchange differences arising, if any, are recognized in equity.

2.7. Defined contribution pension funds

The contributions payable to defined contribution retirement schemes are recognized as an expense in the period to which they relate. On the payment of the contribution the Group has no further liability.

2.8. Business combinations

There were no new business combinations as defined by IFRS 3 during 2020, 2021 or 2022.

All goodwill is attributed to an acquisition that occurred in 2005. Goodwill represents the excess of the cost of the acquisition over the Group's interest in the recognized amount (generally fair value) of the identifiable assets, liabilities and contingent liabilities of the acquiree.

2.9. Property, plant and equipment

The Group holds no property assets other than leased property assets classified as right-of-use assets. See note 2.14 for further details.

All equipment and furniture is stated in the financial statements at its cost of acquisition less a provision for depreciation.

Depreciation is charged to write off the cost less estimated residual values of furniture and equipment on a straight-line basis over their estimated useful lives. All equipment and furniture is estimated to have a useful economic life of between three and ten years. Estimated useful economic lives and residual values are reviewed each year and amended if necessary.

2.10. Goodwill

Goodwill is stated at cost less any accumulated impairment losses; it is allocated to the operating segment that is expected to benefit from synergies of the related business combination and represent the lowest level within the Group at which management controls the related cash flows. Goodwill is not amortized but is tested for impairment annually, or sooner when an indication of impairment has been identified. Goodwill arising on the acquisition of a subsidiary represents the excess of the cost of acquisition over the Group's interest in the net fair value of the identifiable assets, liabilities and contingent liabilities of the subsidiary at the date of acquisition. On disposal of a subsidiary, the attributable amount of goodwill is included in the determination of the profit or loss on disposal.

2.11. Other intangible assets

Other intangible assets that are acquired by the Group are stated at cost less accumulated amortization and less accumulated impairment losses.

Amortization

Amortization is charged to the income statement on a straight-line basis over the estimated useful lives of intangible assets unless such lives are indefinite. Intangible assets with an indefinite useful life and goodwill are systematically tested for impairment at each balance sheet date. Other intangible assets are amortized from the date they are available for use. The estimated useful lives are as follows:

Licenses and software 10 – 15 years.

Capitalization of research and development costs

Costs associated with research activities are treated as an expense in the period in which they are incurred.

Costs that are directly attributable to the development phase of an internal project will only be recognized as intangible assets provided they meet the following requirements:

- an asset is created that can be separately identified;
- the technical feasibility exists to complete the intangible asset so that it will be available for sale or use and the Group has the intention and ability to do so;
- it is probable that the asset created will generate future economic benefits either through internal use or sale;
- sufficient technical, financial and other resources are available for completion of the asset; and
- the expenditure attributable to the intangible asset during its development can be reliably measured.

Careful judgment by management is applied when deciding whether recognition requirements for development costs have been met. This is necessary as the economic success of any product development is uncertain and may be subject to future technical problems at the time of recognition. Judgments are based on the information available at each balance sheet date.

To date, no development costs have been capitalized in respect of the internal projects on the grounds that the costs to date are either for the research phase of the projects or, if relating to the development phase, then the work so far does not meet the recognition criteria set out above. In most cases recognition would not occur until regulatory approval.

2.12. Impairment testing of goodwill, other intangible assets and property, plant and equipment

At each balance sheet date non-financial assets are assessed to determine whether there is an indication that the asset or the asset's cash generating unit may be impaired. At least annually or if there is such an indication, the recoverable amount of the asset or asset's cash generating unit is compared to the carrying amount.

The recoverable amount of the asset or asset's cash generating unit is the higher of the fair value less costs to sell and value in use.

Impairment losses recognized for cash generating units to which goodwill has been allocated are credited initially to the carrying amount of goodwill. Any remaining impairment loss is charged pro rata to the other assets in the cash generating unit.

2.13. Financial instruments

Financial assets and financial liabilities are recognized on the balance sheet when the Group becomes a party to the contractual provisions of the instrument.

For the periods presented in these financial statements, financial assets were classified in the following categories: derivative financial instruments, and financial assets at amortized cost. Currently other categories of financial asset are not used. Management determines the classification of its financial assets at initial recognition.

The de-recognition of financial instruments occurs when the rights to receive cash flows from investments expire or are transferred and substantially all of the risks and rewards of ownership have been transferred.

Derivative financial instruments

The Group uses forward contracts to manage exposure to risks from foreign exchange movements. Derivatives are initially recognized at fair value at the date that the contract is entered into and subsequently remeasured at each balance sheet date. The resulting gain or loss is recognized in the income statement.

Financial assets at amortized cost

Financial assets at amortized cost include trade receivables held in order to collect contractual cash flows, U.S. Treasury Bills and a term deposit held collect solely payment of the principal and interest, and deposits on property operating leases and for the procurement of materials. These are measured at initial recognition at fair value plus, if appropriate, directly attributable transaction costs and are subsequently measured at amortized cost using the effective interest method, less provision for impairment. Premiums and discounts, if any, are amortized or accreted as interest expense or income over the life of the related asset using the effective interest method. Any impairment is assessed using the Expected Credit Losses (ECL) model. The Group applies the IFRS 9 simplified approach to measuring expected credit losses which uses a lifetime expected loss allowance for trade receivables. Any impairment is recognized in the income statement.

Cash and cash equivalents

Cash and cash equivalents comprise cash on hand and demand deposits with original maturities of three months or less that are readily convertible to a known amount of cash and are subject to an insignificant risk of change in value.

Financial liabilities and equity

Financial liabilities and equity instruments issued are classified according to the substance of the contractual arrangements entered into and the definitions of a financial liability and an equity instrument. A financial liability is a contractual obligation to either deliver cash or another financial asset to another entity or to exchange a financial asset or financial liability with another entity, including obligations which may be settled using its equity instruments. An equity instrument is any contract that evidences a residual interest in the assets after deducting all of its liabilities. The accounting policies adopted for specific financial liabilities and equity instruments are set out below.

Financial liabilities

At initial recognition, financial liabilities are measured at their fair value minus, if appropriate, any transaction costs that are directly attributable to the issue of the financial liability. After initial recognition, all financial liabilities are measured at amortized cost using the effective interest method.

Equity instruments

Equity instruments issued by the Group are recorded as the proceeds received, net of direct issue costs.

2.14. Leased assets

For any new contracts entered into on or after 1 January 2019, the Group considers whether a contract is, or contains a lease. A lease is defined as ‘a contract, or part of a contract, that conveys the right to use an asset (the underlying asset) for a period of time in exchange for consideration’. To apply this definition, the Group assesses whether the contract meets two key evaluations, which are whether:

- the contract contains an identifiable asset;
- the Group has the right to obtain substantially all of the economic benefits from use of the identified asset throughout the period of use

Measurement and recognition

At lease commencement date, the Group recognizes a right-of-use asset (as part of the appropriate underlying class of assets in property, plant and equipment) and a lease liability on the balance sheet.

The right-of-use asset is measured at cost comprising the following: the amount of the initial measurement of lease liability, any lease payments made at or before the commencement date less any lease incentives received, any initial

direct costs, and restoration costs. The Group depreciates the right-of-use assets on a straight-line basis from the lease commencement date to the earlier of the end of the useful life of the right-of-use asset or the end of the lease term. The Group also assesses the right-of-use asset for impairment when such indicators exist.

At the commencement date, the Group measures the lease liability at the present value of the lease payments unpaid at that date, discounted using the Group's incremental borrowing rate. Lease payments included in the measurement of the lease liability are made up of fixed payments (including in substance fixed), variable payments based on an index or rate, amounts expected to be payable under a residual value guarantee and payments arising from options reasonably certain to be exercised. Subsequent to initial measurement, the liability will be reduced for payments made and increased for interest.

The Group has elected to account for short-term leases (leases with a duration of less than 12 months) and leases of low-value assets using the practical expedients. Instead of recognizing a right-of-use asset and lease liability, the payments in relation to these are recognized as an expense in profit or loss on a straight-line basis over the lease term.

The interest payments for leases are recognized in the statement of cashflows under finance and other expenses.

Lease break clauses and extension options

When the Group has the option to extend a lease, management uses its judgment to determine whether or not an option would be reasonably certain to be exercised. Management considers all facts and circumstances including past practice and any cost that will be incurred to change the asset if an option to extend is not taken, to help determine the lease term.

Similarly, when a break clause exists in the lease agreement, management must consider the likelihood of this option to curtail the lease being exercised.

2.15. Share-based payments

Historically the Group has issued equity settled share-based payments to certain employees (see note 25). Equity settled share-based payments are measured at fair value (excluding the effect of non-market-based vesting conditions) at the date of grant. The fair value so determined is expensed on a straight-line basis over the vesting period, based on the Group of the number of shares that will eventually vest and adjusted for the effect of non-market-based vesting conditions.

The value of the charge is adjusted to reflect expected and actual levels of award vesting, except where failure to vest is as a result of not meeting a market condition.

Cancellations of equity instruments are treated as an acceleration of the vesting period and any outstanding charge is reversed in full immediately.

Fair value is measured using a Black Scholes model, binomial pricing model, or Monte Carlo model. The key assumptions used in the model have been adjusted, based on management's best estimate, for the effects of non-transferability, exercise restrictions and behavioral considerations.

Any payment made to a counterparty on the cancellation or settlement of a grant of equity instruments (even if this occurs after the vesting date) should be accounted for as a repurchase of an equity interest (that is, as a deduction from equity). But, if the payment exceeds the fair value of the equity instruments repurchased (measured at the repurchase date), any such excess should be recognized as an expense.

2.16. Equity

Share capital is determined using the nominal value of shares that have been issued.

The share premium account includes any premiums received on the initial issuing of the share capital. Any transaction costs associated with the issuing of shares are deducted from the share premium account, net of any related income tax benefits.

The merger reserve represents the difference between the nominal value and the market value at the date of issue of shares issued in connection with the acquisition by the Group of an interest in over 90% of the share capital of another company.

Equity settled share-based payments are credited to a share-based payment reserve as a component of equity until related options or warrants are exercised.

Foreign currency translation differences are included in the translation reserve.

Profit and loss account (deficit) includes all current and prior period results as disclosed in the income statement.

2.17. Taxation

Current tax payable is based on taxable profit for the year. Taxable profit differs from profit as reported in the income statement because it excludes items of income or expense that are taxable or deductible in other years and it further excludes items that are never taxable or deductible. Current tax liabilities are calculated using tax rates that have been enacted or substantively enacted by the balance sheet date.

Tax receivable arises from the U.K. legislation regarding the treatment of certain qualifying research and development costs, allowing for the surrender of tax losses attributable to such costs in return for a tax rebate. Research and development tax credits are recognized when the receipt is probable. Research and development costs which are not eligible for reimbursement under the U.K. Research and Development Tax Credit scheme, such as expenditure incurred on research projects for which the group receives income, may be reimbursed under the U.K. Research and Development Expenditure Credit ("RDEC") scheme. Amounts receivable under the RDEC scheme are presented within the Income Statement within Research and Development costs.

Deferred tax is recognized on differences between the carrying amounts of assets and liabilities in the financial statements and the corresponding tax bases used in the computation of taxable profit and is accounted for using the balance sheet liability method. Deferred tax liabilities are generally recognized for all taxable temporary differences and deferred tax assets are recognized to the extent that it is probable that taxable profits will be available against which deductible temporary differences can be utilized.

Such assets and liabilities are not recognized if the temporary difference arises from initial recognition of goodwill or from the initial recognition (other than in a business combination) of other assets and liabilities in a transaction that affects neither the taxable profit nor the accounting profit.

Deferred tax liabilities are recognized for taxable temporary differences arising on investments in subsidiaries except where the Group is able to control the reversal of the temporary difference and it is probable that the temporary difference will not reverse in the foreseeable future.

The carrying amount of deferred tax assets is reviewed at each balance sheet date and reduced to the extent that it is no longer probable that sufficient taxable profits will be available to allow all or part of the asset to be recovered.

Deferred tax is calculated at the tax rates that are expected to apply in the period when the liability is settled, or the asset realized. Deferred tax is charged or credited to the income statement, except when it relates to items charged or credited directly to equity, in which case the deferred tax is also dealt with in equity.

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 Group intends to settle its current tax assets and liabilities on a net basis.

Withholding tax is payable on gross income from dividends, interest, lease of property, royalties, and other China-source passive income since the Group does not have an establishment or place of business in China.

2.18. Critical accounting estimates and judgments and key sources of estimation uncertainty

In the process of applying the entity's accounting policies, management makes estimates and judgments that have an effect on the amounts recognized in the financial statements. Although these estimates are based on management's best knowledge of current events and actions, actual results may ultimately differ from those estimates.

The critical judgments concerning the future, and other key sources of estimation uncertainty at the balance sheet date, that have a significant risk of causing a material adjustment to the carrying amounts of assets and liabilities within the next financial year, are described below:

- Application of IFRS 15 in determining revenue from contracts with customers specifically:

  - The determination of the numbers of performance obligations. Judgment was previously required in determining whether the license and the R&D activities are distinct performance obligations or not at the time collaboration agreements were executed. It is considered the license of the IP and the R&D activities are not distinct as the R&D services are essential to discover and develop a drug candidate and enhance the value in the underlying IP. In addition, the gene targets are highly specialized such that only the Group has the specialist knowledge to apply the IP to the specific target. On this basis, it was concluded that there is only one single performance obligation covering both the R&D services and licenses of the IP in respect of each target at the time the agreements were executed;

  - The allocation of the upfront payments between performance obligations (judgment). Mallinckrodt paid the Group $20 million in 2019, AstraZeneca paid the Group $60 million in 2020 and 2021, and Hansoh paid $16 million upfront in 2021.These upfront payments were considered the initial transaction price. A judgment was required to determine how this should be allocated across the contracted targets. In 2019, due to the compounds being at similar stages of development at the time of contract execution, the $20 million paid by Mallinckrodt was allocated evenly, on the basis of a benchmarking exercise considering the standalone selling price per target of past deals announced to the market by comparable companies; Similarly the $60 million paid by AstraZeneca was allocated evenly across target options for AstraZeneca. The Hansoh $16 million upfront payment was allocated $4 million for each of the two targets in Greater China, Hong Kong, Macau and Taiwan and $8 million for the global target based on the benchmarking exercise, as well as consideration for geography licensed and other contractual terms. These initial transaction amounts are recognized as revenue over the life of the performance obligations for each contract.

  - The estimate of future costs to be incurred to determine percentage of completion of revenue contracts:

    In determining the percentage of completion of the revenue projects, the Group estimated the total future costs expected to be incurred through the life of the performance obligations per the contract. An increase in future costs could arise as a result of a requested change in scope by the collaboration partner or through higher than anticipated internal costs incurred by Silence. The impact of a change in scope would be largely neutral on revenue recognition because there would be consequential increases in revenue to match the additional costs. There is no experience of internal costs being higher than anticipated to date, but if this were the case then a 10% increase in future estimated costs would lead to a 0.4% increase in revenue.

2.19. Segment reporting

- Operating segments are reported in a manner consistent with the internal reporting provided to the Board. The chief operating decision maker (CODM), who is responsible for allocating resources and assessing performance of the operating segments, has been identified as the Group's Chief Executive Officer. The Group has a single reportable segment (see note 4).

3. Revenue

Revenue from collaboration agreements for the year ended December 31, 2022 predominately relates to the research collaboration agreements the Company entered into with Mallinckrodt in July 2019 and AstraZeneca in March 2020.

Revenue comprised £0.6 million of royalty income (2021: £0.4 million; 2020: £0.2 million) and £16.9 million of Research collaboration income (2021: £12.0 million; 2020: £5.3 million). Disaggregation of revenue from contracts with customers is as follows:

	Year ended December 31,		
	2022	2021	2020
	£000s	£000s	£000s
Revenue from Contracts with Customers			
Research collaboration - Mallinckrodt plc	**11,658**	8,748	3,817
Research collaboration - AstraZeneca	**5,081**	2,652	22
Research collaboration - Other	**184**	623	1,414
Research collaboration - total	**16,923**	12,023	5,253
Royalties	**578**	392	226
Total revenue from contracts with customers	**17,501**	12,415	5,479

Under our collaboration agreement with Mallinckrodt, we received an upfront cash payment of £16.4 million ($20 million) in 2019 and are eligible to receive specified development, regulatory and commercial milestone payments. We received milestone payments totaling £2.2 million or $3 million (2021: £2.9 million; 2020: £1.4 million) during the year ended December 31, 2022. In addition to these payments, Mallinckrodt has agreed to fund some of our research personnel and preclinical development costs. We recognize the upfront payment, milestone payments, payments for personnel costs and other research funding payments over time, in accordance with IFRS 15 para 35 c). During the year ended December 31, 2022, we recognized a total of £11.7 million in revenue under this agreement (2021: £8.7 million; 2020: £3.8 million).

Under our collaboration agreement with AstraZeneca, we received an upfront cash payment of £17.1 million ($20 million) in 2020 with a further amount of £30.8 million ($40 million) received in May 2021. We are also eligible to receive specified development and commercial milestone payments as well as tiered royalties on net sales, if any. We recognize the upfront payment and milestone payments over time, in accordance with IFRS 15 para 35 c). During the year ended December 31, 2022, we recognized a total of £5.1 million in revenue under this agreement (2021: £2.7 million; 2020: £22 thousand).

We entered into a collaboration agreement with Hansoh on October 15, 2021. We received a $16 million (equivalent to approximately £11.9 million based on the exchange rate at the payment date and $14.4 million or £10.7 million, net of taxes) upfront payment to us in December 2021. We are eligible to receive development, regulatory and commercial milestones as well as royalties on Hansoh net product sales. During the year ended December 31, 2022, the Company triggered milestone payments totaling $2.0 million (£1.5 million) (2021: £nil). We recognize the upfront payment and milestone payments over time, in accordance with IFRS 15 para 35 c). During the year ended December 31, 2022, we recognized a total of £0.2 million in revenue under this agreement (2021: £32 thousand; 2020: nil).

In December 2018, we entered into a settlement and license agreement with Alnylam Pharmaceuticals Inc., or Alnylam, pursuant to which we settled outstanding patent litigation with Alnylam related to its RNAi product ONPATTRO. As part of the settlement, we license specified patents to Alnylam, and Alnylam pays us a tiered royalty of up to one percent of net sales of ONPATTRO in the European Union. We are eligible to receive these royalties through December 2023. We invoice Alnylam quarterly in arrears based on sales data for that quarter as reported to us by Alnylam. Royalty revenue is recognized based on the level of sales when the related sales occur. During the year ended December 31, 2022, we recognized a total of £0.6 million in royalty income from Alnylam (2021: £0.4 million; 2020: £0.2 million).

4. Segment reporting

In 2022, the Group operated in the specific technology field of RNA therapeutics.

Business segments

The Group has identified the Chief Executive Officer as the CODM. For the 12 months ended December 31, 2022 and 2021, the CODM determined that the Group had one business segment, the development of RNAi-based medicines. This is consistent with reporting to senior management. The information used internally by the CODM is the same as that disclosed in the financial statements.

An analysis of the group's assets and revenues by location is shown below:

	U.S.A.	U.K.	Germany	Total
	£000s	£000s	£000s	£000s
Non-current assets				
As at December 31, 2021	17	516	9,328	9,861
As at December 31, 2022	**-**	**1,166**	**9,648**	**10,814**
Revenue analysis for the year ended December 31, 2020				
Research collaboration	-	5,253	-	5,253
Royalties	-	-	226	226
	-	5,253	226	5,479
Revenue analysis for the year ended December 31, 2021				
Research collaboration	-	12,023	-	12,023
Royalties	-	-	392	392
	-	12,023	392	12,415
Revenue analysis for the year ended December 31, 2022				
Research collaboration	**-**	**16,923**	**-**	**16,923**
Royalties	**-**	**-**	**578**	**578**
.	**-**	**16,923**	**578**	**17,501**

5. Operating loss

This is stated after charging/(crediting):

	Year ended December 31,		
	2022	2021	2020
	£000s	£000s	£000s
Depreciation of property, plant and equipment	**478**	411	476
Amortization of intangibles	**4**	16	20
Share-based payments charge	**10,252**	8,632	4,395
(Gain)/loss on disposal of property, plant and equipment	**-**	-	(3)
Short lease payments on premises	**410**	332	347
Fees payable to the Company's auditors for the audit of the Company and the consolidation:			
- audit fees	**463**	403	284
- other assurance services	**150**	180	431

6. Directors and staff costs

Staff costs, including Directors' remuneration, during the year for the Group were as follows:

	Year ended December 31,		
	2022	2021	2020
	£000s	£000s	£000s
Wages and salaries	**14,760**	10,837	6,656
Social security costs	**1,434**	1,491	827
Other pension costs	**429**	319	201
Share-based payments charge	**10,252**	8,632	4,395
Total aggregate remuneration	**26,875**	21,279	12,079

	Year ended December 31,		
	2022	2021	2020
	Number	Number	Number
Research and development and related support services	**88**	66	39
Administration	**28**	26	26
Total average number of employees	**116**	92	65

7. Other losses

	Year ended December 31,		
	2022	**2021**	**2020**
	£000s	£000s	£000s
Net foreign exchange losses	**-**	-	(4,864)
Net fair value gain on derivative	**-**	-	1,492
Total Other losses	**-**	-	(3,372)

8. Finance and other expenses

	Year ended December 31,		
	2022	2021	2020
	£000s	£000s	£000s
Lease liability interest expense	**47**	8	16
Net foreign exchange losses	**-**	44	307
Total Finance and other expenses	**47**	52	323

9. Finance and other income

	Year ended December 31,		
	2022	2021	2020
	£000s	£000s	£000s
Bank interest receivable	**23**	10	129
Accretion on U.S Treasury Bills	**203**	-	-
Net foreign exchange gains	**1,046**	-	-
Total Finance and other income	**1,272**	**10**	**129**

10. Taxation

The entire tax credit of £6.9m relates to current tax as shown below. No deferred tax was recognized in the year.

	December 31 2022 £000s	2021 £000s
Current Tax Expense		
Current Year	**(7,280)**	**(5,571)**
Changes in estimate related to prior years	**401**	**(875)**
Total current tax	**(6,879)**	(6,446)
Deferred Tax Expense		
Origination and reversal of temporary differences	**-**	**-**
Change in tax rate	**-**	**-**
Recognition of previously unrecognized tax losses	**-**	**-**
Recognition of previously unrecognized tax losses (derecognition of previously recognised) deductible temporary differences	-	-
Taxation	**(6,879)**	**(6,446)**

The deferred tax charge in 2022 was nil (2021: nil; 2020: nil). Reconciliation of tax credit at standard rate of U.K. corporation tax to the current tax credit:

	Year ended December 31, 2022 £000s	2021 £000s	2020 £000s
Loss before tax	**(47,368)**	(45,856)	(36,041)
Tax credit at the standard rate of U.K. corporation tax of 19% (2020: 19%; 2019: 19%)	9,000	8,713	6,848
Effect of overseas tax rate	544	(264)	(85)
Impact of unrelieved tax losses not recognized	(9,948)	(8,639)	(6,763)
Adjustment in respect of prior year	(401)	875	(42)
Research and development tax credit in respect of current year	7,836	6,945	3,536
Effect of overseas taxes	(152)	(1,184)	-
	6,879	6,446	3,494

Estimated tax losses of £167.8 million (2021: £154.1 million; 2020: £135.6 million) are available for relief against future profits.

The deferred tax asset not recognized in these financial statements on the estimated losses and the treatment of the equity settled share- based payments, net of any other temporary differences is detailed in note 23. During the year, the Group had not yet received a research and development tax credit related to the prior year (2021: £4.4 million; 2020: £3.02 million). The Group has accrued £7.8 million (2021: £6.95 million; 2020: £3.54 million) recognizing a current tax asset in respect of 2022 research and development tax credits. Research and development tax credit in respect of the current year includes amounts for unfunded projects that are permissible to claim under the Small or Medium Enterprise ('SME') R&D tax scheme. In addition to this we have also recognised £0.5m of income from the RDEC scheme in the income statement within research and development costs. The company had a foreign tax expense of £0.4 million. (2021: £0.2 million; 2020: £nil).

The corporation tax main rate during 2022 was 19% (2021: 19%; 2020: 19%). In the Spring Budget 2021, the U.K. Government announced that from 1 April 2023 the corporation tax rate will increase to 25%. As the company has not recognized any related deferred tax assets as at 31, December 2022, the tax rate increase has no impact.

Since the Group does not have an establishment or place of business in China, the Group is subject to withholding tax on gross income from dividends, interest, lease of property, royalties, and other China-source passive income. In 2021 the Group entered into a collaboration agreement with Hansoh, a biopharmaceutical company in China and received a $16 million upfront payment, which required withholding tax of $1.6 million. In 2022 the Group received a milestone payment of £1.5 million ($2.0 million), which required withholding tax of £0.2 million.

11. Loss per ordinary equity share (basic and diluted)

The calculation of the loss per share is based on the loss for the financial year after taxation of £40.5 million (2021: loss of £39.4 million; 2020: loss of £32.5 million) and on the weighted average of 96,584,512 (2021: 88,950,441; 2020: 81,772,124) ordinary shares in issue during the year.

The options outstanding at December 31, 2022, December 31, 2021 and December 31, 2020 are considered to be anti-dilutive as the Group is loss-making.

12. Property, plant and equipment

	Equipment and furniture	Right-of-use asset	Total
	£000s	£000s	£000s
Cost			
At January 1, 2021	4,066	456	4,522
Additions	1,311	-	1,311
Disposals	(46)	(111)	(157)
Translation adjustment	(219)	-	(219)
At December 31, 2021	5,112	345	5,457
At January 1, 2022	5,112	345	5,457
Additions	140	499	639
Disposals	(506)	(346)	(852)
Translation adjustment	240	-	240
At December 31, 2022	**4,986**	**498**	**5,484**
Accumulated depreciation			
At January 1, 2021	3,274	121	3,395
Charge for the year	238	173	411
Eliminated on disposal	(46)	(74)	(120)
Translation adjustment	(173)	-	(173)
At December 31, 2021	3,293	220	3,513
At January 1, 2022	3,293	220	3,513
Charge for the year	306	172	478
Eliminated on disposal	(506)	(346)	(852)
Translation adjustment	144	-	144
At December 31, 2022	**3,237**	**46**	**3,283**
Net book value			
As at December 31, 2021	1,819	125	1,944
As at December 31, 2022	**1,749**	**452**	**2,201**

13. Goodwill

	Year ended December 31,	
	2022	2021
	£000s	£000s
Balance at start of year	**7,592**	8,125
Translation adjustment	**417**	(533)
Balance at end of year	**8,009**	7,592

The recoverable amount is based on fair value less cost of disposal.

The key assumptions used in the valuation models to determine the fair value less cost of disposal are as follows:

- Fair value has been determined as market capitalization (share price x number of shares in issue) at December 31, 2022
- Disposal costs have been estimated to be minimal

Goodwill is assessed at a segment level. As there is only one operating segment, we have considered the fair value of the entire business as market capitalization at December 31, 2022, which was £453.3 million (2021:£528.8 million), with share price not dropping significantly below its December 31, 2022 value at any point so far in 2023, and therefore a sensitivity analysis has not been presented.

14. Other intangible assets

	Licenses & software
	£000s
Cost	
At January 1, 2021	107
Additions	23
Translation adjustment	
At December 31, 2021	130
At January 1, 2022	130
Additions	300
Translation adjustment	-
At December 31, 2022	**430**
Accumulated depreciation	
At January 1, 2021	90
Charge for the year	16
Translation adjustment	
At December 31, 2021	106
At January 1, 2022	106
Charge for the year	4
Translation adjustment	-
At December 31, 2022	**110**
Net book value	
As at December 31 2021	24
As at December 31 2022	**320**

The intangible assets included above have finite useful lives estimated to be of 10–15 years from the date of acquisition, over which period they are amortized or written down if they are considered to be impaired. Internally generated patent costs are only recorded where they are expected to lead directly to near-term revenues, none have been capitalized to date.

15. Cash and cash equivalents

	December 31, 2022	2021
	£000s	£000s
Cash at bank and in hand	**41,986**	73,537
US Treasury Bills	**12,376**	-
Short term bank deposits	**454**	-
Total Cash and cash equivalents	**54,816**	73,537

Cash at bank comprises balances held by the Group in current, short-term bank deposits, and U.S. Treasury Bills with an original maturity of three months or less. The carrying amount of these assets approximates to their fair value.

16. DERIVATIVE FINANCIAL INSTRUMENTS

Derivative financial instruments related to an open forward currency contract measured at fair value through the income statement. The fair value was calculated from data sourced from an independent financial market data provider using mid-market-end-of-day data as of December 31, 2020. The derivative contract that was in place at December 31, 2020 was closed out on May 28, 2021.

The fair value of the derivative is calculated based on level 2 inputs under IFRS 13.

The fair value of financial instruments that are not traded in active market, in the case of an over-the-counter derivative, is determined using valuation techniques which maximize the use of observable market data and rely as little as possible on entity specific estimates. As all significant inputs required to fair value an instrument are observable, this derivative financial instrument is included in level 2.

The specific valuation technique used to value this derivative is the present value of future cash flow based on the forward exchange rate relative to its value based on the year-end exchange rate.

The derivative fair value movement is disclosed in the Income Statement under “Other (losses)/gains – net”. For the year ended December 31, 2021 the gain on the derivative financial instrument (£1.02 million), which was closed out in May 2021, matched the related foreign exchange loss (£1.02 million) on the receivable, resulting in a net nil impact on the Income Statement.

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17. Financial assets at amortized cost

Non-current financial assets at amortized cost primarily relate to deposits for properties.

Current financial assets at amortized cost, other than trade receivables as disclosed in note 19, include U.S. Treasury Bills (with maturities from purchase date over three months) of £16.3 million (2021: nil).

	December 31, 2022	2021
	£000s	£000s
Current financial assets at amortized cost – U.S Treasury Bills	**16,328**	-
Total financial assets at amortized cost - current	**16,328**	-
Non-current financial assets at amortized cost	**284**	301
Total financial assets at amortized cost	**16,612**	**301**

18. Other current assets

	December 31, 2022	2021
	£000s	£000s
Prepayments	**8,200**	4,309
VAT receivable	**1,545**	1,211
Total other current assets	**9,745**	5,520

19. Trade receivables

	December 31, 2022	2021
	£000s	£000s
Trade receivables	**915**	331

The Directors consider that the carrying amount of trade receivables approximates to their fair value.

No interest is charged on outstanding receivables. There were no overdue trade receivables balances.

The Group has applied an expected credit loss model to the balance and determined that £nil (2021: £nil) provision is required.

20. Trade and other payables

	December 31, 2022	2021
	£000s	£000s
Trade payables	**3,186**	4,065
Social security and other taxes	**467**	318
Accruals and other payables	**8,391**	6,215
Corporate income tax payable	**589**	185
Total trade and other payables	**12,633**	10,783

The Directors consider that the carrying amount of trade and other payables approximates to their fair value.

21. Lease liability

	December 31, 2022	2021
	£000s	£000s
Lease liability	**446**	137
Total lease liability	**446**	137

The lease liability recognized on the face of the balance sheet comprises the Group's London office, which was renegotiated upon completion of the original term, with the new term beginning in September 2022. The repayment of the principal portion of these lease liabilities for the year-ending December 31, 2022 was £0.2 million (2021: £0.2 million).

There are 2 short-term leases in Berlin, Germany and three leases in Hoboken, U. S., not included in the lease liability above. Both leases in Berlin are on a rolling contract basis with either party being able to end the lease with a cancellation notice period of 11.5 months, while the leases in the U. S. are on a rolling contract basis with a notice period of three months, thus allowing exemption using the practical expedient, without significant cost.

22. Contract liabilities

Contract liabilities comprise entirely deferred revenue in respect of the Mallinckrodt, AstraZeneca plc, and Hansoh research collaborations. The current contract liabilities represent the amount of estimated revenue to be reported in the next 12 months related to amounts invoiced to our partners. Current and non-current contract liabilities include future revenue from collaboration recharged expenses, upfront payments, and milestones achieved to December 31, 2022.

	December 31, 2022	December 31, 2021
	£000s	£000s
Contract liabilities:		
Current	**8,864**	**4,247**
Non-current	**63,485**	**72,501**
Total contract liabilities	**72,349**	**76,748**

	Total
	£000s
Contract liabilities:	
At January 1, 2021	68,379
Additions during period	20,392
Revenue unwound during period	(12,023)
At December 31, 2021	**76,748**
At January 1, 2022	76,748
Additions during period	12,519
Revenue unwound during period	(16,918)
At December 31, 2022	**72,349**

23. Deferred tax

The Group has the following unrecognized deferred tax assets as at December 31, 2022:

	December 31,			
	Gross	Net	Gross	Net
	2022	2022	2021	2021
	£000s			£000s
Trading losses	**167,828**	**44,136**	152,060	33,910
Share based payments	**8,995**	**2,249**	16,625	3,159
Capital losses	**7,873**	**1,968**	7,873	1,496
Total unrecognized deferred tax asset	**184,696**	**48,353**	176,558	38,565

To total unrecognized deferred tax assets are calculated based on the main corporate tax rate of 25% (19% for 2021 and 2020) as this is the tax rate applicable to when we expect to utilize the these deferred tax assets. Unrecognized deferred tax assets from foreign trading losses are calculated at the tax rate applicable to the related jurisdiction.

Deferred tax assets are recognized where it is probable that future taxable profit will be available to utilize losses. Due to the uncertainty of future capital gains, a deferred tax asset in respect of capital losses was not recognized at December 31, 2022 (2021: nil).

24. Share capital

	December 31,		
	2022	2021	2020
	£000s	£000s	£000s
Authorized, allotted, called up and fully paid ordinary shares, par value £0.05	5,390	4,489	4,165
	Number	Number	Number
Number of shares in issue	107,808,472	89,784,720	83,306,259

The Group has only one class of share. All ordinary shares have equal voting rights and rank pari passu for the distribution of dividends.

On February 5, 2021 the Group announced a private placement of 2,022,218 of the Company's American Depositary Shares ("ADSs"), each representing three ordinary shares, at a price of US $22.50 per ADS, with new and existing institutional and accredited investors (the "Private Placement"). The aggregate gross proceeds of the Private Placement was US $45 million (approximately £33 million) before deducting approximately £2.4 million in placement agent fees and other expenses. The financing syndicate included Adage Capital Management LP, BVF Partners L.P., Consonance Capital, Great Point Partners, LLC, and other investors.

On October 15, 2021, the Company filed a registration statement on Form F-3 with the SEC to cover the offering, issuance and sale of securities from time to time in one or more offerings of up to $300,000,000 in aggregate, which includes a sale of up to $100,000,000 of ADSs that may be issued and sold under an Open Market Sale Agreement, dated October, 15, 2021, with Jefferies LLC.

On November 30, 2021, the Company completed delisting from AIM. As a result, the Company converted the existing employee share options to ADSs which represents three ordinary shares and the exercise price was also converted to represent an ADS price at an exchange rate equal to the average of the last five business trading days currency conversion of sterling pounds to US dollars, which was 1.334058 sterling pounds to 1 US dollar. This is not a modification of the existing share option grants, as the value or timing of the grants was unchanged.

On August 11, 2022 the Group announced a registered direct offering (the "Offering") of 5,950,000 of the Company's ADSs, each representing three ordinary shares, at a price of $9.50 per ADS, with new and existing institutional and accredited investors. The aggregate gross proceeds of the Offering was $56.5 million (approximately £46.4 million) before deducting $4.1 million (approximately £3.3 million) in underwriting discounts, commissions and estimated offering expenses.

Details of the shares issued during the current and previous year are as follows:

Number of shares in issue at January 1, 2020	78,370,265
Shares issued during the year	4,276,580
Options exercised at £0.05	496,666
Options exercised at £0.85	56,470
Options exercised at £1.00	60,000
Options exercised at £1.90	46,278
Number of shares in issue at December 31, 2020	83,306,259
Shares issued during the year	6,066,654
Options exercised at £0.05	66,114
Options exercised at £0.85	121,854
Options exercised at £1.00	25,000
Options exercised at £1.28	720
Options exercised at £1.90	198,119
Number of shares in issue at December 31, 2021	89,784,720
Shares issued during the year	17,850,000
Options exercised at $0.20/ADS or $0.07/ordinary share	84,835
Options exercised at $4.16/ADS or $1.39/ordinary share	16,968
Options exercised at $5.12/ADS or $1.72/ordinary share	12,951
Options exercised at $5.88/ADS or $1.96/ordinary share	24,000
Options exercised at $7.32/ADS or $2.44/ordinary share	15,000
Options exercised at $7.60/ADS or $2.53/ordinary share	19,998
Number of shares in issue at December 31, 2022	**107,808,472**
Number of equivalent ADS in issue at December 31, 2022	**35,936,157**

At December 31, 2022, there were options outstanding of 11,571,487 (2021: 8,052,699; 2020: 6,768,894) unissued ordinary shares.

Details of the options outstanding are as follows:

Year of issue	Weighted average Exercise price (£)	WeightedaverageExerciseprice($)	At January 1, 2022	Options granted	Options forfeited	Options expired	Options exercised	At December 31, 2022	Weighted average years to expiry date
2014	3.50	4.23	4,000	-	-	-	-	4,000	1.67
2015	3.50	4.23	3,333	-	-	-	-	3,333	2.52
2016	4.25	5.14	19,832	-	-	-	(9,973)	9,859	3.35
2017	6.00	7.25	46,240	-	-	-	(8,000)	38,240	4.83
2018	0.18	0.21	70,233	-	-	-	(14,876)	55,357	5.22
2019	4.31	5.21	763,260	-	(12,666)	-	(25,068)	725,526	6.73
2020	18.38	22.22	1,040,023	-	(316,573)	-	-	723,450	7.58
2021	17.33	20.95	737,312	-	(36,839)	-	-	700,473	8.27
2022	18.44	22.30	-	1,940,377	(343,453)	-	-	1,596,924	9.28
Total (ADSs)			**2,684,233**	**1,940,377**	**(709,531)**	**-**	**(57,917)**	**3,857,162**	
Total (Ordinary Shares)			**8,052,699**	**5,821,131**	**(2,128,593)**	**-**	**(173,752)**	**11,571,487**	

ADSs represent three ordinary shares and the exercise price was also converted to represent an ADS price at an exchange rate equal to the closing current year currency conversion of sterling pounds to US dollars, which was 1.208971 sterling pounds to 1 US Dollar.

The market price of Company shares at the year-end was $15.25/ADS or ($5.08 or 420 pence/share). (2021: $23.89/ADS ($7.96 or 590 pence/share); 2020: 514 pence). During the year the minimum and maximum prices were $7.80 and $24.66 per ADS (215 pence and 680 pence per ordinary share), respectively (2021: 443 pence and 680 pence; 2020: 304 pence and 515 pence).

25. Equity-settled share-based payments

The Group has issued share options under the 2018 Long Term Incentive Plan (LTIP), 2018 Non-Employee Long Term Inventive Plan (Non-Employee LTIP), and individual share option contracts, open to all employees of the Group, as well as EMI shares (none of which remain outstanding at December 31, 2022). Under the LTIP, Non-Employee LTIP, individual contracts and schemes available, the options typically vest after 3 years, with the exception of some options granted to certain members of key management personnel. The vesting period for these options ranges from 3 to 33 months. The options usually lapse after one year following the employee leaving the Group.

	2022			2021		2020	
	Number of ADSs(1)	**Weighted Average Exercise price**	**Weighted Average Exercise price**	Number Of Shares	Weighted Average Exercise price	Number Of Shares	Weighted Average Exercise price
		$	**Pence**		Pence		Pence
Options							
Outstanding at the beginning of the year	**2,684,233**	**7.32**	**605.63**	6,768,894	226.83	4,302,617	102.46
Granted during the year	**1,940,377**	**22.30**	**1,844.41**	2,259,153	554.60	3,178,216	351.90
Lapsed or forfeited during the year	**(709,531)**	**29.25**	**2,419.76**	(563,541)	146.02	(52,525)	5.00
Exercised during the year	**(57,917)**	**3.20**	**265.05**	(411,807)	116.62	(659,414)	33.48
Outstanding at the year-end (ordinary shares/pence)				8,052,699	329.74	6,768,894	226.83
Outstanding at the year-end (ADS/$)	**3,857,162**	**15.10**	**1,248.95**	2,684,233	7.32		
Exercisable at the year-end	**1,889,460**	**13.24**	**1,095.01**	2,503,504	263.45	1,079,609	151.33

The table above shows the number of options in relation to ordinary shares and equivalent ADSs outstanding and exercisable at year end, on the conversion ratio of three ordinary share options to one ADS as disclosed in note 24.

The options outstanding at the year-end have a weighted average remaining contractual life of 8.2 years (2021: 8.3 years; 2020: 7.4 years). The weighted average share price at the time of exercise during the year was 318.31 pence per ordinary share or $10.97 per ADS (2021: 575.39 pence; 2020: 435.19 pence).

The Group granted 5,821,131 share options during the year (2021: 2,259,153; 2020: 3,178,216). The fair value of options granted were calculated using Black Scholes model for 2022. Prior to January 1, 2022, the fair value of options granted were calculated using a Binomial or Monte Carlo model. Inputs into the model were as follows:

	2022	2021	2020
Inputs and assumptions for options granted in the year:			
Weighted average share price (pence)	**537.4**	586	461
Weighted average ADS price ($)	**19.5**		
Weight average hurdle price (pence)	**n/a**	n/a	90.0
Weighted average exercise price (pence)	**673.8**	520.0	352.0
Weighted average ADS price ($)	**24.4**		
Option life (years)	**8.9**	10.0	10.0
Expected volatility	**56%-74%**	65%-70%	70%-72%
Risk free rate	**1.16%-3.57%**	0.28%-1.04%	0.19%-0.44%
Expected dividend yield	**nil**	nil	nil

The Group recognized total charges of £10.3 million (2021: £8.6 million; 2020: £4.4 million) related to equity settled share-based payment transactions during the year.

Fair value of the grants has been calculated using volatility assumptions between 56% and 74%, based on the three year historical volatility as at the respective date of grant.

The Group does not bear any responsibility to settle any employee tax obligations that arise on the exercise of share options. The estimated employer tax obligation on outstanding options at the year-end was £0.4 million (2021: £0.6 million; 2020: £0.5 million;).

26. Capital reserves

The capital redemption reserve was created in 2012 following the reduction of nominal share capital to 0.1p per share. It is required under Section 733 of the Companies Act 2006, held to maintain the capital of the Company when shares are bought back and subsequently cancelled without court approval.

Due to the size of the deficit on the accumulated losses account, the Company has no distributable reserves.

The share premium account reflects the premium to nominal value paid on issuing shares less costs related to the issue. The merger reserve was created on issuance of shares relating to the acquisition of Silence Therapeutics GmbH.

The share-based payments reserve reflects the cost to issue share-based compensation, primarily employee share options.

	Share Premium account	Merger reserve	Share-based Payment reserve	Capital redemption reserve	Total
	£000s	£000s	£000s	£000s	£000s
At January 1, 2020	138,150	22,248	1,651	5,194	167,243
Shares issued	15,396	-	-	-	15,396
On options in issue during the year	-	-	4,395	-	4,395
On options exercised during the year	188	-	(331)	-	(143)
Movement in the year	15,584	-	4,064	-	19,648
At December 31, 2020	153,734	22,248	5,715	5,194	186,891
Shares issued	32,585	-	-	-	32,585
On options in issue during the year	-	-	8,632	-	8,632
On options exercised during the year	460	-	(659)	-	(199)
Costs capitalized in respect of issuance of shares during the period	(2,447)				(2,447)
Movement in the year	30,598	-	7,973	-	38,571
At December 31, 2021	184,332	22,248	13,688	5,194	225,462
Shares issued	45,533	-	-	-	45,533
On options in issue during the year	-	-	10,252	-	10,252
On options exercised during the year	153	-	(192)	-	(39)
Costs capitalized in respect of issuance of shares during the period	(3,348)				(3,348)
Movement in the year	42,338	-	10,060	-	52,398
At December 31, 2022	**226,670**	**22,248**	**23,748**	**5,194**	**277,860**

27. Capital commitments and contingent liabilities

There were no capital commitments at December 31, 2022 (2021: nil; 2020: nil).

28. Commitments under short leases

At December 31, 2022, the Group had a gross commitment on its office rental and service charge in Berlin, Germany and the Hoboken, U.S. lease equal to £0.3 million (2021: £0.3 million; 2020: £0.1 million) in the next year. No amounts are payable after more than one year.

In addition, the Group enters into contracts in the normal course of business with contract research organizations to assist in the performance of research and development activities and other services and products for operating purposes. These contracts generally provide for termination on notice, and therefore are cancellable contracts and not reflected in the disclosure above.

29. Financial instruments and risk management

The Group's financial instruments comprise primarily cash and other financial assets and various items such as receivables and trade payables which arise directly from its operations. The main purpose of these financial instruments is to provide working capital for the Group's operations. The Group assesses counterparty risk on a regular basis. Board approval is required for adoption of any new financial instrument or counterparty. The primary focus of the treasury function is preservation of capital.

The Directors consider that the carrying amount of these financial instruments approximates to their fair value.

Financial assets by category

The categories of financial assets included in the balance sheet and the heading in which they are included are as follows. The measurement of financial assets is at amortized cost unless otherwise stated:

	December 31,	
	2022	2021
	£000s	£000s
Trade receivables	**915**	331
Cash and cash equivalents	**54,816**	73,537
Financial assets at amortized costs - U.S.Treasury Bills	**16,328**	
Non-current financial assets at amortized cost	**284**	301
	72,343	74,169

Financial liabilities by category

	December 31,	
	2022	2021
	£000s	£000s
Trade and other payables	**12,166**	10,464
Lease liability	**446**	137
	12,612	10,601

All amounts are short-term with trade and other payables due in less than 6 months. The lease liability is £0.1 million due within 6 months and £0.1 million due in 6 to 12 months. £0.2 million is due between 1 to 2 years.

Credit quality of financial assets (fixed term deposits and receivables)

The maximum exposure to credit risk at the reporting date by class of financial asset was:

	December 31,	
	2022	2021
	£000s	£000s
Trade receivables	**915**	331
Financial assets at amortized cost – non-current	**284**	301
Financial assets at amortized cost – current	**16,328**	
	17,527	632

Cash and cash equivalents, term deposits and U.S. Treasury Bills are not considered to be exposed to significant credit risk due to the fact they are held in a financial institution with an "A" rating. The Group considers the possibility of significant loss in the event of non-performance by a financial counterparty to be unlikely.

The Group regularly monitors the creditworthiness of its collaborators and at the reporting date, no financial assets are credit impaired.

Capital management

The Group considers its capital to be equal to the sum of its total equity. The Group monitors its capital using a number of measures including cash flow projections, working capital ratios, the cost to achieve preclinical and clinical milestones and potential revenue from existing partnerships and ongoing licensing activities. The Group's objective when managing its capital is to ensure it obtains sufficient funding for continuing as a going concern. The Group funds its capital requirements through the issue of new shares to investors, milestone and research support payments received from existing licensing partners and potential new licensees.

Interest rate risk

The nature of the Group's activities and the basis of funding are such that the Group has significant liquid resources. The Group uses these resources to meet the cost of future research and development activities. Consequently, it seeks to minimize risk in the holding of its bank deposits while maintaining a reasonable rate of interest. The Group is not financially dependent on the income earned on these resources and therefore the risk of interest rate fluctuations is not significant to the business. Nonetheless, the Directors take steps to secure rates of interest which generate a return for the Group.

Credit and liquidity risk

Credit risk is managed on a Group basis. Funds are deposited with financial institutions with a credit rating equivalent to, or above, the main U.K. clearing banks. The Group's liquid resources are invested having regard to the timing of payments to be made in the ordinary course of the Group's activities. All financial liabilities are payable in the short term (between zero and three months) and the Group maintains adequate bank balances in either instant access or short-term deposits to meet those liabilities as they fall due.

The Group only enters into collaboration agreements with large, reputable companies and the creditworthiness of collaborators is monitored on an ongoing basis.

The Group applies the IFRS 9 simplified approach to measuring expected credit losses which uses a lifetime expected loss allowance for all trade receivables. Expected loss rates are based on payment profiles of past receivables and the aging profiles of outstanding balances at the reporting period end date. The historical loss rates are adjusted to reflect
current and forward-looking information on macroeconomic factors affecting the ability of the customer to settle the receivables. At the year-end there were no debts that were past due or are expected to be past due. It was therefore concluded on this basis that there were no expected credit losses for the trade receivable.

Trade receivables are written off where there is no reasonable expectation of recovery. Indicators that there is no reasonable expectation of recovery includes, but is not limited to, a failure to engage in a repayment plan with the Group.

Currency risk

The Group operates in a global market with revenue possibly arising in a number of different currencies, principally in US dollars, sterling or euros. The majority of the operating costs are incurred in euros with the rest predominantly in sterling. Additionally, to a lesser extent, a number of operating costs are incurred in US dollars. The Group makes use of forward contracts to reduce its exposure to foreign currency risk where the existence, timing and quantum of future cash inflows can be accurately predicted.

Financial assets and liabilities denominated in euros and translated into sterling at the closing rate were:

	December 31, 2022	2021
	£000s	£000s
Financial assets	**2,302**	1,918
Financial liabilities	**(1,279)**	(3,278)
Net financial liabilities	**1,023**	(1,360)

Financial assets and liabilities denominated in US dollars and translated into sterling at the closing rate were:

	December 31, 2022	2021
	£000s	£000s
Financial assets	**53,086**	11,248
Financial liabilities	**(2,947)**	(876)
Net financial assets	**50,139**	10,372

The following table illustrates the sensitivity of the net result for the year and the reported financial assets of the Group in regard to the exchange rate for sterling against the euro.

During the year sterling rose by 1% (2021: 4%) against the euro. The table shows the impact of an additional weakening or strengthening of sterling against the euro by 20%.

	As reported	If sterling rose 20%	If sterling fell 20%
	£000s	**£000s**	**£000s**
2022			
Group result for the year	(40,489)	(37,572)	(44,865)
Euro denominated net financial liabilities	1,023	853	1,279
Total equity at December 31, 2022	22,072	21,902	22,328
2021			
Group result for the year	(39,410)	(35,618)	(45,099)
Euro denominated net financial liabilities	(1,360)	(1,133)	(1,700)
Total equity at December 31, 2021	8,526	8,753	8,186
2020			
Group result for the year	(32,547)	(29,056)	(37,784)
Euro denominated net financial liabilities	(723)	(603)	(904)
Total equity at December 31, 2020	9,059	9,180	8,878

The following table illustrates the sensitivity of the net result for the year and the reported financial assets of the Group in regards to the exchange rate for sterling against the U.S. dollar.

During the year sterling dropped by 10% (2021: 7%) against the U.S. dollar. The table shows the impact of an additional weakening or strengthening of sterling against the US dollar by 20%.

	As reported	If sterling rose 20%	If sterling fell 20%
	£000s	£000s	£000s
2022			
Group result for the year	(40,489)	(37,013)	(45,703)
U.S. dollar denominated net financial assets	50,139	41,783	62,674
Total equity at December 31, 2022	22,072	13,716	34,607
2021			
Group result for the year	(39,410)	(36,308)	(44,063)
U.S. dollar denominated net financial assets	10,372	8,643	12,965
Total equity at December 31, 2021	8,526	6,797	11,119
2020			
Group result for the year	(32,547)	(31,283)	(34,442)
U.S. dollar denominated net financial assets	27,304	22,753	34,130
Total equity at December 31, 2020	9,059	4,508	15,885

30. Notes to the cash flow statement

Changes in liabilities arising from financing activities.

	January 1, 2022 £000s	Cash flows from financing activities : Repayments £000s	Non-cash flows: New lease liabilities £000s	December 31, 2022 £000s
Lease liabilities	137	(190)	499	446
Total liabilities from financing activities	137	(190)	499	446

31. Related party transactions

Since January 1, 2020, we have engaged in the following transactions with our directors, executive officers or holders of more than 10% of our outstanding share capital and their affiliates, which we refer to as our related parties.

In 2022, we paid Gladstone Consultancy Partnership, a company controlled by our Non-Executive Chairman, £60 thousand for consulting and advisory services to be provided by Iain Ross (2021:nil; 2020: £75 thousand). The amounts payable were settled before the relevant year ends.

Key management are considered to be Directors of the Group. Directors' compensation is discussed in Item 6.

32. Post balance sheet events

There were no post balance sheet events as of the filing date.

Exhibit 2.3

DESCRIPTION OF SHARE CAPITAL AND ARTICLES OF ASSOCIATION

Set forth below is a summary of certain information concerning our share capital as well as a description of certain provisions of our articles of association, or the Articles, and relevant provisions of the U.K. Companies Act 2006, or the Companies Act. The summary below contains only material information concerning our share capital and corporate status and does not purport to be complete and is qualified in its entirety by reference to the Articles, which are filed as Exhibit 1.1 to the Annual Report on Form 20-F (the "Annual Report"). Further, please note that holders of our American Depositary Shares, or ADSs, will not be treated as one of our shareholders and will not have any shareholder rights.

General

We were incorporated as a public limited company under the laws of England and Wales on November 18, 1994 under the name Stanford Rook Holdings plc with company number 2992058. On June 21, 1999 we changed our name to SR Pharma plc. On April 26, 2007, we changed our name to Silence Therapeutics plc. Our principal executive offices are located at 72 Hammersmith Road, London W14 8TH, United Kingdom and our telephone number is +44 (0)20-3457-6900. Our registered office address is 27 Eastcastle Street, London, W1W 8DH. Our ADSs were listed on the Nasdaq Capital Market under the symbol "SLN" in September 2020. In June 2021, we moved our Nasdaq listing from the Nasdaq Capital Market tier to the Nasdaq Global Market tier. Our ordinary shares were traded on AIM under the symbol "SLN," but were delisted with effect from November 30, 2021. Our website address is *www.silence-therapeutics.com*. The information contained on, or that can be accessed from, our website does not form part of this summary. Our agent for service of process in the United States is Silence Therapeutics Inc., with a registered address at 221 River Street, Hoboken, New Jersey 07030 USA.

The principal legislation under which we operate and under which our ordinary shares are issued is the Companies Act.

As of March 1, 2022, we had 89,784,720 ordinary shares issued and outstanding, with a nominal value of £0.05 per ordinary share. Each issued ordinary share is fully paid.

Ordinary Shares

In accordance with the Articles, 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 on all matters to be voted on by shareholders generally;
- 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.

Options

As at March 1, 2022, there were options to purchase 10,707,271 ordinary shares outstanding with a weighted average exercise price of £3.93 per ordinary share. The options generally lapse after 10 years from the date of the grant.

Share Register

We are required by the Companies Act to keep a register of our shareholders. Under the laws of England and Wales, the ordinary shares are deemed to be 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 Market Services Limited, trading as Link Group.

Holders of our ADSs will not be treated as one of our 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. Holders of our ADSs have a right to receive the ordinary shares underlying their ADSs. For discussion on our ADSs and ADS holder rights see "Description of American Depositary Shares" filed as Exhibit 2.4 to the Annual Report.

Under the Companies Act, we must enter an allotment of shares in our share register as soon as practicable and in any event within two months of the allotment. We also are required by the Companies Act to register a transfer of shares (or give the transferee notice of and reasons for refusal) 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 wrongly entered in or omitted from our register of shareholders; or

- there is a default or unnecessary delay in entering on the register the fact of any person having ceased to be a shareholder 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.

Preemptive Rights

The laws of England and Wales generally provide shareholders with preemptive rights when new shares are issued for cash; however, it is possible for the articles of association, or shareholders in a general meeting, to disapply preemptive rights. Such a disapplication of preemptive rights may be for a maximum period of up to five years from the date of adoption of the articles of association, if the disapplication is contained in the articles of association, or from the date of the shareholder resolution, if the disapplication is by shareholder resolution. In either case, this disapplication would need to be renewed by our shareholders upon its expiration (*i.e.*, at least every five years). Typically UK public companies seek the disapplication of preemption rights (in relation to a specified aggregate nominal amount) on an annual basis at their annual general meeting.

On June 15, 2021, our shareholders approved the disapplication of preemptive rights until the earlier of our next annual general meeting or the date that is 15 months after such approval in respect of the allotment of up to a maximum aggregate nominal amount of £893,988.41 of ordinary shares of £0.05 each.

Articles of Association

Our Articles were adopted on November 1, 2021.

A summary of the terms of the Articles is set out below. The summary below is not a complete copy of the terms of the Articles. Please refer to the full version of the Articles, which are filed as Exhibit 1.1 to the Annual Report.

Objects

The objects of our company are unrestricted.

Shares and Rights Attaching to Them

Share Rights

Subject to any special rights attaching to shares or class of shares already in issue, our shares may be issued with or have attached to them any preferred, deferred or other special rights or be subject to such restrictions, whether in regard to dividend, voting, return of capital or otherwise, as we may by ordinary resolution of the shareholders determine or, in the absence of any such determination, as our board may determine.

Voting Rights

Subject to any rights or restrictions attached to any shares from time to time, the voting rights attaching to our shares are as follows:

- on a show of hands, every shareholder present in person 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;
- on a show of hands, each duly authorised corporate representative has one vote;
- on a poll every shareholder who is present in person or by proxy or by corporate representative shall have one vote for each share of which he or she is the holder or in respect of which their appointment as proxy or corporate representative is made; and
- in the case of joint holders of a share, the vote of the senior holder who votes shall be accepted to the exclusion of the votes of the other joint holders (and seniority shall be determined by the order in which the names stand in the register in respect of the share).

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 (before or on the declaration of the result of the show of hands) demanded. Subject to the provisions of the Companies Act, as described in “Differences in Corporate Law—Voting Rights,” a poll may be demanded by:

- the chairman of the meeting;
- at least five shareholders present in person or by proxy and entitled to vote on the resolution;

- any shareholder(s) present in person or by proxy and representing in the aggregate not less than one-tenth of the total voting rights of all shareholders having the right to attend and vote at the meeting (excluding the shares held in treasury); or

- any shareholder(s) present in person or by proxy and holding shares conferring a right to vote on the resolution at the meeting on which there have been paid up sums in the aggregate equal to not less than one-tenth of the total sums paid up on all shares conferring that right (excluding the shares held in treasury).

A resolution put to the vote at a general meeting held partly by means of electronic facility or facilities shall, unless the chairman of the meeting determines that it shall be decided on a show of hands, be decided on a poll.

Restrictions on Voting

No shareholder shall, unless the directors otherwise determine, be entitled to vote, either in person or by proxy, at any general meeting or at any separate class meeting in respect of any share held by such shareholder unless all calls or other sums payable by such shareholder 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 us serving on such shareholder at least 14 days' notice specifying the time or times and place of payment) pay at the time or times so specified the amount called on such holder's shares.

Dividends

We may 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 directors may from time to time pay shareholders such interim dividends as they think fit and may also pay the fixed dividends payable on any shares of the company half-yearly or otherwise on fixed dates. If the directors act in good faith, they shall not incur any liability to the holders of shares conferring preferred rights for any loss they may suffer in consequence of the payment of an interim dividend on any shares having non-preferred or deferred rights.

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 proportionately 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.

Subject to any rights attaching to or the terms of issue of any shares, no dividend or other monies payable by us on or in respect of any share shall bear interest against us. Any dividend unclaimed after a period of 12 years from the date such dividend became due for payment shall be forfeited and shall revert to us.

Dividends may be declared or paid in any currency or currencies 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.

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 specific assets other than cash, and in particular of paid up shares or debentures of any other company. The directors may, if authorized by ordinary resolution of shareholders, offer any holders of ordinary shares the right to elect to receive in lieu of a dividend an allotment of ordinary shares credited as fully paid up, subject to such exclusions and other arrangements as the board may deem necessary or expedient to deal with legal or practical problems in respect of overseas shareholders or in respect of shares represented by depositary receipts.

Change of Control

There is no specific provision in the Articles that would have the effect of delaying, deferring or preventing a change of control.

Distributions on Winding Up

On a winding up, the liquidator may, with the sanction of a special resolution of shareholders and any other sanctions required by law, divide amongst the shareholders (excluding the company itself to the extent it is a shareholder by virtue only of its holding of shares as treasury shares) in specie or in kind the whole or any part of our assets (whether they shall consist of property of the same kind or not) and may set such values as he or she deems fair upon any property to be divided and may determine how such division shall be carried out as between the shareholders or different classes of shareholder. The liquidator may, with the sanction of a special resolution of the shareholders and any other sanctions required by law, vest the whole or any part of such assets in trustees upon such trusts for the benefit of the shareholders as the liquidator shall think fit, 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 restrictions attached to any class of shares issued may be abrogated or varied with the consent in writing of the holders of at least three-quarters 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 class of shares, subject to the Companies Act and the terms of their issue. The Companies Act 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 an aggregate of 15% 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 nominal 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 shareholders, confirmed by the court, reduce our share capital, any capital redemption reserve or any share premium account in any manner authorized by the Companies Act. We may redeem or purchase all or any of our shares as described in “Other English Law Considerations—Purchase of Own Shares.”

Preemption Rights

In certain circumstances, our shareholders may have statutory preemption rights under the Companies Act in respect of the allotment of new shares as described in “Preemptive Rights” and “Differences in Corporate Law—Preemptive Rights.”

Transfer of Shares

Any certificated shareholder may transfer all or any of his, her or its shares by an instrument of transfer in any usual or common form or in any other manner which is permitted by the Companies Act and 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.

The board may decline to register any transfer of any share:

- which is not a fully paid share, provided that, where any such shares or securities are listed on any stock exchange, such discretion may not be exercised in a way in which the U.K. Financial Conduct Authority, the London Stock Exchange or any other relevant regulator or stock exchange regards as preventing dealing in shares or other securities from taking place on an open and proper basis;

- unless any written instrument of transfer, duly stamped (if required), is deposited with us at our registered office or such other place as the board may from time to time determine, accompanied by the certificate for the shares to which it relates;

- unless there is provided such evidence as the board may reasonably require to show the right of the transferor to make the transfer and if the instrument of transfer is executed by some other person on his, her or its behalf, the authority of that person to do so;

- where the transfer is in respect of more than one class of share; and

- in the case of a transfer to joint holders, the number of joint holders to whom the share is to be transferred exceeds four.

If the board declines to register a transfer of a certificated share it shall, as soon as practicable and in any event within two months after the date on which the transfer is lodged, send to the transferee notice of the refusal, together with reasons for the refusal.

Shareholder Meetings

Annual General Meetings

In accordance with the Companies Act, 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 at such time and place and with such additional means of attendance and participation (including at such other place(s) and/or by means of an electronic facility or facilities) as the board sees fit, subject to the requirements of the Companies Act, as described in "Differences in Corporate Law—Annual General Meeting" and "Differences in Corporate Law—Notice of General Meetings."

Notice of General Meetings

The arrangements for the calling of general meetings are described in "Differences in Corporate Law—Notice of General Meetings."

Quorum of General Meetings

No business 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.

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 except that:

- the quorum for such class meeting shall be two holders in person or by proxy representing not less than one-third in nominal value of the issued shares of the class (excluding any shares held in treasury);

- at the class meeting, a holder of shares of the class present in person or by proxy may demand a poll and shall on a poll be entitled to one vote for every share of the class held by him or her; and

- if at any adjourned meeting of such holders a quorum is not present at the meeting, one holder of shares of the class present in person or by proxy at an adjourned meeting constitutes a quorum.

Directors

Number of Directors

Unless and until otherwise determined by an ordinary resolution of shareholders, we may not have less than two directors on the board of directors but are not subject to any maximum number of directors.

Appointment of Directors

Subject to the provisions of the Articles, we may, by ordinary resolution of the shareholders, elect any person who is willing to act to be a director, either to fill a casual vacancy or as an addition to the existing board. However, any person that is not a director retiring from the existing board must be recommended by the board of directors, or be proposed by a shareholder not less than seven and not more than 42 days before the date appointed for the meeting in order to be eligible for election.

Without prejudice to the power to appoint any person to be a director by shareholder resolution, the board has power to appoint any person to be a director, either to fill a casual vacancy or as an addition to the existing board but so that the total number of directors does not exceed any maximum number fixed by or in accordance with the Articles.

Any director appointed by the board will hold office only until the following annual general meeting. Such a director is eligible for re-appointment at that meeting.

Rotation of Directors

At every annual general meeting, there shall retire from office any director who shall have been a director at each of the preceding two annual general meetings and who was not appointed or re-appointed by us in general meeting at, or since, either such meeting. A retiring director shall be eligible for re-appointment. A director retiring at a meeting shall, if he or she is not re-appointed at such meeting, retain office until the meeting appoints someone in his or her place, or if it does not do so, until the conclusion of such meeting.

Directors' Interests

The directors may authorize, to the fullest extent permitted by law, any matter proposed to them which would otherwise result in a director infringing his or her duty to avoid a situation in which he or she has, or can have, a direct or indirect interest that conflicts, or possibly may conflict, with our interests. A director shall not, save as otherwise agreed by him or her, be accountable to us for any benefit which he or she derives from any matter authorized by the directors and any contract, transaction or arrangement relating thereto shall not be liable to be avoided on the grounds of any such benefit.

Subject to the requirements under sections 175, 177 and 182 of the Companies Act, a director who is any way, whether directly or indirectly, interested in a proposed or existing transaction or arrangement with us shall declare the nature of his interest at a meeting of the directors.

A director shall not vote in respect of any contract, arrangement or transaction whatsoever in which he or she has an interest which is to his or her knowledge a material interest otherwise than by virtue of interests in shares or debentures or other securities of or otherwise in or through our company. A director shall not be counted in the quorum at a meeting in relation to any resolution on which he or she is debarred from voting.

A director shall be entitled to vote (and be counted in the quorum) in respect of any resolution concerning any of the following matters:

- the giving of any guarantee, security or indemnity in respect of money lent or obligations incurred by him or her or by any other person at the request of or for the benefit of our company or any of our subsidiary undertakings;

- the giving of any guarantee, security or indemnity in respect of a debt or obligation of our company or any of our subsidiary undertakings for which he or she has assumed responsibility in whole or in part under a guarantee or indemnity or by the giving of security;

- any proposal concerning an offer of securities of or by our company or any of our subsidiary undertakings in which offer he or she is or may be entitled to participate as a holder of securities or in the underwriting or sub-underwriting of which he or she is to participate;

- any contract, arrangement or transaction concerning any other body corporate in which he or she or any person connected with him or her (within the meaning of sections 252-5 of the Companies Act) is interested, directly or indirectly and whether as an officer or shareholder or otherwise howsoever, provided that he or she and any persons so connected with him or her do not to his or her knowledge hold an interest (within the meaning of sections 820 to 825 of the Companies Act) in one percent or more of any class of the equity share capital of such body corporate or of the voting rights available to members of the relevant body corporate;

- any contract, arrangement or transaction for the benefit of employees of our company or any of our subsidiary undertakings which does not accord to him or her any privilege or advantage not generally accorded to the employees to whom the scheme relates;

- any contract, arrangement or transaction concerning any insurance which our company is to purchase and/or maintain for, or for the benefit of, any directors or persons including directors;

- the giving of an indemnity in relation to another director; and

- the provision of funds to any director to meet, or the doing of anything to enable a director to avoid incurring, expenditure of the nature described in section 205(1) or 206 of the Companies Act.

If a question arises at a meeting of the board or of a committee of the board as to the right of a director to vote or be counted in the quorum, and such question is not resolved by his or her voluntarily agreeing to abstain from voting or not to be counted in the quorum, the question shall be determined by the chairman and his or her ruling in relation to any director other than himself or herself shall be final and conclusive except in a case where the nature or extent of the interest of the director concerned has not been fairly disclosed.

Directors' Fees and Remuneration

Each of the directors shall be paid a fee in such sums as may from time to time be determined by the directors provided that the aggregate of all such fees so paid to directors shall not exceed £500,000 per annum, or such higher amount as may from time to time be determined by ordinary resolution of shareholders.

Each director may be paid all his or her reasonable traveling, hotel and other expenses properly incurred in attending and returning from meetings of the directors or committees of the directors or general meetings of the company or separate meetings of the holders of any class of shares or debentures of the company or otherwise in connection with the business of our company.

Any director who is appointed to any executive office or who serves on any committee or who devotes special attention to the business of our company, or who otherwise performs services which in the opinion of the directors are outside the scope of the ordinary duties of a director, may be paid such extra remuneration by way of salary, percentage of profits or otherwise as the directors may determine.

Borrowing Powers

The board may exercise all the powers to borrow money and to mortgage or charge our undertaking, property and assets (present or future) and uncalled capital or any part thereof and to issue debentures, debenture stock and other securities, whether outright or as collateral security for any debt, liability or obligation of us or of any third party.

The board must restrict the borrowings of the Company and exercise all voting and other rights or powers of control exercisable by the Company in relation to its subsidiaries so as to secure that the aggregate amount remaining outstanding of all monies borrowed by the Company and its subsidiaries shall not at any time, without the previous sanction of an ordinary resolution of the shareholders, exceed a sum equal to five (5) times the aggregate of:

- the amount paid up on the issued share capital of the Company; and

- the total of the capital and revenue reserves of the Company and its subsidiaries (including any share premium account, capital redemption reserve and credit balance on the profit and loss or income account) in each case, whether or not such amounts are available for distribution;

all as shown in the latest audited consolidated balance sheet, subject to certain adjustments.

Indemnity

Every director or other officer of our group may be indemnified against all costs, charges, expenses, losses and liabilities sustained or incurred by him or her in connection with the actual or purported execution and/or discharge of his or her duties (including those duties, powers and discretions in relation to any members of our group) including all costs, charges, expenses, losses and liabilities suffered or incurred in disputing, defending, investigating or providing evidence in connection with any actual or threatened claims or otherwise. Every director or other officer of our group may also be provided with funds to meet, or do anything to enable a director or other officer of the Company to avoid incurring, expenditure of the nature described in sections 205(1) or 206 of the Companies Act.

Exclusive jurisdiction

The Articles will provide that, unless we consent in writing to the selection of an alternative forum in the United States of America, the federal district courts of the United States of America shall be the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act. Save in respect of any cause of action arising under the Securities Act, by subscribing for or acquiring shares, a shareholder submits all disputes between him or herself and us or our directors to the exclusive jurisdiction of the English courts.

Other English Law Considerations

Mandatory Purchases and Acquisitions

Pursuant to Sections 979 to 991 of the Companies Act, 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, she or it 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 squeeze-out of the minority shareholders 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 squeeze-out 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 Companies Act must, in general, be the same as the consideration that was available under the takeover offer.

Sell Out

The Companies Act also gives 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, her or its shares if, prior to the expiry of the acceptance period for such offer, (1) the offeror has acquired or unconditionally agreed to acquire not less than 90% in value of the voting shares, and (2) 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, her or its 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 Companies Act, we are empowered by notice in writing to any person whom we know or have reasonable cause to believe to be interested in our shares, or at any time during the three years immediately preceding the date on which the notice is issued has been so interested, within a reasonable time to disclose to us particulars of that person's interest and (so far as is within such person's knowledge) particulars of any other interest that subsists or subsisted in those shares.

Under the Articles, if a person defaults in supplying us with the required particulars in relation to the shares in question, or default shares, within the prescribed period of 14 days from the date of the service of notice, 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; and

- 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 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).

Purchase of Own Shares

Under the laws of England and Wales, 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 of association. 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.

We may purchase our own fully paid shares 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, she or it 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 Companies Act, 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 the laws of England and Wales.

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

The Takeover Code applies to an offer for a public company whose securities have been admitted to trading on a multilateral trading facility in the United Kingdom, which includes AIM, at any time during the 10 years prior to the relevant date of an offer, provided that (i) the registered office of the company is in the United Kingdom and (ii) the company is considered by the Panel on Takeovers and Mergers, or the Takeover Panel, to have its place of central management and control in the United Kingdom. The way in which the test for central management and control is applied for the purposes of the Takeover Code may be different from the way in which it is applied by the United Kingdom tax authorities. Under the Takeover Code, the Takeover Panel looks to where the majority of the directors are resident, amongst other factors, for the purposes of determining where a company has its place of central management and control. The Takeover Panel has confirmed that based on the current composition of our board, the Takeover Code will continue to apply to us. However, the Takeover Code could cease to apply if in the future if any changes to the board composition result in the majority of the directors not being resident in the United Kingdom, Channel Islands and Isle of Man. Our articles of association have been amended to include certain important protections which would apply in the event that the Takeover Code ceases to apply.

We are therefore currently subject to the Takeover Code.

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

- acquires an interest in our shares which, when taken together with shares in which he or 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 or her, 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 or her, 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 twelve months.

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 representing our ordinary shares, other than withholding tax requirements. There is no limitation imposed by the laws of England and Wales or in the Articles on the right of non-residents to hold or vote our shares.

Differences in Corporate Law

The applicable provisions of the Companies Act differ from laws applicable to U.S. corporations and their shareholders. Set forth below is a summary of certain differences between the provisions of the Companies Act applicable to us and the General Corporation Law of the State of Delaware relating to shareholders' rights and protections. This summary is not intended to be a complete discussion of shareholder rights under the laws of Delaware and the laws of England and Wales.

	England and Wales	**Delaware**
Number of Directors	Under the Companies Act, a public limited company must have at least two directors and the number of directors may be fixed by or in the manner provided in a company's articles of association.	Under Delaware law, a corporation must have at least one director and the number of directors shall be fixed by or in the manner provided in the bylaws.
Removal of Directors	Under the Companies Act, shareholders may remove a director without cause by an ordinary resolution (which is passed by a simple majority of those voting in person or by proxy at a general meeting) irrespective of any provisions of any service contract the director has with the company, provided 28 clear days' notice of the resolution has been given to the company and its shareholders. On receipt of notice of an intended resolution to remove a director, the company must forthwith send a copy of the notice to the director concerned. Certain other procedural requirements under the Companies Act must also be followed such as allowing the director to make representations against his or her removal either at the meeting or in writing.	Under Delaware law, any director or the entire board of directors may be removed, with or without cause, by the holders of a majority of the shares then entitled to vote at an election of directors, except (a) unless the certificate of incorporation provides otherwise, in the case of a corporation whose board of directors is classified, shareholders may effect such removal only for cause, or (b) in the case of a corporation having cumulative voting, if less than the entire board of directors is to be removed, no director may be removed without cause if the votes cast against his or her removal would be sufficient to elect him or her if then cumulatively voted at an election of the entire board of directors, or, if there are classes of directors, at an election of the class of directors of which he or she is a part.
Vacancies on the Board of Directors	Under the laws of England and Wales, the procedure by which directors, other than a company's initial directors, are appointed is generally set out in a company's articles of association, provided that where two or more persons are appointed as directors of a public	Under Delaware law, vacancies and newly created directorships may be filled by a majority of the directors then in office (even though less than a quorum) or by a sole remaining director unless (a) otherwise provided in the certificate of incorporation or by-laws of the corporation or (b)

	England and Wales	Delaware
	limited company by resolution of the shareholders, resolutions appointing each director must be voted on individually.	the certificate of incorporation directs that a particular class of stock is to elect such director, in which case a majority of the other directors elected by such class, or a sole remaining director elected by such class, will fill such vacancy.
Annual General Meeting	Under the Companies Act, a public limited company must hold an annual general meeting in each six-month period following our annual accounting reference date.	Under Delaware law, the annual meeting of stockholders shall be held at such place, on such date and at such time as may be designated from time to time by the board of directors or as provided in the certificate of incorporation or by the bylaws.
General Meeting	Under the Companies Act, a general meeting of the shareholders of a public limited company may be called by the directors. Shareholders holding at least 5% of the paid-up capital of the company carrying voting rights at general meetings (excluding any paid up capital held as treasury shares) can require the directors to call a general meeting and, if the directors fail to do so within a certain period, may themselves convene a general meeting.	Under Delaware law, special meetings of the stockholders may be called by the board of directors or by such person or persons as may be authorized by the certificate of incorporation or by the bylaws.
Notice of General Meetings	Under the Companies Act, at least 21 clear days' notice must be given for an annual general meeting and any resolutions to be proposed at the meeting. Subject to a company's articles of association providing for a longer period, 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. The shareholders of a company may in all cases consent to a shorter notice period, the proportion of shareholders' consent required being 100% of those entitled to attend and vote in the case of an annual general meeting and, in the case of any other general meeting, a majority in number of the members having a right to attend and vote at the meeting, being a majority who together hold not less than 95% in nominal value of the shares giving a right to attend and vote at the meeting (excluding any shares held as treasury shares).	Under Delaware law, unless otherwise provided in the certificate of incorporation or bylaws, written notice of any meeting of the stockholders must be given to each stockholder entitled to vote at the meeting not less than 10 nor more than 60 days before the date of the meeting and shall specify the place, date, hour, and purpose or purposes of the meeting.
Quorum	Subject to the provisions of a company's articles of association, the Companies Act provides that two 'qualifying persons' present at a meeting (in person, by proxy or authorized representative under the Companies Act (provided that the proxies and/or authorized representatives, represent different shareholders)) shall constitute	The certificate of incorporation or bylaws may specify the number of shares, the holders of which shall be present or represented by proxy at any meeting in order to constitute a quorum, but in no event shall a quorum consist of less than one-third of the shares entitled to vote at the meeting. In the absence of such specification in

	England and Wales	Delaware
	a quorum for companies with more than one shareholder.	the certificate of incorporation or bylaws, a majority of the shares entitled to vote, present in person or represented by proxy, shall constitute a quorum at a meeting of stockholders.
Proxy	Under the Companies Act, at any meeting of shareholders, a shareholder may designate another person to attend, speak and vote at the meeting on their behalf by proxy.	Under Delaware law, at any meeting of stockholders, a stockholder may designate another person to act for such stockholder by proxy, but no such proxy shall be voted or acted upon after three years from its date, unless the proxy provides for a longer period. A director of a Delaware corporation may not issue a proxy representing the director's voting rights as a director.
Preemptive Rights	Under the Companies Act, "equity securities," being (1) shares in the company other than shares that, with respect to dividends and capital, carry a right to participate only up to a specified amount in a distribution, referred to as "ordinary shares," or (2) rights to subscribe for, or to convert securities into, ordinary shares, proposed to be allotted for cash must be offered first to the existing equity shareholders in the company in proportion to the respective nominal value of their holdings, unless an exception applies or a special resolution to the contrary has been passed by shareholders in a general meeting or the articles of association provide otherwise in each case in accordance with the provisions of the Companies Act.	Under Delaware law, shareholders have no preemptive rights to subscribe to additional issues of stock or to any security convertible into such stock unless, and except to the extent that, such rights are expressly provided for in the certificate of incorporation.
Authority to Allot	Under the Companies Act, the directors of a company must not allot shares or grant of rights to subscribe for or to convert any security into shares unless an exception applies or an ordinary resolution to the contrary has been passed by shareholders in a general meeting or the articles of association provide otherwise in each case in accordance with the provisions of the Companies Act.	Under Delaware law, if the corporation's charter or certificate of incorporation so provides, the board of directors has the power to authorize the issuance of stock. It may authorize capital stock to be issued for consideration consisting of cash, any tangible or intangible property or any benefit to the corporation or any combination thereof. It may determine the amount of such consideration by approving a formula. In the absence of actual fraud in the transaction, the judgment of the directors as to the value of such consideration is conclusive.
Liability of Directors and Officers	Under the Companies Act, any provision, whether contained in a company's articles of association or any contract or otherwise, that purports to exempt a director of a company, to any extent, from any liability that would otherwise attach to him or her in connection with any negligence,	Under Delaware law, a corporation's certificate of incorporation may include a provision eliminating or limiting the personal liability of a director to the corporation and its stockholders for damages arising from a breach of fiduciary duty as a director. However, no provision can limit the liability of a director for:

	England and Wales	Delaware
	default, breach of duty or breach of trust in relation to the company is void. Any provision by which a company directly or indirectly provides an indemnity, to any extent, for a director of the company or of an associated company against any liability attaching to him or her in connection with any negligence, default, breach of duty or breach of trust in relation to the company of which he or she is a director is also void except as permitted by the Companies Act, which provides exceptions for the company to (a) purchase and maintain insurance against such liability; (b) provide a "qualifying third party indemnity" (being an indemnity against liability incurred by the director to a person other than the company or an associated company or criminal proceedings in which he or she is convicted); and (c) provide a "qualifying pension scheme indemnity" (being an indemnity against liability incurred in connection with our activities as trustee of an occupational pension plan).	• any breach of the director's duty of loyalty to the corporation or its stockholders; • acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law; • intentional or negligent payment of unlawful dividends or stock purchases or redemptions; or • any transaction from which the director derives an improper personal benefit.
Voting Rights	Under the laws of England and Wales, unless a poll is demanded by the shareholders of a company or is required by the chairman of the meeting or our articles of association, shareholders shall vote on all resolutions on a show of hands. Under the Companies Act, a poll may be demanded by (a) not fewer than five shareholders having the right to vote on the resolution; (b) any shareholder(s) representing not less than 10% of the total voting rights of all the shareholders having the right to vote on the resolution (excluding any voting rights attaching to treasury shares); or (c) any shareholder(s) holding shares in the company conferring a right to vote on the resolution (excluding any voting rights attaching to treasury shares) being shares on which an aggregate sum has been paid up equal to not less than 10% of the total sum paid up on all the shares conferring that right. A company's articles of association may provide more extensive rights for shareholders to call a poll. Under the laws of England and Wales, an ordinary resolution is passed on a show of hands if it is approved by a simple majority (more than 50%) of the votes cast by shareholders present (in person or by proxy) and entitled to vote. If a poll is demanded, an ordinary resolution is passed if it is approved by holders representing a simple	Delaware law provides that, unless otherwise provided in the certificate of incorporation, each stockholder is entitled to one vote for each share of capital stock held by such stockholder.

	England and Wales	Delaware
	majority of the total voting rights of shareholders present, in person or by proxy, who, being entitled to vote, vote on the resolution. Special resolutions require the affirmative vote of not less than 75% of the votes cast by shareholders present, in person or by proxy, at the meeting. If a poll is demanded, a special resolution is passed if it is approved by holders representing not less than 75% of the total voting rights of shareholders in person or by proxy who, being entitled to vote, vote on the resolution.	
Shareholder Vote on Certain Transactions	The Companies Act provides for schemes of arrangement, which are arrangements or compromises between a company and any class of shareholders or creditors and used in certain types of reconstructions, amalgamations, capital reorganizations, or takeovers. These arrangements require: • the approval at a shareholders' or creditors' meeting convened by order of the court, of a majority in number of shareholders or creditors representing 75% in value of the capital held by, or debt owed to, the class of shareholders or creditors, or class thereof present and voting, either in person or by proxy; and • the approval of the court.	Generally, under Delaware law, unless the certificate of incorporation provides for the vote of a larger portion of the stock, completion of a merger, consolidation, sale, lease or exchange of all or substantially all of a corporation's assets or dissolution requires: • the approval of the board of directors; and • approval by the vote of the holders of a majority of the outstanding stock or, if the certificate of incorporation provides for more or less than one vote per share, a majority of the votes of the outstanding stock of a corporation entitled to vote on the matter.
Standard of Conduct for Directors	Under the laws of England and Wales, a director owes various statutory and fiduciary duties to the company, including: • to act in the way he or she considers, in good faith, would be most likely to promote the success of the company for the benefit of its members as a whole(and in doing so have regard (amongst other matters) to: (i) the likely consequences of any decision in the long-term, (ii) the interests of the company's employees, (iii) the need to foster the company's business relationships with suppliers, customers and others, (iv) the impact of the company's operations on the community and the environment, (v) the desirability to maintain a reputation for high standards of business conduct, and (vi) the need to act fairly as between members of the company);	Delaware law does not contain specific provisions setting forth the standard of conduct of a director. The scope of the fiduciary duties of directors is generally determined by the courts of the State of Delaware. In general, directors have a duty to act without self-interest, on a well-informed basis and in a manner they reasonably believe to be in the best interest of the stockholders. Directors of a Delaware corporation owe fiduciary duties of care and loyalty to the corporation and to its shareholders. The duty of care generally requires that a director act in good faith, with the care that an ordinarily prudent person would exercise under similar circumstances. Under this duty, a director must inform himself or herself of all material information reasonably available regarding a significant transaction. The duty of loyalty requires that a director act in a manner he or she

	England and Wales	Delaware
	• to avoid a situation in which he or she has, or can have, a direct or indirect interest that conflicts, or possibly conflicts, with the interests of the company; • to act in accordance with our constitution and only exercise his or her powers for the purposes for which they are conferred; • to exercise independent judgment; • to exercise reasonable care, skill, and diligence; • not to accept benefits from a third party conferred by reason of his or her being a director or doing, or not doing, anything as a director; and • a duty to declare any interest that he or she has, whether directly or indirectly, in a proposed or existing transaction or arrangement with the company.	reasonably believes to be in the best interests of the corporation. He or she must not use his or her corporate position for personal gain or advantage. In general, but subject to certain exceptions, actions of a director are presumed to have been made on an informed basis, in good faith and in the honest belief that the action taken was in the best interests of the corporation. However, this presumption may be rebutted by evidence of a breach of one of the fiduciary duties. Delaware courts have also imposed a heightened standard of conduct upon directors of a Delaware corporation who take any action designed to defeat a threatened change in control of the corporation. In addition, under Delaware law, when the board of directors of a Delaware corporation approves the sale or break-up of a corporation, the board of directors may, in certain circumstances, have a duty to obtain the highest value reasonably available to the shareholders.
Stockholder Suits	Under the laws of England and Wales, 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 our internal management. Notwithstanding this general position, the Companies Act 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 where our affairs have been or are being conducted in a manner that is unfairly prejudicial to some of its shareholders.	Under Delaware law, a stockholder may initiate a derivative action to enforce a right of a corporation if the corporation fails to enforce the right itself. The complaint must: • state that the plaintiff was a stockholder at the time of the transaction of which the plaintiff complains or that the plaintiffs shares thereafter devolved on the plaintiff by operation of law; and • allege with particularity the efforts made by the plaintiff to obtain the action the plaintiff desires from the directors and the reasons for the plaintiff's failure to obtain the action; or • state the reasons for not making the effort. Additionally, the plaintiff must remain a stockholder through the duration of the derivative suit. The action will not be dismissed or compromised without the approval of the Delaware Court of Chancery.

Stock Exchange Listing

Our ADSs were listed on the Nasdaq Capital Market under the symbol "SLN" in September 2020. In June 2021, we moved our Nasdaq listing from the Nasdaq Capital Market tier to the Nasdaq Global Market tier.

Our ordinary shares were traded on AIM, a market operated by the London Stock Exchange, under the ticker symbol “SLN”. On October 15, 2021, we announced our intention to cancel the admission of our ordinary shares to trading on AIM, subject to shareholder approval which was obtained. The final day of trading of the ordinary shares on AIM was November 29, 2021 and the delisting took effect at 7:00 a.m. on November 30, 2021.

Registrar of Shares, Depositary for ADSs

Our share register is maintained by Link Market Services Limited. The share register reflects only registered holders of our ordinary shares. Holders of ADSs representing our ordinary shares will not be treated as our shareholders and their names will therefore not be entered in our share register. The Bank of New York Mellon has agreed to act as the depositary for the ADSs representing our ordinary shares and the custodian for ordinary shares represented by ADSs is The Bank of New York Mellon, acting through an office located in England. Holders of ADSs representing our ordinary shares have a right to receive the ordinary shares underlying such ADSs. For discussion on ADSs representing our ordinary shares and rights of ADS holders, see “Description of American Depositary Shares” filed as Exhibit 2.4 to the Annual Report.

Exhibit 2.4

DESCRIPTION OF AMERICAN DEPOSITARY SHARES

American Depositary Shares

The Bank of New York Mellon, as depositary, will register and deliver American Depositary Shares, or ADSs. Each ADS will represent three ordinary shares (or a right to receive three ordinary shares) deposited with The Bank of New York Mellon, acting through an office located in the United Kingdom, as custodian. Each ADS will also represent any other securities, cash or other property that may be held by the depositary. The deposited ordinary shares together with any other securities, cash or other property held by the depositary are referred to as the deposited securities. The depositary's office at which the ADSs will be administered and its principal executive office are located at 240 Greenwich Street, New York, New York 10286.

You may hold ADSs either (A) directly (i) by having an American Depositary Receipt, or ADR, which is a certificate evidencing a specific number of ADSs, registered in your name, or (ii) by having uncertificated ADSs registered in your name, or (B) indirectly by holding a security entitlement in ADSs through your broker or other financial institution that is a direct or indirect participant in The Depository Trust Company, also called DTC. If you hold ADSs directly, you are a registered ADS holder, also referred to as an ADS holder. This description assumes you are an ADS holder. If you hold the ADSs indirectly, you must rely on the procedures of your broker or other financial institution to assert the rights of ADS holders described in this section. You should consult with your broker or financial institution to find out what those procedures are.

Registered holders of uncertificated ADSs will receive statements from the depositary confirming their holdings.

As an ADS holder, we will not treat you as one of our shareholders and you will not have shareholder rights. Shareholder rights are governed by the laws of England and Wales. The depositary will be the holder of the ordinary shares underlying your ADSs. As a registered holder of ADSs, you will have ADS holder rights. A deposit agreement among us, the depositary, ADS holders and all other persons indirectly or beneficially holding ADSs sets out ADS holder rights as well as the rights and obligations of the depositary. New York law governs the deposit agreement and the ADSs.

The following is a summary of the material provisions of the deposit agreement. For more complete information, you should read the entire deposit agreement and the form of ADR, which are filed as Exhibits 2.1 and 2.2, respectively, to the Annual Report on Form 20-F.

Dividends and Other Distributions

How will you receive dividends and other distributions on the ordinary shares?

The depositary has agreed to pay or distribute to ADS holders the cash dividends or other distributions it or the custodian receives on ordinary shares or other deposited securities, upon payment or deduction of its fees and expenses, or withholding of taxes. You will receive these distributions in proportion to the number of ordinary shares your ADSs represent.

Cash

The depositary will convert any cash dividend or other cash distribution we pay on the ordinary shares into U.S. dollars, if it can do so on a reasonable basis and can transfer the U.S. dollars to the United States. If that is not possible or if any government approval is needed and cannot be obtained, the deposit agreement allows the depositary to distribute the foreign currency only to those ADS holders to whom it is possible to do so. It will hold the foreign currency it cannot convert for the account of the ADS holders who have not been paid. It will not invest the foreign currency and it will not be liable for any interest.

Before making a distribution, any withholding taxes, or other governmental charges that must be paid will be deducted. See "Material Income Tax Considerations." The depositary will distribute only whole U.S. dollars and cents and will

round fractional cents to the nearest whole cent. *If the exchange rates fluctuate during a time when the depositary cannot convert the foreign currency, you may lose some of the value of the distribution.*

Ordinary Shares

The depositary may distribute additional ADSs representing any ordinary shares we distribute as a dividend or free distribution. The depositary will only distribute whole ADSs. It will sell ordinary shares which would require it to deliver a fraction of an ADS (or ADSs representing those ordinary shares) and distribute the net proceeds in the same way as it does with cash. If the depositary does not distribute additional ADSs, the outstanding ADSs will also represent the new ordinary shares. The depositary may sell a portion of the distributed ordinary shares (or ADSs representing those ordinary shares) sufficient to pay its fees and expenses in connection with that distribution.

Rights to Purchase Additional Ordinary Shares.

If we offer holders of our securities any rights to subscribe for additional ordinary shares or any other rights, the depositary may (i) exercise those rights on behalf of ADS holders, (ii) distribute those rights to ADS holders or (iii) sell those rights and distribute the net proceeds to ADS holders, in each case after deduction or upon payment of its fees and expenses. To the extent the depositary does not do any of those things, it will allow the rights to lapse. *In that case, you will receive no value for them.* The depositary will exercise or distribute rights only if we ask it to and provide satisfactory assurances to the depositary that it is legal to do so. If the depositary will exercise rights, it will purchase the securities to which the rights relate and distribute those securities or, in the case of ordinary shares, new ADSs representing the new ordinary shares, to subscribing ADS holders, but only if ADS holders have paid the exercise price to the depositary. U.S. securities laws may restrict the ability of the depositary to distribute rights or ADSs or other securities issued on exercise of rights to all or certain ADS holders, and the securities distributed may be subject to restrictions on transfer.

Other Distributions

The depositary will send to ADS holders anything else we distribute on deposited securities by any means it thinks is legal, fair and practical. If it cannot make the distribution in that way, the depositary has a choice. It may decide to sell what we distributed and distribute the net proceeds, in the same way as it does with cash. Or, it may decide to hold what we distributed, in which case ADSs will also represent the newly distributed property. However, the depositary is not required to distribute any securities (other than ADSs) to ADS holders unless it receives satisfactory evidence from us that it is legal to make that distribution. The depositary may sell a portion of the distributed securities or property sufficient to pay its fees and expenses in connection with that distribution. U.S. securities laws may restrict the ability of the depositary to distribute securities to all or certain ADS holders, and the securities distributed may be subject to restrictions on transfer.

The depositary is not responsible if it decides that it is unlawful or impractical to make a distribution available to any ADS holders. We have no obligation to register ADSs, ordinary shares, rights or other securities under the Securities Act. We also have no obligation to take any other action to permit the distribution of ADSs, ordinary shares, rights or anything else to ADS holders. *This means that you may not receive the distributions we make on our ordinary shares or any value for them if it is illegal or impractical for us to make them available to you*.

Deposit, Withdrawal and Cancellation

How are ADSs issued?

The depositary will deliver ADSs if you or your broker deposits ordinary shares or evidence of rights to receive ordinary shares with the custodian. Upon payment of its fees and expenses and of any taxes or charges, such as stamp taxes or stock transfer taxes or fees, the depositary will register the appropriate number of ADSs in the names you request and will deliver the ADSs to or upon the order of the person or persons that made the deposit.

How can ADS holders withdraw the deposited securities?

You may surrender your ADSs to the depositary for the purpose of withdrawal. Upon payment of its fees and expenses and of any taxes or charges, such as stamp taxes or stock transfer taxes or fees, the depositary will deliver the ordinary shares and any other deposited securities underlying the ADSs to the ADS holder or a person the ADS holder designates at the office of the custodian. Or, at your request, risk and expense, the depositary will deliver the deposited securities at its office, if feasible. However, the depositary is not required to accept surrender of ADSs to the extent it would require delivery of a fraction of a deposited share or other security. The depositary may charge you a fee and its expenses for instructing the custodian regarding delivery of deposited securities.

How do ADS holders interchange between certificated ADSs and uncertificated ADSs?

You may surrender your ADR to the depositary for the purpose of exchanging your ADR for uncertificated ADSs. The depositary will cancel that ADR and will send to the ADS holder a statement confirming that the ADS holder is the registered holder of uncertificated ADSs. Upon receipt by the depositary of a proper instruction from a registered holder of uncertificated ADSs requesting the exchange of uncertificated ADSs for certificated ADSs, the depositary will execute and deliver to the ADS holder an ADR evidencing those ADSs.

Voting Rights

How do you vote?

ADS holders may instruct the depositary how to vote the number of deposited shares their ADSs represent. If we request the depositary to solicit your voting instructions (and we are not required to do so), the depositary will notify you of a shareholders' meeting and send or make voting materials available to you. Those materials will describe the matters to be voted on and explain how ADS holders may instruct the depositary how to vote. For instructions to be valid, they must reach the depositary by a date set by the depositary. The depositary will try, as far as practical, subject to the laws of England and Wales and the provisions of our articles of association or similar documents, to vote or to have its agents vote the ordinary shares or other deposited securities as instructed by ADS holders. If we do not request the depositary to solicit your voting instructions, you can still send voting instructions, and, in that case, the depositary may try to vote as you instruct, but it is not required to do so.

Except by instructing the depositary as described above, you will not be able to exercise voting rights unless you surrender your ADSs and withdraw the ordinary shares. However, you may not know about the meeting enough in advance to withdraw the ordinary shares. In any event, the depositary will not exercise any discretion in voting deposited securities and it will only vote or attempt to vote as instructed.

We cannot assure you that you will receive the voting materials in time to ensure that you can instruct the depositary to vote your ordinary shares. In addition, the depositary and its agents are not responsible for failing to carry out voting instructions or for the manner of carrying out voting instructions. *This means that you may not be able to exercise voting rights and there may be nothing you can do if your ordinary shares are not voted as you requested.*

In order to give you a reasonable opportunity to instruct the depositary as to the exercise of voting rights relating to Deposited Securities, if we request the Depositary to act, we agree to give the depositary notice of any such meeting and details concerning the matters to be voted upon at least 30 days in advance of the meeting date.

Fees and Expenses

Persons depositing or withdrawing ordinary shares or ADS holders must pay:	**For:**
$5.00 (or less) per 100 ADSs (or portion of 100 ADSs)	Issuance of ADSs, including issuances resulting from a distribution of ordinary shares or rights or other property

Persons depositing or withdrawing ordinary shares or ADS holders must pay:	For:
	Cancellation of ADSs for the purpose of withdrawal, including if the deposit agreement terminates
$.05 (or less) per ADS	Any cash distribution to ADS holders
A fee equivalent to the fee that would be payable if securities distributed to you had been ordinary shares and the ordinary shares had been deposited for issuance of ADSs	Distribution of securities distributed to holders of deposited securities (including rights) that are distributed by the depositary to ADS holders
$.05 (or less) per ADS per calendar year	Depositary services
Registration or transfer fees	Transfer and registration of ordinary shares on our share register to or from the name of the depositary or its agent when you deposit or withdraw ordinary shares
Expenses of the depositary	Cable (including SWIFT) and facsimile transmissions (when expressly provided in the deposit agreement)
	Converting foreign currency to U.S. dollars
Taxes and other governmental charges the depositary or the custodian has to pay on any ADSs or ordinary shares underlying ADSs, such as stock transfer taxes, stamp duty or withholding taxes	As necessary
Any charges incurred by the depositary or its agents for servicing the deposited securities	As necessary

The depositary collects its fees for delivery and surrender of ADSs directly from investors depositing ordinary shares or surrendering ADSs for the purpose of withdrawal or from intermediaries acting for them. The depositary collects fees for making distributions to investors by deducting those fees from the amounts distributed or by selling a portion of distributable property to pay the fees. The depositary may collect its annual fee for depositary services by deduction from cash distributions or by directly billing investors or by charging the book-entry system accounts of participants acting for them. The depositary may collect any of its fees by deduction from any cash distribution payable (or by selling a portion of securities or other property distributable) to ADS holders that are obligated to pay those fees. The depositary may generally refuse to provide fee-attracting services until its fees for those services are paid.

From time to time, the depositary may make payments to us to reimburse us for costs and expenses generally arising out of establishment and maintenance of the ADS program, waive fees and expenses for services provided to us by the depositary or share revenue from the fees collected from ADS holders. In performing its duties under the deposit agreement, the depositary may use brokers, dealers, foreign currency dealers or other service providers that are owned by or affiliated with the depositary and that may earn or share fees, spreads or commissions.

The depositary may convert currency itself or through any of its affiliates, or the custodian or we may convert currency and pay U.S. dollars to the depositary. Where the depositary converts currency itself or through any of its affiliates, the depositary acts as principal for its own account and not as agent, advisor, broker or fiduciary on behalf of any other person and earns revenue, including, without limitation, transaction spreads, that it will retain for its own account. The revenue is based on, among other things, the difference between the exchange rate assigned to the currency conversion made under the deposit agreement and the rate that the depositary or its affiliate receives when buying or selling foreign currency for its own account. The depositary makes no representation that the exchange rate used or obtained by it or its affiliate in any currency conversion under the deposit agreement will be the most favorable rate that could be obtained at the time or that the method by which that rate will be determined will be the most favorable to ADS

holders, subject to the depositary's obligation to act without negligence or bad faith. The methodology used to determine exchange rates used in currency conversions made by the depositary is available upon request.

Where the custodian converts currency, the custodian has no obligation to obtain the most favorable rate that could be obtained at the time or to ensure that the method by which that rate will be determined will be the most favorable to ADS holders, and the depositary makes no representation that the rate is the most favorable rate and will not be liable for any direct or indirect losses associated with the rate. In certain instances, the depositary may receive dividends or other distributions from the us in U.S. dollars that represent the proceeds of a conversion of foreign currency or translation from foreign currency at a rate that was obtained or determined by us and, in such cases, the depositary will not engage in, or be responsible for, any foreign currency transactions and neither it nor we make any representation that the rate obtained or determined by us is the most favorable rate and neither it nor we will be liable for any direct or indirect losses associated with the rate.

Payment of Taxes

You will be responsible for any taxes or other governmental charges payable on your ADSs or on the deposited securities represented by any of your ADSs. The depositary may refuse to register any transfer of your ADSs or allow you to withdraw the deposited securities represented by your ADSs until those taxes or other charges are paid. It may apply payments owed to you or sell deposited securities represented by your ADSs to pay any taxes owed and you will remain liable for any deficiency. If the depositary sells deposited securities, it will, if appropriate, reduce the number of ADSs to reflect the sale and pay to ADS holders any proceeds, or send to ADS holders any property, remaining after it has paid the taxes.

Tender and Exchange Offers; Redemption, Replacement or Cancellation of Deposited Securities

The depositary will not tender deposited securities in any voluntary tender or exchange offer unless instructed to do so by an ADS holder surrendering ADSs and subject to any conditions or procedures the depositary may establish.

If deposited securities are redeemed for cash in a transaction that is mandatory for the depositary as a holder of deposited securities, the depositary will call for surrender of a corresponding number of ADSs and distribute the net redemption money to the holders of called ADSs upon surrender of those ADSs.

If there is any change in the deposited securities such as a sub-division, consolidation or other reclassification, or any merger, scheme of arrangement, recapitalization or reorganization affecting the issuer of deposited securities in which the depositary receives new securities in exchange for or in lieu of the old deposited securities, the depositary will hold those replacement securities as deposited securities under the deposit agreement. However, if the depositary decides it would not be lawful and practical to hold the replacement securities because those securities could not be distributed to ADS holders or for any other reason, the depositary may instead sell the replacement securities and distribute the net proceeds upon surrender of the ADSs.

If there is a replacement of the deposited securities and the depositary will continue to hold the replacement securities, the depositary may distribute new ADSs representing the new deposited securities or ask you to surrender your outstanding ADRs in exchange for new ADRs identifying the new deposited securities.

If there are no deposited securities underlying ADSs, including if the deposited securities are cancelled, or if the deposited securities underlying ADSs have become apparently worthless, the depositary may call for surrender of those ADSs or cancel those ADSs upon notice to the ADS holders.

Amendment and Termination

How may the deposit agreement be amended?

We may agree with the depositary to amend the deposit agreement and the ADRs without your consent for any reason. If an amendment adds or increases fees or charges, except for taxes and other governmental charges or expenses of the depositary for registration fees, facsimile costs, delivery charges or similar items, or prejudices a substantial right

of ADS holders, it will not become effective for outstanding ADSs until 30 days after the depositary notifies ADS holders of the amendment. *At the time an amendment becomes effective, you are considered, by continuing to hold your ADSs, to agree to the amendment and to be bound by the ADRs and the deposit agreement as amended*.

How may the deposit agreement be terminated?

The depositary will initiate termination of the deposit agreement if we instruct it to do so. The depositary may initiate termination of the deposit agreement if:

- 60 days have passed since the depositary told us it wants to resign but a successor depositary has not been appointed and accepted its appointment;
- we delist the ADSs from an exchange in the United States on which they were listed and, within 30 days, do not list the ADSs on another exchange in the United States or make arrangements for trading of ADSs on the U.S. over-the-counter market;
- we delist our ordinary shares from an exchange outside the United States on which they were listed and do not list the ordinary shares on another exchange outside the United States;
- the depositary has reason to believe the ADSs have become, or will become, ineligible for registration on Form F-6 under the Securities Act of 1933;
- we appear to be insolvent or enter insolvency proceedings;
- all or substantially all the value of the deposited securities has been distributed either in cash or in the form of securities;
- there are no deposited securities underlying the ADSs or the underlying deposited securities have become apparently worthless; or
- there has been a replacement of deposited securities.

If the deposit agreement will terminate, the depositary will notify ADS holders at least 90 days before the termination date. At any time after the termination date, the depositary may sell the deposited securities. After that, the depositary will hold the money it received on the sale, as well as any other cash it is holding under the deposit agreement, unsegregated and without liability for interest, for the pro rata benefit of the ADS holders that have not surrendered their ADSs. Normally, the depositary will sell as soon as practicable after the termination date.

After the termination date and before the depositary sells, ADS holders can still surrender their ADSs and receive delivery of deposited securities, except that the depositary may refuse to accept a surrender for the purpose of withdrawing deposited securities or reverse previously accepted surrenders of that kind that have not settled if it would interfere with the selling process. The depositary may refuse to accept a surrender for the purpose of withdrawing sale proceeds until all the deposited securities have been sold. The depositary will continue to collect distributions on deposited securities, but, after the termination date, the depositary is not required to register any transfer of ADSs or distribute any dividends or other distributions on deposited securities to the ADSs holder (until they surrender their ADSs) or give any notices or perform any other duties under the deposit agreement except as described in this paragraph.

Limitations on Obligations and Liability

Limits on our Obligations and the Obligations of the Depositary; Limits on Liability to Holders of ADSs

The deposit agreement expressly limits our obligations and the obligations of the depositary. It also limits our liability and the liability of the depositary. We and the depositary:

- are only obligated to take the actions specifically set forth in the deposit agreement without negligence or bad faith, and the depositary will not be a fiduciary or have any fiduciary duty to holders of ADSs;

- are not liable if we are or it is prevented or delayed by law or by events or circumstances beyond our or its ability to prevent or counteract with reasonable care or effort from performing our or its obligations under the deposit agreement;

- are not liable if we or it exercises discretion permitted under the deposit agreement;

- are not liable for the inability of any holder of ADSs to benefit from any distribution on deposited securities that is not made available to holders of ADSs under the terms of the deposit agreement, or for any special, consequential or punitive damages for any breach of the terms of the deposit agreement;

- have no obligation to become involved in a lawsuit or other proceeding related to the ADSs or the deposit agreement on your behalf or on behalf of any other person;

- may rely upon any documents we believe or it believes in good faith to be genuine and to have been signed or presented by the proper person;

- are not liable for the acts or omissions of any securities depository, clearing agency or settlement system; and

- the depositary has no duty to make any determination or provide any information as to our tax status, or any liability for any tax consequences that may be incurred by ADS holders as a result of owning or holding ADSs or be liable for the inability or failure of an ADS holder to obtain the benefit of a foreign tax credit, reduced rate of withholding or refund of amounts withheld in respect of tax or any other tax benefit.

In the deposit agreement, we and the depositary agree to indemnify each other under certain circumstances.

Requirements for Depositary Actions

Before the depositary will deliver or register a transfer of ADSs, make a distribution on ADSs, or permit withdrawal of ordinary shares, the depositary may require:

- payment of stock transfer or other taxes or other governmental charges and transfer or registration fees charged by third parties for the transfer of any ordinary shares or other deposited securities;

- satisfactory proof of the identity and genuineness of any signature or other information it deems necessary; and

- compliance with regulations it may establish, from time to time, consistent with the deposit agreement, including presentation of transfer documents.

The depositary may refuse to deliver ADSs or register transfers of ADSs when the transfer books of the depositary or our transfer books are closed or at any time if the depositary or we think it advisable to do so.

Your Right to Receive the Ordinary Shares Underlying your ADSs

ADS holders have the right to cancel their ADSs and withdraw the underlying ordinary shares at any time except:

- when temporary delays arise because: (i) the depositary has closed its transfer books or we have closed our transfer books; (ii) the transfer of ordinary shares is blocked to permit voting at a shareholders' meeting; or (iii) we are paying a dividend on our ordinary shares;

- when you owe money to pay fees, taxes and similar charges; or
- when it is necessary to prohibit withdrawals in order to comply with any laws or governmental regulations that apply to ADSs or to the withdrawal of ordinary shares or other deposited securities.

This right of withdrawal may not be limited by any other provision of the deposit agreement.

Direct Registration System

In the deposit agreement, all parties to the deposit agreement acknowledge that the Direct Registration System, also referred to as DRS, and Profile Modification System, also referred to as Profile, will apply to the ADSs. DRS is a system administered by DTC that facilitates interchange between registered holding of uncertificated ADSs and holding of security entitlements in ADSs through DTC and a DTC participant. Profile is a feature of DRS that allows a DTC participant, claiming to act on behalf of a registered holder of uncertificated ADSs, to direct the depositary to register a transfer of those ADSs to DTC or its nominee and to deliver those ADSs to the DTC account of that DTC participant without receipt by the depositary of prior authorization from the ADS holder to register that transfer.

In connection with and in accordance with the arrangements and procedures relating to DRS/Profile, the parties to the deposit agreement understand that the depositary will not determine whether the DTC participant that is claiming to be acting on behalf of an ADS holder in requesting registration of transfer and delivery as described in the paragraph above has the actual authority to act on behalf of the ADS holder (notwithstanding any requirements under the Uniform Commercial Code). In the deposit agreement, the parties agree that the depositary's reliance on and compliance with instructions received by the depositary through the DRS/Profile system and in accordance with the deposit agreement will not constitute negligence or bad faith on the part of the depositary.

Shareholder Communications; Inspection of Register of Holders of ADSs

The depositary will make available for your 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. The depositary will send you copies of those communications or otherwise make those communications available to you if we ask it to. You have a right to inspect the register of holders of ADSs, but not for the purpose of contacting those holders about a matter unrelated to our business or the ADSs.

Jury Trial Waiver

The deposit agreement provides that, to the extent permitted by law, ADS holders waive the right to a jury trial of any claim they may have against us or the depositary arising out of or relating to our ordinary shares, the ADSs or the deposit agreement, including any claim under the U.S. federal securities laws. If we or the depositary opposed a jury trial demand based on the waiver, the court would determine whether the waiver was enforceable in the facts and circumstances of that case in accordance with applicable case law.

You will not, by agreeing to the terms of the deposit agreement, be deemed to have waived our or the depositary's compliance with U.S. federal securities laws or the rules and regulations promulgated thereunder.

Each holder of ADSs may be required from time to time to provide certain information, including proof of taxpayer status, residence and beneficial ownership (as applicable), from time to time and in a timely manner as we, the depositary or the custodian may deem necessary or proper to fulfill obligations under applicable law.

Exhibit 4.7

THE SYMBOL [***] DENOTES PLACES WHERE CERTAIN IDENTIFIED INFORMATION HAS BEEN EXCLUDED FROM THE EXHIBIT BECAUSE IT IS BOTH (i) NOT MATERIAL AND (ii) CUSTOMARILY AND ACTUALLY TREATED AS PRIVATE.

EXCLUSIVE RESEARCH COLLABORATION, OPTION AND LICENSE AGREEMENT

by and between

SILENCE THERAPEUTICS PLC

and

HANSOH (SHANGHAI) HEALTHTECH CO., LTD. and JIANGSU HANSOH PHARMACEUTICAL GROUP COMPANY LIMITED

Dated as of October 14, 2021

THIS EXCLUSIVE RESEARCH COLLABORATION, OPTION AND LICENSE AGREEMENT is made and entered into effective as of October 14, 2021 (the "**Effective Date**") by and between

(1) **SILENCE THERAPEUTICS PLC**, a public limited company organized under the laws of England and Wales with a registered office at 27 Eastcastle Street, London, W1W 8DH ("**Silence**"), and

(2) **HANSOH (Shanghai) Healthtech Co., Ltd.**, a corporation organized and existing under the laws of the People's Republic of China having a principal place of business at Room 102, Block 1 No. 298 Xiangke Road, China (Shanghai) Pilot Free Trade Zone, China ("**Hansoh Healthtech**") and **Jiangsu Hansoh Pharmaceutical Group Company Limited**, a corporation organized and existing under the laws of the People's Republic of China having a place of business at No. 9 Dongjin Road, Huaguoshan Avenue, Lianyungang, Jiangsu, China ("**Jiangsu Hansoh**" and together with Hansoh Healthtech, "**Hansoh**"); and

Silence and Hansoh are sometimes referred to herein individually as a "**Party**" and collectively as the "**Parties**".

BACKGROUND

(A) Silence owns certain intellectual property rights with respect to the research and development of RNAi Molecules (as defined below).

(B) Hansoh has expertise in the development, manufacturing, and commercialization of drugs.

(C) The Parties have agreed to collaborate to perform drug discovery and research on certain Licensed Targets, which will be chosen in accordance with this Agreement. Hansoh wishes to obtain, and Silence wishes to grant to Hansoh, an option to obtain a license under Silence's rights in such technology and related intellectual property rights to develop and

commercialize Licensed Compounds and Licensed Products directed to those Licensed Targets.

NOW, THEREFORE, in consideration of the mutual promises and conditions hereinafter set forth, and other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties, intending to be legally bound, do hereby agree as follows:

ARTICLE 1
DEFINITIONS

As used in this Agreement and the Schedules to this Agreement the following capitalized terms, whether used in the singular or plural, shall have the meanings set out below:

1.1 "**Accounting Standards**" means, with respect to either Party, records and books of accounts shall be maintained in accordance with International Financial Reporting Standards (IFRS).

1.2 "**Acquisition**" means: (a) a merger involving Silence or any Holding Company of Silence, in which the shareholders of Silence or such Holding Company immediately prior to such merger cease to control (as defined in Section 1.3) Silence or such Holding Company after such merger; (b) a sale of all or substantially all of the business or assets of Silence to an acquiring entity; or (c) a sale of a controlling (as defined in Section 1.3) interest of Silence to an acquiring entity.

1.3 "**Affiliate**" means, with respect to a Party, any Person that, directly or indirectly, through one (1) or more intermediaries, controls, is controlled by or is under common control with such Party. For the purposes of this definition, "control" and, with correlative meanings, the terms "controlling", "controlled by" and "under common control with", means (a) the possession, directly or indirectly, of the power to direct the management or policies of a Person, whether through the ownership of voting securities, by contract

relating to voting rights or corporate governance, or otherwise; or (b) the ownership, directly or indirectly, of more than fifty percent (50%) of the voting securities or other ownership interest of a Person (or, with respect to a limited partnership or other similar entity, its general partner or controlling entity).

1.4 "**Agreement**" means this agreement and all schedules, appendices and other addenda attached hereto as any of the foregoing may be amended in accordance with the provisions of this Agreement.

1.5 "**Alliance Manager**" has the meaning set forth in Section 2.14.

1.6 "**Annual Gross Sales**" means the total Gross Sales of all Licensed Products directed (whether solely or jointly with any other Licensed Targets) to a particular Licensed Target in a particular Year or, with respect to the Year that includes the First Commercial Sale, the period beginning on such date of First Commercial Sale through to the end of the Year in which such First Commercial Sale occurred.

1.7 "**Applicable Law**" means federal, state, local, national and supra-national laws, statutes, rules, and regulations, including any rules, regulations, guidelines, or other requirements of the Regulatory Authorities, major national securities exchanges or major securities listing organizations, that may be in effect from time to time during the Term and applicable to a particular activity or country or other jurisdiction hereunder.

1.8 "**Business Day**" means a day other than a Saturday or Sunday on which banking institutions in London, England or the People's Republic of China are open for business.

1.9 "**Centralized Approval Procedure**" means the procedure through which a MAA filed with the EMA results in a single marketing authorization valid throughout the European Union.

1.10 "**China Licensed Compound**" means any Licensed Compound directed to either of the China Licensed Targets.

1.11 "**China Licensed Product**" means any Licensed Product directed to either of the China Licensed Targets.

1.12 "**China Licensed Targets**" means the targets set forth in Section 1 of Schedule 1.78, unless otherwise agreed by the Parties in writing.

1.13 "**Claims**" has the meaning set forth in Section 14.1.

1.14 "**Clinical Studies**" means a Phase 1 Trial, Phase 2 Trial, Phase 3 Trial, and such other tests and studies in human subjects that are required by Applicable Law, or otherwise conducted or recommended by any applicable Regulatory Authority, to obtain or maintain Regulatory Approvals for a Licensed Compound or Licensed Product for one (1) or more Indications, including tests or studies that are intended to expand the approved Indications for such Licensed Compounds or Licensed Products.

1.15 "**Collaboration**" means the collaboration between the Parties which is the subject matter of this Agreement.

1.16 "**Combination Product**" means a Licensed Product sold as a single unit for a single price which Licensed Product contains one or more additional agents having a meaningful therapeutic effect (whether coformulated or copackaged) other than a Licensed Compound.

1.17 "**Commercialization**" means any and all activities directed to the preparation for sale of, offering for sale of, or sale of a molecule or product, including activities related to marketing, promoting, distributing, importing and exporting such molecule or product, and, for purposes of setting forth the rights and obligations of the Parties under this

Agreement, shall be deemed to include conducting medical affairs activities and conducting phase 4 trials, and interacting with Regulatory Authorities regarding any of the foregoing. When used as a verb, "**to Commercialize**" and "**Commercializing**" means to engage in Commercialization, and "**Commercialized**" has a corresponding meaning.

1.18 "**Commercially Reasonable Efforts**" means, with respect to the performance of Development or Commercialization activities with respect to a Licensed Compound and/or Licensed Product by a Party, the carrying out of such activities using efforts and resources comparable to the efforts and resources that [***] under similar circumstances acting in good faith would typically devote to compounds or products of similar market potential at a similar stage in development or product life taking into account all relevant factors, including the [***].

1.19 "**Confidential Information**" means any Information or data provided orally, visually, in writing or other form by or on behalf of one (1) Party (or an Affiliate or representative of such Party) to the other Party (or to an Affiliate or representative of such Party) in connection with this Agreement, whether prior to, on, or after the Effective Date, including Information relating to the terms of this Agreement, any Licensed Target, or any Licensed Compound or Licensed Product, any Exploitation of any Licensed Target or any Licensed Compounds or Licensed Product, any Know-How with respect thereto developed by or on behalf of the disclosing Party or its Affiliates (including Hansoh Research Know-How and Silence Research Know-How, as applicable), or the scientific, regulatory, patent or business affairs or other activities of either Party. Notwithstanding the foregoing, (a) Silence Background IP, Silence Research IP and Silence China Product Development IP will be considered Confidential Information of Silence, (b) Hansoh Background IP, Hansoh Research IP and Hansoh China Product Development IP will be

considered Confidential Information of Hansoh, and (c) Joint Research IP shall be deemed to be the Confidential Information of both Parties and both Parties shall be deemed to be the receiving Party and the disclosing Party with respect thereto.

1.20 "**Control**" means, with respect to any item of Information, Know-How, material, Patent, or other property right, the possession of the right, whether directly or indirectly, and whether by ownership, license, covenant not to sue, or otherwise (other than by operation of the license and other grants (but not assignment) in this Agreement), to grant a license, sublicense, or other right to or under such Information, Know-How, material, Patent, or other property right as provided for herein without violating the terms of any agreement or other arrangement with any Third Party existing as of the time such Party would be required hereunder to grant such access or license; provided that where access to or the use of any item of Information, Know-How, material, Patent, or other property right of a Third Party requires or triggers a payment obligation, such Information, Know-How, material, Patent, or other property right shall only be Controlled in the circumstances set out in Section 6.8.

1.21 "**Cover**" means, with respect to a particular subject matter at issue and a relevant Patent, that, in the absence of ownership of or a license under such Patent, the manufacture, use, sale, offer for sale, or importation of such subject matter would infringe one or more Valid Claims of such Patent, or, as to a pending claim included in such Patent, the manufacture, use, sale, offer for sale, or importation of such subject matter would infringe such Patent if such pending claim were to issue in an issued patent.

1.22 "**Development**" means all activities related to pre-clinical and other non-clinical research, testing, test method development and stability testing, toxicology, formulation, process development, drug substance design and synthesis, manufacturing scale-up, qualification and validation, quality assurance/quality control, Clinical Studies, including

Manufacturing in support thereof, statistical analysis and report writing, the preparation and submission of Drug Approval Applications, regulatory affairs with respect to the foregoing, and all other activities necessary or reasonably useful or otherwise requested or required by a Regulatory Authority as a condition or in support of obtaining or maintaining a Regulatory Approval. When used as a verb, "**Develop**" means to engage in Development. For purposes of clarity, Development shall include any submissions (and activities required in support thereof) required by Applicable Laws or a Regulatory Authority as a condition or in support of obtaining a pricing or reimbursement approval for an approved molecule or product.

1.23 "**Dispute**" has the meaning set forth in Section 16.7.

1.24 "**Dollars**" or "**$**" means United States Dollars.

1.25 "**Drug Approval Application**" means (a) a New Drug Application, submitted to the FDA pursuant to 21 CFR § 314.50 ("**NDA**"); (b) a Biologics License Application submitted to the FDA pursuant to Section 351(a) of the Public Health Service Act and the regulations promulgated thereunder ("**BLA**"); (c) an application for authorization to market and/or sell a biological or pharmaceutical product submitted to a Regulatory Authority in any country or jurisdiction other than the U.S., including, (i) with respect to the European Union, a marketing authorization application filed with the EMA pursuant to the Centralized Approval Procedure or with the applicable Regulatory Authority of a country in the European Economic Area with respect to the decentralized procedure, mutual recognition or any national approval procedure ("**MAA**") and (ii) with respect to Mainland China, any drug marketing approval application filed with the NMPA; or (d) with respect to any biological or pharmaceutical product for which a NDA, BLA or MAA has been approved by the applicable Regulatory Authority, an application to supplement

or amend such NDA, BLA or MAA to expand the approved label for such biological product to include use of such biological product for an additional Indication.

1.26 "**Effective Date**" means the effective date of this Agreement as set forth in the preamble hereto.

1.27 "**EMA**" means the European Medicines Agency and any successor agency or authority having substantially the same function.

1.28 "**Enterprise Income Tax**" means the tax levied on payments from the Peoples Republic of China pursuant to The Enterprise Income Tax Law of the People's Republic of China (Order No. 23 of the President of the People's Republic of China) that came into effect as of December 29, 2018.

1.29 "**European Union**" means the economic, scientific, and political organization of member states known as the European Union, as its membership may be altered from time to time, and any successor thereto.

1.30 "**Exploit**" or "**Exploitation**" means to make, have made, import, export, use, have used, sell, have sold, or offer for sale, including to Develop, Commercialize, register, modify, enhance, improve, Manufacture, have Manufactured, hold, or keep (whether for disposal or otherwise), or otherwise dispose of.

1.31 **"Failed Target"** has the meaning described in Section 3.8.

1.32 "**FDA**" means the United States Food and Drug Administration and any successor agency or authority having substantially the same function.

1.33 "**Field**" means all therapeutic, prophylactic, palliative and diagnostic uses in humans and animals.

1.34 "**First Commercial Sale**" means, with respect to a Licensed Product and a country or region, the first sale for monetary value for use or consumption by the end user of such Licensed Product in such country or region after Regulatory Approval for the sale of such Licensed Product has been obtained in such country or region. Sales prior to receipt of Regulatory Approval for such Licensed Product, such as so-called "treatment IND sales", "named patient sales", and "compassionate use sales", shall not constitute a First Commercial Sale.

1.35 "**FTE**" means the equivalent of the work of one appropriately qualified individual working on a full-time basis in performing work in connection with this Agreement for a twelve (12) month period (consisting of at least a total of [***] ([***]) hours per Year of dedicated effort related to scientific, technical or operational work (excluding administrative services)).

1.36 "**FTE Costs**" means the FTE Rate multiplied by the number of FTEs applied by Silence to the performance of the relevant activity in accordance with the applicable Research Plan.

1.37 "**FTE Rate**" means, for the period from 1 January to 31 December of each Year, [***] Dollars ($[***]).

1.38 "**Generic Competition**" means, with respect to a given Licensed Product in a given country or region in the Hansoh Territory, that the unit sales of such Licensed Product in such country or region reduce in any Quarter by [***] ([***]%) or more from the most recent Quarter that was prior to the launch of the first to be launched Generic Product of such Licensed Product in such country or region.

1.39 "**Generic Product**" means, with respect to a Licensed Product, any product that is sold by a Third Party under a Regulatory Approval granted by a Regulatory Authority to a

Third Party which Third Party has not obtained the right to market or sell such product from Hansoh (including as a Sublicensee, subcontractor, or Third Party distributor of Hansoh or any of its Affiliates) and either (a) contains, as an active ingredient, the same compound as the Licensed Compound in the reference Licensed Product, and (b) is approved in reliance, in whole or in part, on the prior approval (or on data supporting safety or efficacy data submitted in support of the prior approval) of such Licensed Product as determined by the applicable Regulatory Authority, including but not limited to any product authorized for sale (i) in the U.S. pursuant to Section 505(b)(2) or Section 505(j) of the FD&C Act (21 U.S.C. 355(b)(2) and 21 U.S.C. 355(j), respectively), (ii) in the E.U. pursuant to a provision of Articles 10, 10a or 10b of Parliament and Council Directive 2001/83/EC as amended (including an application under Article 6.1 of Parliament and Council Regulation (EC) No 726/2004 that relies for its content on any such provision), or (iii) in any other country or jurisdiction pursuant to the equivalents of such provisions, including any amendments and successor statutes with respect to the subsections (i) through (iii). A Licensed Product authorized by Hansoh or any of its Affiliates or Sublicensees as an authorized generic product whether or not marketed by Hansoh or a Third Party will not constitute a Generic Product.

1.40 "**Global Licensed Compound**" means any Licensed Compound directed to the Global Licensed Target.

1.41 "**Global Licensed Product**" means any Licensed Product directed to the Global Licensed Target.

1.42 "**Global Licensed Target**" means the target selected as set forth in Section 2 of Schedule 1.78, unless otherwise agreed by the Parties in writing.

1.43 "**GLP Toxicology Study**" means an animal pharmacology and toxicology study conducted using current good laboratory practice that is used to assess whether a Licensed Compound is reasonably safe for initial testing in humans and to support an IND.

1.44 "**Gross Sales**" means, with respect to a Licensed Product for any period, the total amounts billed or invoiced on sales of such Licensed Product during such period by Hansoh, its Affiliates, or Sublicensees in the Hansoh Territory to Third Parties (including wholesalers or distributors), in bona fide arm's length transactions.

1.45 "**Hansoh Background IP**" means the Hansoh Background Patents and Hansoh Background Know-How.

1.46 "**Hansoh Background Know-How**" means any and all Know-How Controlled by Hansoh or any of its Affiliates (i) on the Effective Date, (ii) which has been generated by or on behalf of Hansoh or its Affiliates during the Term otherwise than in the performance of this Agreement, or (iii) other than Know-How created in undertaking any improvements to any Licensed Compound, Licensed Product or the Manufacturing thereof pursuant to Section 6.6, which has been generated by or on behalf of Hansoh or any of its Affiliates during the Term performing activities under this Agreement and outside the scope of any Research Plan, in each case (i), (ii), and (iii) solely to the extent that such Know-How is necessary or useful to Exploit Licensed Compounds or Licensed Products.

1.47 "**Hansoh Background Patents**" means any and all Patents Controlled by Hansoh or any of its Affiliates on the Effective Date or during the Term that Cover any Hansoh Background Know-How.

1.48 "**Hansoh China Product Development IP**" means the Hansoh China Product Development Patents and Hansoh China Product Development Know-How.

1.49 "**Hansoh China Product Development Know-How**" means any and all Know-How that is developed or invented by or on behalf of Hansoh or any licensee or sublicensee of Hansoh in the research or Development of any China Licensed Compound and/or China Licensed Product after the exercise of the Option by Hansoh in respect of a China Licensed Target.

1.50 "**Hansoh China Product Development Patents**" means any and all Patents Controlled by Hansoh after the Effective Date that Cover any Hansoh China Product Development Know-How.

1.51 "**Hansoh Parties**" means Jiangsu Hansoh and Hansoh Healthtech as defined above.

1.52 "**Hansoh Indemnitees**" has the meaning set forth in Section 14.2.

1.53 "**Hansoh Research IP**" means the Hansoh Research Patents and Hansoh Research Know-How.

1.54 "**Hansoh Research Know-How**" means any and all Know-How that is developed or invented after the Effective Date solely by or on behalf of Hansoh or any licensee or sublicensee of Hansoh in performing activities under any Research Plan or in undertaking any improvements to any Licensed Compound, Licensed Product or the Manufacturing thereof pursuant to Section 6.6. For clarity, Hansoh Research Know-How specifically excludes Hansoh Background Know-How and Joint Research Know-How.

1.55 "**Hansoh Research Patents**" means any and all Patents Controlled by Hansoh after the Effective Date that Cover any Hansoh Research Know-How.

1.56 "**Hansoh Sole Region**" means Mainland China, the Special Administrative Regions of Hong Kong and Macau, and Taiwan.

1.57 "**Hansoh Territory**" means

1.57.1 in respect of the Global Licensed Target and the corresponding Global Licensed Compounds and Global Licensed Products, worldwide; and

1.57.2 in respect of the China Licensed Targets and the corresponding China Licensed Compounds and China Licensed Products, the Hansoh Sole Region.

1.58 "**Holding Company**" has the meaning given to "holding company" in section 1159 of the UK Companies Act 2006.

1.59 "**In-Vivo Study**" means a study using a whole, living organism conducted using current good laboratory practice that is used to assess a Licensed Compound.

1.60 "**IND**" means an application filed with a Regulatory Authority for authorization to commence Clinical Studies, including (a) an Investigational New Drug Application as defined in the United States Federal Food, Drug, and Cosmetic Act, as amended, or any successor application or procedure filed with the FDA, (b) any equivalent of a United States IND in other countries or regulatory jurisdictions, (e.g., a Clinical Trial Application ("**CTA**")), and (c) all supplements, amendments, variations, extensions, and renewals thereof that may be filed with respect to the foregoing.

1.61 "**Indemnitee**" has the meaning set forth in Section 14.3.

1.62 "**Indemnitor**" has the meaning set forth in Section 14.3.

1.63 "**Indication**" means a disease, disorder, illness, or health condition and all of its associated signs, symptoms, stages, or any progression of the foregoing (including precursor conditions), in each case, for which a separate Phase 3 Trial is required.

1.64 "**Information**" means all knowledge of a technical, scientific, business and other nature, including know-how, technology, means, methods, processes, practices, formulae, instructions, skills, techniques, procedures, experiences, ideas, technical assistance, designs, drawings, assembly procedures, computer programs, apparatuses, specifications, data, results and other material, regulatory data, and other biological, chemical, pharmacological, toxicological, pharmaceutical, physical and analytical, pre-clinical, clinical, safety, manufacturing and quality control data and information, including study designs and protocols, reagents (e.g., chemical reactants, intermediates, modifications and products; plasmids, proteins, cell lines, assays and compounds) and chemical and biological methodologies; in each case (whether or not confidential, proprietary, patented or patentable, of commercial advantage or not) in written, electronic, or any other form now known or hereafter developed.

1.65 "**Initiation**" means, with respect to a Clinical Study, the first dosing of the first (1st) human subject in such Clinical Study. "**Initiate**" has a correlative meaning.

1.66 "**Joint Development Activities**" has the meaning set out in Section 7.4.1.

1.67 "**Joint Development Committee**" or "**JDC**" means the committee formed to oversee Joint Development Activities in accordance with Section 2.9.

1.68 "**Joint Development Plan**" means the plan agreed pursuant to Section 7.4.1 which plan shall be in the format set out in Schedule 1.68.

1.69 "**Joint Research IP**" means the Joint Research Patents and Joint Research Know-How.

1.70 "**Joint Research Know-How**" means any and all Know-How that is developed or invented after the Effective Date jointly by or on behalf of Hansoh on the one hand, and by or on behalf of Silence on the other hand, in performing activities under each Research Plan. For clarity, Joint Research Know-How specifically excludes Hansoh Background Know-How, Hansoh Research Know-How, Hansoh China Product Development Know-How, Silence Background Know-How, Silence Research Know-How and Silence China Product Development Know-How.

1.71 "**Joint Research Patents**" means any and all Patents that Cover any Joint Research Know-How.

1.72 "**Joint Steering Committee**" or "**JSC**" has the meaning set forth in Section 2.1.

1.73 "**Know-How**" means any and all computer programs, data (including pharmacological, biological, chemical, biochemical, toxicological, and regulatory data), designs, drawings, experience, results, ideas, improvements, instructions, inventions, know-how, knowledge, methods, methodologies, modifications, observations, procedures, processes, practices, skill, trade secrets, technical assistance, techniques, technology, works of authorship, and other proprietary Information, whether or not protectable under patent, copyrights, trade secret or other laws, but which are not generally known, including assembly procedures, discoveries, formulae, materials (including chemicals), biological materials (including expression constructs, nucleic acid sequences, amino acid sequences, and cell lines), clinical trial and patient selection designs and methodology, test data (including pharmacological, toxicological, pre-clinical and clinical information and test data), analytical and quality control data (including drug stability data), manufacturing technology and data (including formulation data), and sales forecasts, data and descriptions.

1.74 "**Licensed Compound**" means a compound comprising or consisting of RNAi Molecules [***].

1.75 "**Licensed Know-How**" means the Silence Background Know-How, Silence China Product Development Know-How and the Silence Research Know-How that is necessary for the Exploitation of a Licensed Compound.

1.76 "**Licensed Patent**" means any Patent comprised within the Silence Background Patents, Silence Research Patents, Silence China Product Development Patents or Joint Research Patents that, in the absence of a license, would be infringed by the Exploitation of Licensed Compounds or Licensed Products in the Field.

1.77 "**Licensed Product**" means a pharmaceutical product comprising or containing one or more Licensed Compounds as an active pharmaceutical ingredient, whether alone or in combination with one (1) or more other active ingredients, and in any form, formulation, dosage form and strength, and for any mode of delivery.

1.78 "**Licensed Target**" means any one of the China Licensed Targets and/or the Global Licensed Target but, for the avoidance of doubt, excluding any Failed Targets.

1.79 "**Mainland China**" means the People's Republic of China, but excluding the Special Administrative Regions of Hong Kong and Macau, and Taiwan.

1.80 "**Major Market**" means any of [***].

1.81 "**Manufacture**" and "**Manufacturing**" means all activities related to the synthesis, making, production, processing, purifying, formulating, filling, finishing, packaging, labelling, shipping, and holding of any molecule, product or any intermediate thereof, including process development, process qualification and validation, scale-up, pre-clinical, clinical and commercial production and analytic development, product

characterization, supply chain, stability testing, quality assurance testing and release, and quality control.

1.82 "**Net Sales**" means, with respect to a Licensed Product for any period, the Gross Sales, less the following deductions, in each case related specifically to the Licensed Product and actually allowed and taken by such Third Parties and not otherwise recovered by or reimbursed to Hansoh, its Affiliates, or Sublicensees:

(a) trade, cash and quantity discounts;

(b) price reductions, chargebacks or rebates, retroactive or otherwise, imposed by, negotiated with or otherwise paid to governmental authorities, health care organizations, health care insurance carriers, buying groups, distributors, wholesalers or other individual or group payees;

(c) actual non-collectable receivables written off in accordance with applicable accounting standard provided that the foregoing do not exceed one percent (1%) of the Net Sales in any given Quarter;

(d) taxes on sales (such as sales, excise, import, value added, or use taxes) to the extent added to the sale price and set forth separately as such in the total amount invoiced;

(e) amounts repaid or credited by reason of rejections, defects, return goods allowance, recalls or returns, or because of retroactive price reductions;

(f) the portion of administrative fees paid during the relevant time period to group purchasing organizations, pharmaceutical benefit managers or Medicare Prescription Drug Plans relating to such Licensed Product;

(g) freight, insurance, import/export, and other transportation charges to the extent added to the sale price and set forth separately as such in the total amount invoiced; and

(h) [***].

Net Sales shall not include transfers or dispositions for charitable, promotional, pre-clinical, clinical, regulatory, or governmental purposes, provided such transfer takes place for no consideration. Net Sales shall include the amount or fair market value of all other consideration received by Hansoh, its Affiliates, or Sublicensees in respect of the Licensed Product, whether such consideration is in cash, payment in kind, exchange, or other form. Net Sales shall not include sales between or among Hansoh, its Affiliates, or Sublicensees.

Where a Licensed Product is sold as part of a Combination Product, the Net Sales applicable to such transaction will be calculated by multiplying the total Net Sales of such combined product by the fraction A/(A+B), where A is the sale price of the Licensed Product portion of such Combination Product when sold separately and B is the sale price of the other active ingredient(s) in such Combination Product when sold separately; provided, however, that if the Licensed Product portion of such Combination Product or any of the other active ingredients in such Combination Product is not then sold separately, then Net Sales for purposes of determining royalty payments will be agreed upon by the Parties based on the relative value contributed by each component, such agreement not to be unreasonably withheld, conditioned or delayed.

If “A” or “B” cannot be determined by reference to non-Combination Product sales as described above, then Net Sales will be calculated as above, but the sale price in the above equation will be determined by mutual agreement reached in good faith by the Parties

prior to the end of the accounting period in question based on an equitable method of determining the same that takes into account, in the applicable country, variations in dosage units and the relative fair market value of each therapeutically-active component in the Combination Product. If the Parties are unable to reach such an agreement prior to the end of the applicable accounting period, the Parties will refer such matter to a jointly selected Third Party with expertise in the pricing of pharmaceutical products in the Hansoh Territory or relevant part thereof that is not, and has not in the past five (5) years been, an employee, consultant, legal advisor, officer, director or stockholder of, and does not have any conflict of interest with respect to, either Party for resolution.

Subject to the above, Net Sales shall be calculated in accordance with [***], which must be in accordance with Accounting Standards and consistent with the audited net sales reported externally by Hansoh.

For the purposes of calculating Net Sales, all Net Sales shall be converted into Dollars in accordance with Section 10.2.

1.83 "**NMPA**" means The National Medical Products Administration in Mainland China and any successor agency or authority having substantially the same function

1.84 "**Option**" has the meaning set forth in Section 5.1.

1.85 "**Option Exercise Date**" means, on an Option-by-Option basis, the date that Silence receives written notification that Hansoh wishes to exercise such Option, pursuant to Section 5.1.

1.86 "**Option Exercise Payment**" has the meaning set forth in Section 5.2.

1.87 "**Option Term**" means:

1.87.1 in respect of each of the China Licensed Targets, the period of time commencing on the delivery to Hansoh of a Research Plan Data Package (to be delivered within [***] ([***]) days of [***], and expiring on the earlier of: (i) [***] ([***]) calendar days after [***], or [***] ([***]) calendar days after [***] (ii) termination of this Agreement as a whole, or (iii) termination of this Agreement to the extent relating to the relevant China Licensed Target.

1.87.2 in respect of the Global Licensed Target, the period of time commencing on the [***] (to be delivered within [***] ([***]) days of the completion of [***]) in respect of the Global Licensed Target, and expiring on the earlier of (i) [***] ([***]) calendar days after [***], or [***] ([***]) calendar days after [***], (ii) termination of this Agreement as a whole, or (iii) termination of this Agreement to the extent relating to the Global Licensed Target.

1.88 "**Patent Challenge**" has the meaning set forth in Section 15.4.

1.89 "**Patents**" means (a) all national, regional and international patents and patent applications, including provisional patent applications and any and all rights to claim priority thereto, (b) all patent applications filed either from such patents, patent applications, or provisional applications or from an application claiming priority from either of these, including divisionals, continuations, continuations-in-part, provisionals, converted provisionals, and continued prosecution applications, (c) any and all patents that have issued or in the future issue from the foregoing patent applications ((a) and (b)), including utility models, petty patents, and design patents and certificates of invention, (d) any and all extensions or restorations by existing or future extension or restoration mechanisms, including revalidations, reissues, re-examinations, and extensions (including any supplementary protection certificates and the like) of the foregoing patents or patent applications or other patents resulting from post-grant proceedings ((a), (b), and

(c)), and (e) any similar patent rights, including so-called pipeline protection or any importation, revalidation, confirmation, or introduction patent or registration patent or patent of additions to any of such foregoing patent applications and patents.

1.90 "**Person**" means an individual, sole proprietorship, partnership, limited partnership, limited liability partnership, corporation, limited liability company, business trust, joint stock company, trust, unincorporated association, joint venture or other similar entity or organization, including a government or political subdivision, department, or agency of a government.

1.91 "**Phase 1 Trial**" means a human clinical trial of a Licensed Product that satisfies the requirements for a Phase 1 study as defined in 21 CFR § 312.21(a) (or any amended or successor regulations), regardless of where such clinical trial is conducted.

1.92 "**Phase 2 Trial**" means a human clinical trial of a Licensed Product that satisfies the requirements for a Phase 2 study as defined in 21 CFR § 312.21(b) (or any amended or successor regulations), regardless of where such clinical trial is conducted.

1.93 "**Phase 3 Trial**" means a human clinical trial of a Licensed Product that satisfies the requirements for a Phase 3 study as defined in 21 CFR § 312.21(c) (or any amended or successor regulations), regardless of where such clinical trial is conducted.

1.94 "**PMDA**" means Japan's Pharmaceuticals and Medical Devices Agency and any successor agency or authority having substantially the same function.

1.95 "**Preliminarily Identified Target**" means those targets set out in Schedule 1.95.

1.96 "**Product Specific Patent**" means any Licensed Patent that specifically and solely claims the composition of matter, manufacture, or method of use of a Licensed Compound or Licensed Product directed to the relevant Licensed Target.

1.97 "**Publishing Party**" has the meaning set forth in Section 12.5.3.

1.98 "**Quarter**" means each successive period of three (3) calendar months commencing on January 1, April 1, July 1 and October 1, except that the first Quarter of the Term shall commence on the Effective Date and end on the day immediately prior to the first to occur of January 1, April 1, July 1 or October 1 after the Effective Date, and the last Quarter shall end on the last day of the Term.

1.99 "**Regulatory Approval**" means, with respect to a country or other jurisdiction in the Hansoh Territory or Silence Territory, any and all approvals (including Drug Approval Applications), licenses, registrations, or authorizations of any Regulatory Authority necessary to Commercialize a Licensed Product in such country or other jurisdiction, including, where applicable, pricing or reimbursement approval in such country or other jurisdiction.

1.100 "**Regulatory Authority**" means any applicable supra-national, federal, national, regional, state, provincial, or local governmental or regulatory authority, agency, department, bureau, commission, council, or other entities (e.g., the FDA, EMA, NMPA and PMDA) regulating or otherwise exercising authority with respect to activities contemplated in this Agreement, including the Exploitation of any Licensed Products in the Hansoh Territory or the Silence Territory.

1.101 "**Regulatory Documentation**" means all (a) applications (including any agency submissions) and registrations, licenses, authorizations, and approvals (including Regulatory Approvals), (b) material correspondence and reports submitted to or received from Regulatory Authorities (including minutes and official contact reports relating to any communications with any Regulatory Authority) and all supporting documents with respect thereto, including all regulatory drug lists, advertising and promotion documents,

adverse event files, and complaint files, and (c) clinical data and other data contained in any of the foregoing, in each case ((a), (b), and (c)) relating to a Licensed Compound or Licensed Product.

1.102 "**Regulatory Exclusivity**" means, with respect to any country or other jurisdiction in the Hansoh Territory, an additional market protection, other than Patent protection, granted by a Regulatory Authority in such country or other jurisdiction which confers an exclusive Commercialization period during which Hansoh or its Affiliates or Sublicensees have the exclusive right to market and sell a Licensed Product in such country or other jurisdiction through a regulatory exclusivity right (e.g., new chemical entity exclusivity, new use or indication exclusivity, new formulation exclusivity, orphan drug exclusivity, pediatric exclusivity, or any applicable data exclusivity).

1.103 "**Research Budget**" has the meaning set forth in Section 3.2.

1.104 "**Research Collaboration Term**" means the period commencing on the Effective Date and ending upon the earlier of (a) the expiration of the Research Plan Term for all of the Licensed Targets, and (b) termination of this Agreement.

1.105 "**Research Plan**" means the research plan that shall form the basis of the Development work for the particular Licensed Target in respect of which Hansoh expects to exercise an Option, and setting out the information that will form part of the Research Plan Data Package. Each Research Plan for the China Licensed Targets shall identify for each activity whether it is specifically related to the Hansoh Territory, the Silence Territory or both. A template Research Plan is set out in Schedule 1.105.

1.106 "**Research Plan Data Package**" means, with respect to Licensed Compounds and Licensed Products directed to a particular Licensed Target, a report setting out the data generated by or on behalf of Silence in performing activities under the applicable

Research Plan in respect of such Licensed Compounds and/or Licensed Products which shall include the information identified in the applicable Research Plan that is agreed to form part of the Research Plan Data Package.

1.107 "**Research Plan Term**" means the term of any Research Plan, which shall commence on the date that the Parties agree that activities thereunder shall begin and shall, for the Research Plan related to the Global Licensed Target not exceed [***] years, and for the Research Plans related to the China Licensed Targets not exceed [***] years, unless otherwise agreed in writing or which is extended pursuant to Section 3.6 or Section 3.7.

1.108 "**Restricted Information**" means (i) any data generated by any Clinical Study or any preclinical study conducted in animals (including in both cases any study subject follow-up and analysis of study subject samples) in each case that was conducted by either Party in respect of a Licensed Compound or Licensed Product; (ii) any information describing any chemical structure ([***]) and any information describing the mechanism of action of the foregoing, in each case, disclosed by the other Party; and (iii) any information directly related to the Manufacture of any compound that is disclosed to the other Party.

1.109 "**RNA**" means ribonucleic acid.

1.110 "**RNAi Molecule**" means [***].

1.111 "**Royalty Term**" means, with respect to each Licensed Product and each country or region in the Hansoh Territory, the period beginning on the date of the First Commercial Sale of such Licensed Product in such country or region, and ending on the [***] to occur of (a) the expiration of the last-to-expire Valid Claim of any [***] Patent that Covers the composition of matter of the Licensed Compound contained in such Licensed Product in such country or region, (b) the expiration of Regulatory Exclusivity for such Licensed

Product in such country or region, and (c) the [***] ([***]) anniversary of the First Commercial Sale of such Licensed Product in such country or region.

1.112 "**Senior Officer**" means, with respect to Silence, its Chief Executive Officer or his/her designee, and with respect to Hansoh, its Executive Director of the Board or his/her designee.

1.113 "**Silence Background IP**" means the Silence Background Patents and Silence Background Know-How.

1.114 "**Silence Background Know-How**" means any and all Know-How Controlled by Silence or any of its Affiliates (i) on the Effective Date, (ii) which has been generated by or on behalf of Silence or its Affiliates during the Term otherwise than in the performance of this Agreement, or (iii) which has been generated by or on behalf of Silence or any of its Affiliates during the Term performing activities under this Agreement and outside the scope of any Research Plan, in each case (i), (ii), and (iii) solely to the extent that such Know-How is necessary or useful to Exploit Licensed Compounds or Licensed Products.

1.115 "**Silence Background Patents**" means any and all Patents Controlled by Silence or any of its Affiliates on the Effective Date or during the Term that Cover any Silence Background Know-How.

1.116 "**Silence China Product Development IP**" means the Silence China Product Development Patents and Silence China Product Development Know-How.

1.117 "**Silence China Product Development Know-How**" means any and all Know-How that is developed or invented by or on behalf of Silence or any licensee or sublicensee of Silence in the research, Development of any China Licensed Compound and/or China

Licensed Product after the exercise of the Option by Hansoh in respect of a China Licensed Target.

1.118 "**Silence China Product Development Patents**" means any and all Patents Controlled by Silence after the Effective Date that Cover any Silence China Product Development Know-How.

1.119 "**Silence Indemnitees**" has the meaning set forth in Section 14.1.

1.120 "**Silence Research IP**" means the Silence Research Patents and Silence Research Know-How.

1.121 "**Silence Research Know-How**" means any and all Know-How that is developed or invented after the Effective Date solely by or on behalf of Silence or any licensee or sublicensee of Silence in performing activities under any Research Plan, or in undertaking any improvements to any Licensed Compound, Licensed Product or the Manufacturing thereof outside of a Research Plan. For clarity, Silence Research Know-How specifically excludes Silence Background Know-How and Joint Research Know-How.

1.122 "**Silence Research Patents**" means any and all Patents Controlled by Silence or any of its Affiliates after the Effective Date that Cover any Silence Research Know-How.

1.123 "**Silence Technology Transfer Support**" has the meaning set forth in Section 8.4.1.

1.124 "**Silence Territory**" means, in respect of the China Licensed Targets and the corresponding China Licensed Compounds and China Licensed Products, all areas of the world other than the Hansoh Sole Region. It is recognized that since Hansoh's rights in relation to the Global Licensed Target are worldwide, there shall be no Silence Territory

in respect of the Global Licensed Target, Global Licensed Compounds and corresponding Global Licensed Products.

1.125 "**Sublicensee**" means a Third Party to whom Hansoh (or a sublicensee of Hansoh) grants a sublicense to Develop, Manufacture, use, import, promote, offer for sale, sell, have sold, or otherwise Commercialize any Licensed Product in the Field in the Hansoh Territory, beyond the mere right to purchase Licensed Products from Hansoh and its Affiliates, and excluding wholesalers, full-service distributors that do not promote the sale of the Licensed Product, and other similar physical distributors.

1.126 "**Term**" has the meaning set forth in Section 15.1.

1.127 "**Third Party**" means any Person other than Silence, Hansoh, or an Affiliate of Silence or Hansoh.

1.128 "**Valid Claim**" means either: (a) a claim of a pending Patent application, which claim was filed and is being prosecuted in good faith and has not been abandoned or finally disallowed without the possibility of appeal or re-filing of the application provided always that if a particular claim has not issued within [***] ([***]) years of its priority date, it will not be considered a Valid Claim for purposes of this Agreement unless and until such claim is included in an issued or granted Patent, notwithstanding the foregoing definition; or (b) a claim of any issued and unexpired Patent for which the validity, enforceability, or patentability has not been affected by any of the following: (x) irretrievable lapse, abandonment, revocation, dedication to the public, or disclaimer; or (y) a holding, finding, or decision of invalidity, unenforceability, or non-patentability by a court, governmental agency, national or regional patent office, or other appropriate body that has competent jurisdiction, such holding, finding, or decision being final and unappealable or unappealed within the time allowed for appeal.

1.129 "**Withholding Party**" has the meaning set forth in Section 10.3.

1.130 "**Year**" means each successive period of twelve (12) calendar months commencing on January 1 and ending on December 31, except that the first Year of the Term shall commence on the Effective Date and end on December 31 of the year in which the Effective Date occurs and the last Year of the Term shall commence on January 1 of the year in which the Term ends and end on the last day of the Term.

1.131 In this Agreement:

1.131.1 all references to a particular Section or Schedule shall be a reference to that Section or Schedule in or to this Agreement as it may be amended from time to time pursuant to this Agreement;

1.131.2 the headings are inserted for convenience only and shall be ignored in construing this Agreement;

1.131.3 words importing the masculine gender shall include the feminine and vice versa and words in the singular include the plural and vice versa;

1.131.4 the words "include", "included", and "including" are to be construed without conveying any limitation to the generality of the preceding words;

1.131.5 reference to any statute or regulation includes any modification or re-enactment of that statute or regulation;

1.131.6 any reference to notices or consent being sought or given in writing shall require the consent or notice to be signed by an appropriately authorised person and shall not include consents or notices conveyed by email; and

1.131.7 in the event of any inconsistency or conflict between this Agreement and any of the Schedules, this Agreement shall prevail.

ARTICLE 2
COLLABORATION MANAGEMENT

2.1 **Joint Steering Committee**. Within [***] ([***]) days after the Effective Date, or as mutually agreed to by the Parties, the Parties shall establish a joint steering committee (the "**Joint Steering Committee**" or "**JSC**"). The JSC shall consist of [***] ([***]) representatives from each of the Parties in addition to [***] ([***]) Alliance Manager from each Party, each with the requisite experience and seniority to enable such person to make decisions on behalf of the Parties with respect to the issues falling within the jurisdiction of the JSC. From time to time, each Party may substitute one (1) or more of its representatives to the JSC by providing prior written confirmation (which may be by email) to the other Party. The chairperson for each meeting shall rotate between Hansoh and Silence, with one of each Party's JSC representatives acting as chairperson of the JSC on a rotating basis.

2.2 **Specific Responsibilities of the JSC**. Until the expiration of the Research Collaboration Term with respect to a particular Licensed Target, the JSC shall review the strategy for and oversee the Development of the Licensed Compounds and Licensed Products directed to such Licensed Target. In particular, the JSC shall:

2.2.1 agree on the activities to be included in each Research Plan;

2.2.2 establish a project team for each Research Plan;

2.2.3 review and discuss the overall status of each Research Plan and the conduct of research and Development activities under each Research Plan;

2.2.4 review and discuss the results of each activity under each Research Plan, whether completed or ongoing;

2.2.5 review and agree to any amendment to a Research Plan;

2.2.6 review and discuss the prosecution strategy for Silence Research Patents and Joint Research Patents, including using their Commercially Reasonable Efforts to ensure that there are or will be a commercially reasonable set of Product Specific Patents directed to each Licensed Target and to Licensed Products directed to each such Licensed Target;

2.2.7 to review and approve decisions of the JDC and to resolve any failure to agree at the JDC;

2.2.8 review and discuss the Manufacturing requirements for any Licensed Compounds;

2.2.9 review and determine what information will be included as part of the Research Plan Data Package, to the extent not already specified in the applicable Research Plan;

2.2.10 establish a Patent Working Group to review and discuss the prosecution strategy for Product Specific Patents and Joint Research Patents, as set out in Section 11.2;

2.2.11 establish subcommittees to perform specific duties of the JSC, direct each such subcommittee to perform the functions for which it is established, and oversee each subcommittee, including resolution of disputes raised to the JSC by any subcommittee;

2.2.12 perform such other functions, and direct each subcommittee to perform such other functions, as are set forth herein or as the Parties may mutually agree in writing, except where in conflict with any provision of this Agreement.

2.3 **Disbandment**. The JSC shall continue to exist until the Parties mutually agree to disband the JSC and thereafter each Party shall designate, to the extent necessary, a contact person for the exchange of Information under this Agreement or such exchange of Information shall be made through the Alliance Managers, and decisions of the JSC, if any, shall be decisions as between the Parties, subject to the other terms and conditions of this Agreement. For clarity, the Patent Working Group shall survive dissolution of the JSC until such time as the Parties mutually agree to disband it.

2.4 **Location of Meetings**. The JSC shall meet at least once per [***], or as otherwise agreed to by the Parties. JSC meetings may be held in person or by audio or video teleconference; provided that unless otherwise agreed, at least [***] ([***]) per Year shall be held in person. In-person meetings shall be held at locations in the United Kingdom, the United States of America, Germany, or the Hansoh Sole Region, as alternately selected by the Parties.

2.5 **Conduct of Meetings**. The chairperson of the JSC shall be responsible for calling meetings on no less than [***] ([***]) Business Days' notice. Each Party shall make all proposals for agenda items and shall provide all appropriate information with respect to such proposed items at least [***] ([***]) Business Days in advance of the applicable meeting; provided, that if the input by the JSC is required urgently, a Party may provide its agenda items to the other Party within a shorter period of time in advance of the meeting, or may propose that there not be a specific agenda for a particular meeting, so long as the other Party consents to such later addition of such agenda items or the absence of a specific agenda for such meeting, such consent not to be unreasonably withheld,

conditioned, or delayed. An individual designated by the chairperson of the JSC shall prepare and circulate the minutes of each meeting for review and approval of the Parties within [***] ([***]) days after the meeting. The Parties shall agree on the minutes of each meeting promptly, but in no event later than the next meeting of the JSC.

2.6 **Procedural Rules**. The JSC shall have the right to adopt such standing rules as shall be necessary for its work, to the extent that such rules are not inconsistent with this Agreement. A quorum of the JSC shall exist whenever there is present at a meeting at least one (1) representative appointed by each Party. Representation by proxy shall be allowed. The JSC shall take action by consensus of the representatives present at a meeting at which a quorum exists, with each Party having a single vote irrespective of the number of representatives of such Party in attendance, or by a written resolution which may be delivered by way of email confirmation. Employees or consultants of either Party that are not representatives of the Parties on the JSC may attend meetings of the JSC; provided, that (a) unless the other Party agrees, no more than two (2) such persons, in addition to such Party's Alliance Manager, may attend any particular meeting, (b) attendance of any non-employee must be pre-approved by the other Party, such approval not to be unreasonably withheld, conditioned or delayed and (c) such attendees (i) shall not vote or otherwise participate in the decision-making process of the JSC and (ii) are bound by obligations of confidentiality and non-disclosure that are substantially similar to those set forth in ARTICLE 12.

2.7 **Decision Making**.

2.7.1 **JSC Decisions**. All JSC decisions shall be made by unanimous vote, with each Party's representatives collectively having one (1) vote. If after reasonable discussion and good faith consideration of each Party's view on a particular matter, the JSC cannot, or does not, reach consensus on an issue

within the scope of the JSC, then the dispute shall first be referred to the Senior Officers of the Parties, who shall confer in good faith on the resolution of the issue. Any final decision mutually agreed to by the Senior Officers shall be conclusive and binding on the Parties.

2.7.2 **Final Decision Making Authority**. If the Senior Officers are not able to agree on the resolution of any such issue within [***] ([***]) days after such issue was first referred to them, then subject to the remainder of this Section 2.7.2:

(a) [***] Silence shall have final decision-making authority as to [***];

(b) in respect of [***], Hansoh shall have the final say;

(c) in respect of [***];

(i) if the matter relates only to [***] then [***] Hansoh shall have the final say;

(ii) if the matter relates only to [***], then [***]Silence shall have the final say; and

(iii) in respect of all other decisions, the Party conducting such activity shall have the final say.

(d) Notwithstanding the forgoing, neither Party may use its final decision-making authority to (a) require the other Party to violate any Applicable Law or any agreement it may have with a third party, (b) to make changes to any Research Plan that would [***], (c) to require the other Party to incur any additional out of pocket costs in

the conduct of the Research Plan beyond those agreed to and budgeted in accordance with this Agreement, or (d) to increase the applicable Research Budget by more than [***] ([***]%).

2.7.3 **Other Disputes**. For clarity, disputes arising between the Parties in connection with or relating to this Agreement or any document or instrument delivered in connection herewith that are outside of the jurisdiction of the JSC shall be resolved pursuant to Section 16.7.

2.8 **Limitations on Authority**. Each Party shall retain the rights, powers, and discretion granted to it under this Agreement and no such rights, powers, or discretion shall be delegated to or vested in the JSC unless such delegation or vesting of rights is expressly provided for in this Agreement or the Parties expressly so agree in writing. The JSC does not have the power to amend, modify, or waive compliance with this Agreement, and this Agreement may only be amended or modified as provided in Section 16.9 and compliance with this Agreement may only be waived as provided in Section 16.11.

2.9 **Joint Development Committee.** Promptly, and in any event within [***] ([***]) days, after the exercise by Hansoh of its Option in respect of a China Licensed Target, the Parties shall establish a joint development committee (the "**Joint Development Committee**" or "**JDC**") that consists of [***] ([***]) representatives from each of the Parties in addition to [***] ([***]) Alliance Manager from each Party, each with the requisite experience and seniority to enable such person to make decisions on behalf of the Parties with respect to the issues falling within the jurisdiction of the JDC. From time to time, each Party may substitute one (1) or more of its representatives to the JDC by providing prior written confirmation (which may be by email) to the other Party. The chairperson for each meeting shall rotate between Hansoh and Silence, with one of each Party's JDC representatives acting as chairperson of the JDC on a rotating basis.

2.9.1 **Specific Responsibilities.** The JDC shall provide strategic direction for, and monitor, manage, coordinate and oversee the performance of, the Joint Development Activities by the Parties under the Joint Development Plan, and serve as a forum to facilitate communications between the Parties regarding the Joint Development Plan. In particular, the JDC shall:

(a) serve as a forum for discussing proposed Joint Development Activities and periodically review the Joint Development Plan for such Joint Development Activities, and review and submit to the JSC for approval amendments thereto;

(b) oversee the conduct of Joint Development Activities;

(c) perform such other functions as are expressly set forth herein or as the Parties may mutually agree in writing, except where in conflict with any provision of this Agreement.

2.10 **Location of Meetings**. The JDC shall meet at least once per [***], or as otherwise agreed to by the Parties. JDC meetings may be held in person or by audio or video teleconference; provided that unless otherwise agreed, at least [***] ([***]) per Year shall be held in person. In-person meetings shall be held at locations in either the United Kingdom, the United States of America or the Hansoh Sole Region, as alternately selected by the Parties.

2.11 **Conduct of Meetings**. The chairperson of the JDC shall be responsible for calling meetings on no less than [***] ([***]) Business Days' notice (unless agreed to in writing by each Party). Each Party shall make all proposals for agenda items and shall provide all appropriate information with respect to such proposed items at least [***] ([***]) Business Days in advance of the applicable meeting; provided, that if the input by the

JDC is required urgently, a Party may provide its agenda items to the other Party within a shorter period of time in advance of the meeting, or may propose that there not be a specific agenda for a particular meeting, so long as the other Party consents to such later addition of such agenda items or the absence of a specific agenda for such meeting, such consent not to be unreasonably withheld, conditioned, or delayed. An individual designated by the chairperson of the JDC shall prepare and circulate the minutes of each meeting for review and approval of the Parties within [***] ([***]) days after the meeting. The Parties shall agree on the minutes of each meeting promptly, but in no event later than the next meeting of the JDC.

2.12 **Procedural Rules**. Subject to the approval of the JSC, the JDC shall have the right to adopt such standing rules as shall be necessary for its work, to the extent that such rules are not inconsistent with this Agreement. A quorum of the JDC shall exist whenever there is present at a meeting at least one (1) representative appointed by each Party. Representation by proxy shall be allowed. The JDC shall take action by consensus of the representatives present at a meeting at which a quorum exists, with each Party having a single vote irrespective of the number of representatives of such Party in attendance, or by a written resolution which may be delivered by way of email confirmation. Employees or consultants of either Party that are not representatives of the Parties on the JDC may attend meetings of the JDC; provided, that (a) unless the other Party agrees, no more than [***] ([***]) such persons, in addition to such Party's Alliance Manager, may attend any particular meeting, (b) attendance of any non-employee must be pre-approved by the other Party, such approval not to be unreasonably withheld, conditioned or delayed and (c) such attendees (i) shall not vote or otherwise participate in the decision-making process of the JDC and (ii) are bound by obligations of confidentiality and non-disclosure that are substantially similar to those set forth in ARTICLE 12.

2.13 **Decisions of the JDC.** All decisions of the JDC shall be subject to the ratification of such decision at the next JSC. In the event that the members of the JDC cannot reach a unanimous decision on any issue, the matter shall be referred to the JSC and the JSC decision making authority shall apply to such issue.

2.14 **Alliance Manager**. Promptly after the Effective Date, each Party shall appoint [***] who shall oversee contact between the Parties for all matters between meetings of the JSC and shall have such other responsibilities as the Parties may agree in writing after the Effective Date (each, an "**Alliance Manager**"). If not already a member of the JSC and/or JDC, each Alliance Manager shall be permitted to attend JSC and JDC meetings as appropriate as non-voting participants. Each Party may replace its Alliance Manager at any time by notice in writing to the other Party. Each Party shall bear the costs of its Alliance Manager.

2.15 **Expenses**. Each Party shall be responsible for all travel and related costs and expenses for its members and other representatives to attend meetings of, and otherwise participate in, the JSC and JDC.

2.16 **R&D Meetings**. During the Research Plan Term, in addition to meetings of the JSC and JDC, at least one individual from each Party who is involved in the conduct of the Research Plan shall meet as mutually agreed by the Parties, but in no event less than [***] (each an "**R&D Meeting**"), to facilitate and promote the exchange of information between the Parties with respect to the conduct of the Research Plan. The first R&D Meeting shall be held within [***] ([***]) days of the Effective Date. R&D Meetings may be held by telephone or video conference. All in-person R&D Meetings shall be held at locations as mutually agreed upon by the Parties. In the event that both Parties agree that such meetings would be useful after the exercise of the Option in respect of a Licensed Target, the Parties shall use their good faith efforts to agree on how such

meetings will be conducted after the Option Exercise Date for a period and at a frequency to be agreed.

ARTICLE 3
DEVELOPMENT AND REGULATORY

3.1 **Overview**. Subject to the terms and conditions of this Agreement, during the Research Collaboration Term the Parties will collaborate with respect to the performance of the Research Plans and shall keep the JSC informed of such activities.

3.2 **Research Plans**. The Research Plans shall set forth the estimated timeline and details for all activities to be conducted pursuant to such plan, based upon the outline Research Plan set out in Schedule 1.105. The Research Plans shall also: (a) include a reasonably detailed budget of the Development costs for the activities to be conducted pursuant to such plan (the "**Research Budget**") on an activity-by-activity or study-by-study basis, as appropriate, and (b) set out the expected contents of the Research Plan Data Package for each Licensed Target. If the terms of a Research Plan contradict, or create inconsistencies or ambiguities with, the terms of this Agreement, then the terms of this Agreement shall govern. From time to time, the Parties may prepare updates and amendments, as appropriate, to a Research Plan (including any consequential changes to the Research Budget), for review of and approval by the JSC, subject to and in accordance with the applicable provisions of ARTICLE 2, including Section 2.7.

3.3 **Research Plan Timing.** The Parties shall be required to initiate work on:

3.3.1 the [***] Research Plan, being the Research Plan directed to the [***]Licensed Target, no later than [***] ([***]) months after the Effective Date provided that neither Party shall be obliged initiate work pursuant to

such Research Plan earlier than [***] ([***]) months after the Effective Date; and

3.3.2 the [***] Research Plan being the Research Plan directed to the [***] Licensed Target, no later than [***] ([***]) months after the Effective Date provided that neither Party shall be obliged initiate work pursuant to such Research Plan earlier than [***] ([***]) months after the Effective Date.

3.4 **Research Budget Caps.** Except as otherwise provided in this Agreement or mutually agreed in writing by the Parties, neither Party shall be required to perform any activities or incur any costs, fees or expenses under any Research Plan in excess of the relevant Research Budget or for longer than the Research Plan Term.

3.5 **Research Plan Data Package.** On completion of all of the activities in respect of the relevant Research Plan, or if the Research Plan Term in respect of a particular Licensed Target has expired, Silence shall notify the JSC of such, and shall provide the Research Plan Data Package to the JSC for review. The JSC shall promptly review the Research Plan Data Package and, as soon as reasonably possible after receipt of the Research Plan Data Package, and in any event within [***] ([***]) days, the JSC shall inform the Parties:

3.5.1 that the Research Plan Data Package is substantially complete; or

3.5.2 that the Research Plan Data Package is not substantially complete, in which case it shall identify in what respect the Research Plan Data Package is incomplete and the provisions of Section 3.6 shall apply.

3.6 If the JSC considers that the Research Plan Data Package is not substantially complete, then the Parties will discuss in good faith a suitable extension to the relevant Research

Plan, setting out the additional work to be performed. Subject to agreement of an extension to the relevant Research Plan covering the relevant additional work, such work shall be at [***] expense in respect of the [***] Licensed Target and the corresponding [***] Licensed Compound and [***] Licensed Products and the costs shall be [***] in respect of the [***] Licensed Targets and the corresponding [***] Licensed Compounds and [***] Licensed Products. All FTEs involved in performing such work by or on behalf of [***] shall be charged at the FTE Cost. Any Research Plan extension under this Section 3.6 shall be limited to [***] ([***]) months additional work beyond that anticipated by the existing applicable Research Plan, unless otherwise expressly agreed by the Parties in writing. At the end of such additional work, Silence shall deliver an updated Research Plan Data Package to the JSC for review.

3.7 In the event that the JSC considers that the updated Research Plan Data Package delivered pursuant to Section 3.6 remains not substantially complete and if [***] wishes [***] that additional work related to the applicable Licensed Target be undertaken, then the Parties will discuss in good faith a suitable additional extension to the relevant Research Plan, setting out the additional work to be performed by (i) [***], or (ii) if [***] declines to undertake such additional work, [***], in each case (i) and (ii) at [***] expense. In the event that the Parties agree that [***] undertakes such additional work, [***] shall provide reasonable assistance to allow [***] to conduct such additional work, at [***] expense. Hansoh hereby grants to Silence a non-exclusive, worldwide, perpetual, irrevocable, royalty-free license, with the right to grant sublicenses as provided in Section 6.3 to any and all intellectual property rights arising from any work that Hansoh undertakes pursuant to this Section 3.7, provided always that such rights shall be subject to the licenses granted in Section 6.1 to Section 6.3. Any Research Plan extension under this Section 3.7 shall be limited to [***] ([***]) months additional work beyond that anticipated by the existing applicable Research Plan (including any extension thereof),

unless otherwise expressly agreed by the Parties in writing. At the end of such additional work, Silence or Hansoh (as applicable) shall deliver an updated Research Plan Data Package to the JSC for review.

3.8 If (a) the JSC considers that the updated Research Plan Data Package provided pursuant to Sections 3.5, 3.6, and 3.7, as applicable, is not substantially complete for any Licensed Target or (b) the Parties mutually agree to end Development of any Licensed Target (in each case (a) and (b) a "**Failed Target**"), such Failed Target shall not be considered an Expired Target pursuant to Section 5.3 nor shall the termination of efforts related to such Failed Target constitute a voluntary termination by Hansoh pursuant to Section 15.2.

3.9 Diligence.

3.9.1 The Parties shall use their respective Commercially Reasonable Efforts to carry out the tasks allocated to them in each agreed Research Plan (including any extension thereto) taking into account the scope of work covered under such Research Plan. Each Party shall use its Commercially Reasonable Efforts to adhere to any timeframes set forth in a Research Plan.

3.9.2 The Parties acknowledge and agree that no outcome or success is or can be assured and that failure to achieve desired results will not in and of itself constitute a breach or default of any obligation in this Agreement.

3.10 Research Expenses. The costs of conducting each Research Plan shall be as follows:

3.10.1 In relation to the [***] Licensed Targets each Party shall be solely responsible for the costs and expenses incurred by such Party in connection with the performance of the Development activities assigned to such Party under and

in accordance with each Research Plan and applicable Research Budget, except that [***] that are [***] shall be reimbursed [***] in advance.

3.10.2 In relation to the [***] Licensed Target, [***] shall reimburse [***] for [***] utilized in performance of activities under the relevant Research Plan in accordance with the Research Budget attached to the relevant Research Plan. In the event that [***] reasonably expects that it will incur any costs, fees or expenses in any Quarter in excess of [***] ([***]%) above the Research Budget for such Quarter with respect to any Research Plan, then [***] shall notify the JSC in writing thereof, and upon receipt of such notice the JSC may approve any amendment to the applicable Research Budget to cover any such excess costs, fees or expenses. In the event that the JSC delays, conditions or refuses its consent to approve any such amendment then [***] shall not be liable for any delay or failure to perform such activities under the applicable Research Plan, for which such costs, fees or expenses are required to be incurred. Any overspend in any Quarter which constitutes an increase of [***] ([***]%) or below over the Research Budget for such Quarter will be automatically deemed to be approved by the JSC. In the event of any underspend of the Research Budget by [***], then [***] shall be entitled to carry such underspend forward to subsequent Quarters. Based on the information currently available to it, [***] estimates that total resource requirements up to IND filing will be a maximum of [***] ([***]) FTE per Research Plan.

3.11 **Development Updates; Information-Sharing**. At each regularly scheduled JSC meeting, each Party shall update the JSC in respect of any then-ongoing activities for

which such Party is responsible under a Research Plan. The Parties shall discuss the status, progress, and results of all such activities at such JSC meetings.

3.12 **Subcontracting**. Each Party shall have the right to subcontract its obligations under a Research Plan to subcontractors and Affiliates, subject to any limitations, restrictions or other qualifications that are set forth in an applicable Research Plan; provided that, (i) such subcontractors and Affiliates agree in writing to be subject to the applicable terms and conditions of this Agreement, including the confidentiality provisions of ARTICLE 12, (ii) that the subcontracting Party directly owns all Know-How and intellectual property rights that may arise as required by ARTICLE 11, (iii) the appointment of a subcontractor shall not release a Party of its obligations under this Agreement, and (iv) a Party shall be responsible for the management of all of its subcontractors and shall remain fully liable to the other Party for the acts and omissions of each such subcontractor.

3.13 **Materials**. In order to facilitate the performance of activities under the Research Plans, either Party may provide to the other Party certain materials for use by the other Party in furtherance of the Research Plans. All such materials are the Confidential Information of the providing Party and will be used by the receiving Party in accordance with the terms and conditions of this Agreement solely for purposes of exercising its rights and performing its obligations under this Agreement and the applicable Research Plan, and the receiving Party will not transfer such materials to any Third Party unless expressly contemplated by this Agreement or upon the written consent of the supplying Party.

ARTICLE 4
EXCLUSIVITY

4.1 **Mutual Exclusivity During the Term.** During the Term, on a Licensed Target-by-Licensed Target basis, each Party shall not, and shall ensure that its respective Affiliates do not, whether on their own or with or through a Third Party, Exploit [***] (including in any Licensed Product) designed to inhibit the relevant Licensed Target, except in the performance of their respective obligations or the exercise of their respective rights under this Agreement.

ARTICLE 5
OPTION GRANTS

5.1 **Option Grant to Hansoh**. Silence hereby grants to Hansoh, on a Licensed Target-by-Licensed Target basis, the exclusive right and option, exercisable at any time during the Option Term at Hansoh's sole discretion, to obtain and exercise an exclusive license under the Silence Background IP, the Silence Research IP, and Silence's interest in the Joint Research IP as set forth in Section 6.1 with respect to the Exploitation of Licensed Products containing the corresponding Licensed Compounds in the Field in the Hansoh Territory (each, an "**Option**"). Hansoh may exercise its Option in respect of a Licensed Target by providing written notice to Silence of its election to exercise such Option at any time during the Option Term. Upon delivery of such written notice and payment of the applicable Option Exercise Payment, the licenses set forth in Sections 6.1 and 6.2 shall, and thereby does, automatically become effective.

5.2 **Option Exercise Payment**. With respect to each Option exercised by Hansoh, Hansoh shall pay to Silence the non-refundable, non-creditable sum of (i) [***] million Dollars ($[***]) in respect of each China Licensed Target and (ii) [***] million Dollars ($[***])

in respect of the Global Licensed Target, (each an "**Option Exercise Payment**") within [***] ([***]) days after receipt by Hansoh of Silence's invoice.

5.3 **Non-Exercise of the Option**. If Hansoh does not exercise its Option with respect to a Licensed Target during the Option Term, or if Hansoh notifies Silence in writing prior to the expiration of the Option Term that it will not exercise such Option, then such Option shall immediately expire with respect to such Licensed Target (an "**Expired Target**") without any further action required on the part of either Party; provided, however, that a Failed Target shall not be considered an Expired Target. In such an event, Hansoh will:

5.3.1 deliver to Silence all its right, title and interest in and to all Licensed Compounds and Licensed Products Developed pursuant to this Agreement and which are directed to such Expired Target, and Silence will be free to Exploit such Expired Target, together with the, Licensed Compounds and Licensed Products directed to such Expired Target as Silence, in its sole discretion, deems appropriate; provided that, notwithstanding the foregoing or anything to the contrary in this Agreement, Hansoh shall not, and shall not be obligated, to transfer ownership of any Hansoh Background IP, Hansoh Research IP, and Hansoh China Product Development IP other than such Licensed Compounds and Licensed Products; and

5.3.2 grant to Silence the licenses set out in Section 15.6.1 in respect of each Expired Target, and all associated Licensed Compounds and Licensed Products.

ARTICLE 6
LICENSE GRANTS

6.1 License Grants to Hansoh.

6.1.1 Research Collaboration License. Silence hereby grants to Hansoh, during the Research Collaboration Term, a non-exclusive license, with the right to grant sublicenses to Affiliates and subcontractors (subject to Section 3.12), under the Silence Background IP and Silence Research IP, solely to conduct the activities assigned to Hansoh under the Research Plans.

6.1.2 Global Target Option License. Subject to Section 6.4, Silence, for itself and its Affiliates, hereby grants to Hansoh upon Hansoh exercising its Option in respect of the Global Licensed Target and paying the Option Exercise Payment with respect thereto, an exclusive (even as to Silence and its Affiliates), royalty-bearing license, with the right to grant sublicenses as provided in Section 6.3, under the Silence Background IP, Silence Research IP, and Silence's interest in the Joint Research IP solely to Exploit the Global Licensed Compounds and Global Licensed Products directed to such Global Licensed Target in the Field anywhere in the world.

6.1.3 China Target Option License. Subject to Section 6.4, Silence, for itself and its Affiliates, hereby grants to Hansoh upon Hansoh exercising its Option in respect of the relevant China Licensed Target and paying the Option Exercise Payment with respect thereto, an exclusive (even as to Silence and its Affiliates), royalty-bearing license, with the right to grant sublicenses as provided in Section 6.3, under the Silence Background IP, Silence Research IP, Silence China Product Development IP and Silence's interest in the Joint

Research IP solely to Exploit the China Licensed Compounds and China Licensed Products directed to such China Licensed Target in the Field in the Hansoh Sole Region. Subject to Silence's prior written consent (such consent to be in Silence's absolute discretion in respect of [***]), Hansoh may be authorised to [***]. Subject to Silence's prior written consent (such consent not to be unreasonably withheld, delayed or conditioned), Hansoh may be authorised to [***].

6.2 License Grants to Silence.

6.2.1 Research Collaboration License. Subject to Section 6.4, Hansoh hereby grants to Silence, during the Research Collaboration Term, a non-exclusive license, with the right to grant sublicenses to Affiliates and subcontractors (subject to Section 3.12), under the Hansoh Background IP and Hansoh Research IP, solely to conduct the activities assigned to Silence under the Research Plans with respect to the Licensed Compounds and Licensed Products.

6.2.2 China Target License. Subject to Section 6.4, Hansoh, for itself and its Affiliates, hereby grants to Silence (i) an exclusive (even as to Hansoh and its Affiliates), royalty-free license, with the right to grant sublicenses as provided in Section 6.3, under the Hansoh Research IP, Hansoh China Product Development IP and Hansoh's interest in the Joint Research IP, and (ii) a non-exclusive, royalty-free license, with the right to grant sublicenses as provided in Section 6.3, under the Hansoh Background IP, in each case (i) and (ii) solely to Exploit China Licensed Compounds and China Licensed Products directed to each China Licensed Target in the Field in the Silence Territory. Subject to Hansoh's prior written consent (such consent to be in Hansoh's

absolute discretion in respect of [***]), Silence may be authorised to undertake [***]. Subject to Hansoh's prior written consent (such consent not to be unreasonably withheld, delayed or conditioned), Silence may be authorised to [***]. In the event that Hansoh does not exercise the Option in respect of either or both China Licensed Targets during the Option Term then the territorial scope of the license granted in this Section 6.2.2 in respect of such China Licensed Target shall be extended to the entire world; provided, however, that this Section 6.2.2 shall not apply with respect to a Failed Target.

6.2.3 **Option Lapse License.** Subject to Section 6.4, in the event that Hansoh does not exercise the Option in respect of the Global Licensed Target within the relevant Option Term, Hansoh, for itself and its Affiliates, hereby grants to Silence (i) an exclusive (even as to Hansoh), royalty-free license, with the right to grant sublicenses as provided in Section 6.3, under the Hansoh Research IP, and Hansoh's interest in the Joint Research IP, and (ii) a non-exclusive, royalty-free license, with the right to grant sublicenses as provided in Section 6.3, under the Hansoh Background IP, in each case (i) and (ii) solely to Exploit Global Licensed Compounds and Global Licensed Products directed to the Global Licensed Target in the Field anywhere in the world; provided, however, that this Section 6.2.3 shall not apply with respect to a Failed Target.

6.3 **Sublicenses**. Each Party shall have the right to grant sublicenses, through multiple tiers of sublicenses, under the licenses granted in Sections 3.7, 6.1.1, 6.1.2, 6.1.3, 6.2.1, 6.2.2 and 6.2.3 to Sublicensees; provided that any such sublicenses shall (a) be in writing, (b) be consistent with the terms and conditions of this Agreement, and (c) require the applicable Sublicensee to comply with all applicable terms of this Agreement. The

granting Party shall be responsible for the performance of any Sublicensee as if such Sublicensee was the granting Party hereunder, and shall, within a reasonable period of a request by the other Party, provide a redacted copy of any sublicense with the other Party. Each sublicense granted by a Party to any rights licensed or granted will terminate immediately upon the termination of the license to the granting Party with respect to such rights.

6.4 **Retention of Rights**. Notwithstanding the exclusive licenses granted by either Party pursuant to Sections 6.1 or 6.2:

6.4.1 Silence hereby expressly reserves the right (a) under the Silence Background IP, Silence Research IP, Silence China Product Development IP and Silence's interest in the Joint Research IP for internal research purposes and/or to exercise its rights and perform its obligations under this Agreement, whether directly or through one or more Affiliates or subcontractors, including the right to perform those activities assigned to it under the Research Plans, and (b) to practice, and to grant licenses under, the Silence Background IP, Silence Research IP, Silence China Product Development IP and Silence's interest in the Joint Research IP outside the scope of the licenses granted to Hansoh in Section 6.1 and outside the scope of its covenants under Section 4.1; and

6.4.2 Hansoh hereby expressly reserves the right (a) under the Hansoh Background IP, Hansoh Research IP, Hansoh China Product Development IP and Hansoh's interest in the Joint Research IP for internal research purposes and/or to exercise its rights and perform its obligations under this Agreement, whether directly or through one or more Affiliates or subcontractors, including the right to perform those activities assigned to it under the Research Plans, and (b) to practice, and to grant licenses under, the Hansoh

Background IP, Hansoh Research IP, Hansoh China Product Development IP and Hansoh's interest in the Joint Research IP outside the scope of the licenses granted to Silence in Section 6.2 and outside the scope of its covenants under Section 4.1.

6.5 **No Implied Licenses**. Except as expressly provided in this Agreement, neither Party shall acquire any license or other intellectual property interest, by implication, estoppel, or otherwise, under or to any Patents, Know-How, Information, or other intellectual property owned or controlled by the other Party.

6.6 **No [***]**. Notwithstanding anything to the contrary in this Agreement, Hansoh shall not, directly or indirectly, [***].

6.7 **Confirmatory Patent License**. Each Party shall, if requested to do so by the other, promptly enter into confirmatory license agreements in the form or substantially the form reasonably requested by the requesting Party for purposes of recording the licenses granted under this Agreement with such patent offices in the Hansoh Territory and/or the Silence Territory as the requesting Party considers appropriate.

6.8 **Third Party Payment Obligations**. In the event that either Party (the "**Using Party**") intends to use, in the course of a Research Plan or the Development of any Licensed Compound or Licensed Product, any item of Information, Know-How, material, Patent, or other property right of a Third Party for which access under this Agreement requires or triggers a payment obligation, the Using Party will promptly provide written notice to the other Party (the "**Other Party"**) of such payment obligation prior to its use in the Research Plan and at least Annually in other cases. Following such notification, the Parties will negotiate in good faith the terms on which the Other Party will (i) assume such payment obligation with respect thereto, and (ii) be bound by any obligations that

are required to be passed on to any sublicensees with respect thereto. If the Parties are not able to reach agreement with respect to such terms, such Information, Know-How, material, Patent, or other property right of a Third Party shall not be Controlled pursuant to this Agreement and, if the Parties do agree on the payments, subject to the Other Party making the agreed payments, such Information, Know-How, material, Patent, or other property right of a Third Party shall, subject to the Other Party complying with such payment obligations and terms be Controlled for the purposes of this Agreement. For the avoidance of doubt, the Using Party shall not require the Other Party to pay a greater share of the payment obligation to the Third Party for access to such Information, Know-How, material, Patent, or other property right of a Third Party than is reasonably attributable to the Using Party's use of such Information, Know-How, material, Patent, or other property right of a Third Party.

ARTICLE 7
DEVELOPMENT AND COMMERCIALIZATION

7.1 **Overview**.

7.1.1 On a Licensed Target-by-Licensed Target basis, following exercise of an Option by Hansoh and for the remainder of the Term with respect to such Licensed Target, as between the Parties, Hansoh shall have the sole right to Exploit, whether by itself or through its Affiliates or Sublicensees, the Licensed Compounds and Licensed Products in the Field and in the Hansoh Territory at its own cost and expense (except as otherwise expressly set forth herein).

7.1.2 On a China Licensed Target-by-China Licensed Target basis, for the Term with respect to such China Licensed Target, as between the Parties, Silence shall have the sole right to Exploit, whether by itself or through its Affiliates or Sublicensees, the China Licensed Compounds and China Licensed Products in the Field and in the Silence Territory at its own cost and expense (except as otherwise expressly set forth herein).

7.2 **Diligence**. On a Licensed Target-by-Licensed Target basis, following exercise of an Option by Hansoh and for the remainder of the Term with respect to such Licensed Target, Hansoh shall itself, or through its Affiliates or Sublicensees, use its Commercially Reasonable Efforts:

7.2.1 To Develop and obtain Regulatory Approval for [***] Global Licensed Product [***], and to Exploit [***] Global Licensed Product for use in humans in the Field[***];

7.2.2 To Develop and obtain Regulatory Approval for [***] China Licensed Product in respect of each China Licensed Target in Mainland China, and to Exploit[***] China Licensed Product [***] for use in humans in the Field in Mainland China.

7.3 **Reporting**. Hansoh shall update Silence regarding its Exploitation activities with respect to the Licensed Compounds and Licensed Products in the Hansoh Territory at [***] meeting between the Parties, which may take place in person or via audio or video conference. At each such update meeting, Hansoh shall summarize the Exploitation activities undertaken by it, its Affiliates and its Sublicensees in the Hansoh Territory with respect to Licensed Compounds or Licensed Products directed to each Licensed Target at a level of detail reasonably required to determine Hansoh's compliance with its

obligations under Section 7.2 of this Agreement. Hansoh shall provide further information as Silence may reasonably request regarding the foregoing.

7.4 Co-Development of China Licensed Products.

7.4.1 Joint Development Plan. Promptly following the exercise by Hansoh of its Option in respect of a China Licensed Target, the Parties shall develop and agree to a plan for the conduct of the Development activities to be undertaken by each Party in the further Development of China Licensed Compounds and China Licensed Products directed to such China Licensed Target (such activities, "**Joint Development Activities**" and such plan the "**Joint Development Plan**") and the Joint Development Plan shall assign responsibility for the Joint Development Activities (including any regulatory activities) between the Parties.

7.4.2 Updates; Amendments. The JDC shall review each Joint Development Plan covering all Joint Development Activities periodically for the purpose of considering appropriate amendments thereto. The JDC shall, subject to JSC approval, manage the proposed updating and/or amending of the Joint Development Plan. In addition, either Party, through its representatives on the JDC, may propose amendments to the Joint Development Plan for Joint Development Activities at any time.

7.4.3 Obligations; Cooperation. Each Party shall use Commercially Reasonable Efforts to perform the responsibilities assigned to it under each Joint Development Plan for Joint Development Activities in accordance with the budget set forth therein. The Parties shall cooperate and collaborate in good

faith with respect to the Joint Development Activities and the implementation and execution of the Joint Development Plan.

7.4.4 **Development Costs.** Except as expressly provided otherwise in the Joint Development Plan, each Party shall be solely responsible for and shall bear all development costs incurred by such Party in connection with the performance of the Joint Development Activities assigned to it in the Joint Development Plan. In performing such activities, the Parties will use their respective Commercially Reasonable Efforts to reduce such development costs and to leverage efficiencies to best advance the Joint Development Plan.

7.4.5 **Development Reports**. Each Party shall provide to the other Party an update at each JDC meeting describing in reasonable detail such Party's activities and progress related to the Development, including non-clinical and clinical studies, technical development and regulatory activities, of the relevant China Licensed Products pursuant to the Joint Development Plan.

7.4.6 **Subcontracting**. Each Party shall have the right to subcontract its obligations under the Joint Development Plan to subcontractors and Affiliates, subject to any limitations, restrictions or other qualifications that are set forth in the Joint Development Plan; provided, that (i) such subcontractors and Affiliates agree in writing to be subject to the applicable terms and conditions of this Agreement, including the confidentiality provisions of ARTICLE 12, (ii) that the subcontracting Party directly owns all intellectual property rights that may arise as required by ARTICLE 11, (iii) the appointment of a subcontractor shall not release a Party of its obligations under this Agreement, and (iv) a Party shall be responsible for the management of all of its subcontractors and

shall remain fully liable to the other Party for the acts and omissions of each such subcontractor.

7.4.7 **Regulatory Matters.** As between the Parties, Hansoh shall have the sole right to seek, prepare, obtain, and maintain the Regulatory Approvals in the Hansoh Territory for the Global Licensed Compounds and Global Licensed Products as set out in Section 7.2.1 and for the China Licensed Compounds and China Licensed Products as set out in Section 7.2.2, and Silence shall have the sole right (but not obligation) to seek, prepare, obtain, and maintain the Regulatory Approvals for China Licensed Compounds or China Licensed Products in the Silence Territory.

7.4.8 **Cooperation; Information Sharing.** The Parties shall at all times cooperate in good faith with respect to any and all regulatory activities pertaining to the China Licensed Compound or China Licensed Product. Each Party will provide the other Party [***] with copies of (i) Regulatory Documentation in [***] prior to any submission of such Regulatory Documentation and (ii) any non-clinical or clinical data Controlled by or generated by such Party in the development of the [***] on a timely basis (clinical data shall be in SAS data sets), to the extent permitted by the Applicable Laws, when and as such data becomes available or at such other times as the Parties may agree. Each Party shall use (and cause its Affiliates to use) Commercially Reasonable Efforts to share such Regulatory Documentation and data with the other Party, and shall use Commercially Reasonable Efforts to include substantially similar obligations in all sublicenses and subcontracts pertaining to the Development of the China Licensed Compound or China Licensed Product. Such Regulatory Documentation and data sharing activities shall include, without

limitation, the creation of a worldwide dossier containing all data relating to the clinical studies conducted by the Parties in their respective territories.

7.4.9 **Translations.** Hansoh will provide English translations of all of the foregoing documentation if the foregoing are reasonably available to or are created by Hansoh, its Affiliates or its Sublicensees or subcontractors. If translations are not available to Hansoh, then Hansoh shall provide a summary of such document in the English language.

(a) Silence shall be entitled to request a copy of such document and to arrange for its translation using a Third Party translation service that has been agreed by the Parties (acting in good faith) and the costs of such translation shall be [***] in respect of [***] of a Licensed Compound or Licensed Product. [***]; and

(b) Silence shall be solely responsible for translation, [***], of all documents that Silence requires to be translated other than those referenced in Section 7.4.9(a).

7.4.10 **Rights of Reference.**

(a) Hansoh may use any of the Regulatory Documentation or data provided to it by Silence in Section 7.4.8 in support of the Development or filing of any Regulatory Approval for the China Licensed Product in the Hansoh Sole Region. Subject to ARTICLE 4, Silence hereby grants, and agrees to grant, to Hansoh a royalty-free right of reference for so long as such China Licensed Product remains subject to this Agreement, with the right to grant sublicenses and further rights of reference, under the Regulatory

Approvals and any other Regulatory Documentation for the China Licensed Compounds or China Licensed Products Controlled by Silence for purposes of Exploiting the China Licensed Compounds or China Licensed Products in the Field in the Hansoh Sole Region. Silence shall, and shall cause its Affiliates to, include in any of its sublicenses or subcontractors pertaining to the China Licensed Compound or China Licensed Product a right of reference to any Regulatory Documentation or data generated or Controlled by such Affiliate, sublicensee, or subcontractor consistent with the right of reference set forth in this Section 7.4.10(a);

(b) Silence may use any of the Regulatory Documentation or data provided to it by Hansoh in Section 7.4.8 in support of the Development or filing of any Regulatory Approval for products in the Silence Territory. Subject to ARTICLE 4, Hansoh hereby grants, and agrees to grant, to Silence a perpetual, irrevocable, royalty-free right of reference, with the right to grant sublicenses and further rights of reference, under the Regulatory Approvals and any other Regulatory Documentation for the China Licensed Compounds or China Licensed Products Controlled by Hansoh or its Affiliates for purposes of Exploiting China Licensed Compounds or China Licensed Products in the Silence Territory. Hansoh shall include, and shall cause its Affiliates to include, in any of its sublicenses or subcontracts pertaining to the China Licensed Compound or China Licensed Product a right of reference to any Regulatory Documentation or data generated or Controlled by such

Affiliate, Sublicensee or subcontractor consistent with the right of reference set forth in this Section 7.4.10(b).

7.4.11 Records.

(a) **Creation**. Each Party shall maintain complete and accurate records (including both paper and electronic records) in sufficient detail and in good scientific manner appropriate for patent and regulatory purposes, and in compliance with Applicable Law and regulatory guidance, of all work done and results achieved in the performance of any activities under each Joint Development Plan. Such records shall be retained by each Party for at least [***] ([***]) years after [***], or for such longer period as may be required by Applicable Law.

(b) **Inspection**. Each Party shall have the right to reasonably inspect the other Party's records arising from the performance of any activities under each Joint Development Plan, and shall provide copies of all such requested records, to the extent reasonably required for the exercise or performance of the requesting Party's rights under this Agreement; provided, however, that the requesting Party shall maintain such records and the Information of the other Party as Confidential Information of the other Party in accordance with ARTICLE 12 hereof and shall not use such records or Information except to the extent otherwise permitted by this Agreement.

ARTICLE 8
MANUFACTURING & SUPPLY

8.1 **Silence Manufacturing During Research Plan.** Silence, through one or more Third Party contract manufacturers, shall be responsible for all Manufacturing activities necessary to perform any of its obligations under a Research Plan.

8.2 **Global Licensed Compound Manufacture.** Following the Option Exercise Date in relation to the Global Licensed Target, Silence shall provide a technology transfer to Hansoh pursuant to Section 8.4.

8.3 **China Licensed Compound Manufacture.** The Parties will discuss the optimal strategy for the manufacture of the relevant China Licensed Compounds and China Licensed Products with a view to cooperating in the most appropriate manufacturing strategy for such China Licensed Compounds and China Licensed Products. In particular, the Parties recognise the lead times for Manufacture by or on behalf of a Party may be significant and shall discuss appropriate timing of such supply at meetings of the JSC. Where a Party contracts with a Third Party for such Manufacture, any supply to the other shall be on a pass-through basis, such that the supplying Party does not assume any liabilities or indemnities for such supply above those which it has received from its Third Party contract manufacturer. Following the Option Exercise Date in relation to each China Licensed Target, Silence shall provide a technology transfer to Hansoh pursuant to Section 8.4.

8.4 **Cooperation and Technology Transfer**.

8.4.1 Following the exercise of each Option in respect of a particular Licensed Target, Silence shall use Commercially Reasonable Efforts to initiate and facilitate technology transfer to Hansoh of all Information related to

Manufacturing of the relevant Licensed Compound and Licensed Product Controlled by Silence ("**Silence Manufacturing Information**") which is [***] to allow Hansoh to manufacture such Licensed Products, including by sharing any manufacturing-related Silence Background Know-How and Silence Research Know-How and introducing Hansoh to any relevant contract manufacturing organisations utilised by Silence with respect to a China Licensed Target prior to the exercise of such Option and in the course of carrying out the relevant Research Plan with respect to a Global Licensed Target in order to allow Hansoh to source materials directly from the provider used by Silence with respect to a China Licensed Target prior to the exercise of such Option and in the course of carrying out the relevant Research Plan with respect to a Global Licensed Product. Such Commercially Reasonable Efforts shall include providing reasonable access to personnel, documentation, materials, and information in the possession and Control of Silence [***] to enable Hansoh to use and practice such Silence Manufacturing Information. For clarity, nothing in this Section 8.4.1 shall require Silence to create any new Know-How, undertake any additional manufacturing activities, or undertake any activity not specified in the relevant Research Plan and Silence's obligation to conduct such technology transfer at no cost to Hansoh shall be limited to [***] ([***]) FTE hours of effort to be taken within [***] ([***]) months of the relevant Option Exercise Date. Upon the reasonable request of Hansoh, such request to be made within [***] ([***]) months of the Option Exercise Date, Silence shall use its reasonable efforts to provide technology transfer support in excess of [***] ([***]) FTE hours of effort pursuant to this Section and at Hansoh's sole cost and expense up to a maximum of an additional [***] ([***]) FTE hours to be taken within [***] ([***]) months of the relevant Option Exercise Date (the

provision of such requested technology transfer support being the "**Silence Technology Transfer Support**"). In the event that Hansoh terminates this Agreement with respect to any Licensed Target, Licensed Compound or Licensed Product Hansoh shall provide technology transfer support to Silence on an equivalent basis to Silence's obligations under this Section 8.4.1.

8.4.2 Throughout the Term of this Agreement, each Party will promptly disclose to the other Party any new Manufacturing Information generated in relation to any China Licensed Compound or China Licensed Product that comes into their possession and Control.

8.5 **Hansoh Obligations**. Subject to Section 8.3, and Silence having provided the Silence Technology Transfer Support, following the Option Exercise Date in respect of Licensed Products directed to a Licensed Target, Hansoh, either directly or through one or more Third Party contract manufacturers, shall be responsible, at its own expense, for all Manufacturing activities necessary for the Exploitation by Hansoh of the Licensed Products directed to such Licensed Target in the Hansoh Territory in accordance with this Agreement.

ARTICLE 9
PAYMENTS AND RECORDS

9.1 **Upfront Payment**. Within [***] ([***]) days after receipt by Hansoh of Silence's invoice in respect thereof, which invoice may be delivered by Silence on or following the Effective Date, Hansoh shall pay to Silence the non-refundable, non-creditable sum of sixteen Million Dollars ($16,000,000).

9.2 **Research Collaboration Milestones**.

9.2.1 **China Licensed Product Development Milestone Payments**. In partial consideration of the rights granted by Silence to Hansoh hereunder and subject to the terms and conditions set forth in this Agreement, Hansoh shall pay to Silence the non-refundable, non-creditable milestone payments upon the achievement of each of the following milestone events for the first China Licensed Compound or China Licensed Product with respect to a particular China Licensed Target to achieve such milestone event (whether by or on behalf of Hansoh, its Affiliates or Sublicensees):

Milestone Event	Milestone Payment
[***]	$[***]
[***]	$[***]
[***]	$[***]
[***]	$[***]
[***]	$[***]
[***]	$[***]
[***]	$[***]
Total	**$37,000,000**

9.2.2 **Global Licensed Product Development Milestone Payments**. In partial consideration of the rights granted by Silence to Hansoh hereunder and

subject to the terms and conditions set forth in this Agreement, Hansoh shall pay to Silence the non-refundable, non-creditable milestone payments upon the achievement of each of the following milestone events for the first Global Licensed Compound or Global Licensed Product with respect to a particular Global Licensed Target to achieve such milestone event (whether by or on behalf of Hansoh, its Affiliates or Sublicensees):

Milestone Event	**Milestone Payment**
[***]	$[***]
[***]	$[***]
[***]	$[***]
[***]	$[***]
[***]	$[***]
[***]	$[***]
[***]	$[***]
[***]	$[***]
[***]	$[***]
[***]	$[***]

Total	**$81,000,000**

9.2.3 **Notice and Payment**. Hansoh shall notify Silence in writing within [***] ([***]) days after the first achievement of any milestone event set forth in this Section 9.2 by or on behalf of Hansoh. Hansoh shall pay to Silence the applicable milestone payment within [***] ([***]) days after receipt by Hansoh of Silence's invoice.

9.2.4 **Once Per Licensed Target**. Each milestone payment in this Section 9.2 shall be payable only upon the achievement of such milestone by the first Licensed Product directed to a particular Licensed Target to achieve such milestone event and no amounts shall be due for subsequent or repeated achievements of such milestone by another Licensed Product directed to the same Licensed Target.

9.3 Sales-Based Milestones

9.3.1 **Licensed Product Sales Milestone Payments**. In partial consideration of the rights granted by Silence to Hansoh hereunder and subject to the terms and conditions set forth in this Agreement, Hansoh shall pay to Silence, on a Licensed Target-by-Licensed Target basis, the following non-creditable, non-refundable milestone payments upon the achievement of each of the following levels of Annual Gross Sales by or on behalf of Hansoh, its Affiliates or Sublicensees.

Annual Gross Sales of Licensed Products directed to a Licensed Target	Sales Milestone Payments
[***]	$[***]
[***]	$[***]
[***]	$[***]
[***]	$[***]
[***]	$[***]
Total	**$367,500,000**

9.3.2 **Notice and Payment**. Hansoh shall notify Silence in writing of the first achievement of any milestone event set forth in this Section 9.3 by or on behalf of Hansoh or its Affiliates or Sublicensees in its report provided pursuant to Section 10.1 and payment of such milestone shall be due within [***] ([***]) days after receipt by Hansoh of Silence's invoice in respect of such milestone. For clarity, each milestone payment set forth in the table above shall be paid only once with respect to a particular Licensed Target, upon first achievement of the corresponding milestone event in respect of the relevant Licensed Target, regardless of the number of times such event is achieved.

9.4 Royalties.

9.4.1 Royalty Rate. As further consideration for the rights granted to Hansoh under this Agreement, subject to the other terms of this Section 9.4, during the Royalty Term, Hansoh shall make [***] non-refundable, non-creditable royalty payments to Silence on the Net Sales of Licensed Products directed to a particular Licensed Target sold in the Hansoh Territory at the applicable rate set forth below:

Net Sales of a Licensed Product	**Royalty Rate**
For that portion of Net Sales of all Licensed Products directed to a particular Licensed Target in any Year which are less than $[***]	[***]%
For that portion of Net Sales of all Licensed Products directed to a particular Licensed Target in any Year which are equal to or greater than $[***] but less than $[***]	[***]%
For that portion of Net Sales of all Licensed Products directed to a particular Licensed Target in any Year which are equal to or greater than $[***] but less than $[***]	[***]%
For that portion of Net Sales of all Licensed Products directed to a particular Licensed Target in any Year	[***]%

which are equal to or greater than $[***] but less than $[***]	
For that portion of Net Sales of all Licensed Products directed to a particular Licensed Target in any Year which are equal to or greater than $[***] but less than $[***]	[***]%
For that portion of Net Sales of all Licensed Products directed to a particular Licensed Target in any Year which are equal to or greater than $[***]	[***]%

9.4.2 **Royalty Term**. Royalties shall be paid on a Licensed Product-by-Licensed Product and country-by-country or region-by-region basis in the Hansoh Territory from the First Commercial Sale of such Licensed Product in a country or region by or on behalf of Hansoh, its Affiliates, or Sublicensees, until the expiration of the Royalty Term for such Licensed Product in such country or region.

9.4.3 **Reductions**.

(a) Subject to Section 9.4.4, in the event that there is no Valid Claim within the Licensed Patents in the United States of America that Covers the relevant Licensed Product in the United States of America absent a license with respect to such Licensed Patent under this Agreement, then the royalty rate set forth in Section 9.4.1 as applied to the sale of such Licensed Product in the United States of America shall be reduced by [***] ([***]%). Hansoh shall not be

permitted to apply the reduction in royalty provided for in this Section 9.4.3(a) where Hansoh has [***] may result in the royalty reduction provided for herein.

(b) Subject to Section 9.4.4, in the event that Hansoh, in order to Exploit a Licensed Product, obtains a license under any Patents owned by a Third Party that has claims that Cover the composition of matter or method of use of the Licensed Compound or RNAi Molecule incorporated in such Licensed Product and, in the absence of such license such Licensed Product would infringe such Third Party Patents, then Hansoh shall be entitled to deduct [***] ([***]%) of the amount of royalties actually paid by Hansoh to such Third Party [***] from the royalties due to Silence [***] (determined in accordance with the Accounting Standards) pursuant to Section 9.4.

(c) Subject to Section 9.4.4, in the event that there is Generic Competition with respect to a Licensed Product in a country or region during [***], then Hansoh shall be entitled to deduct [***] ([***]%) from the royalties due to Silence in [***] (determined in accordance with the Accounting Standards) pursuant to Section 9.4, for so long as there is Generic Competition at such level with respect to such Licensed Product in such country or region.

9.4.4 **Cumulative Reductions Floor**. In no event will the aggregate amount of royalties due to Silence for a Licensed Product in a country in the Hansoh Territory in [***] during the Royalty Term for such Licensed Product in such country be reduced by more than [***] ([***]%) of the amount that otherwise would have been due and payable to Silence in [***] for such Licensed

Product in such country under Section 9.4.1 but for the reductions set forth in Sections 9.4.3(a), 9.4.3(b), and 9.4.3(c) above.

ARTICLE 10
PAYMENT; RECORDS; AUDITS

10.1 **Royalty Payments and Reports**. Hansoh shall calculate all amounts payable to Silence pursuant to Section 9.4 at [***], which amounts shall be converted to Dollars, in accordance with Section 10.2. Hansoh shall provide to Silence within [***] ([***]) days of [***] a statement of (a) the amount of Gross Sales and Net Sales of each Licensed Product in each country or region in the Hansoh Territory during the applicable [***] (including such amounts expressed in local currency and as converted to Dollars), (b) the deductions applied in the calculation of Net Sales from Gross Sales, (c) the applicable royalty rate(s) under this Agreement (including any reduction(s) to such royalty rate(s) under Section 9.4.3), and (d) a calculation of the amount of royalty payment due on such Net Sales for [***]. Hansoh shall pay to Silence the royalty amounts due with respect to [***] within [***] ([***]) days of the [***].

10.2 **Mode of Payment**. All payments to Silence under this Agreement shall be made, without setoff, by deposit of Dollars in the requisite amount to such bank account as Silence may from time to time designate by notice to Hansoh. For the purpose of calculating any sums due under, or otherwise reimbursable pursuant to, this Agreement (including the calculation of Net Sales expressed in currencies other than Dollars), a Party shall convert any amount expressed in a foreign currency into Dollar equivalents using its, its Affiliate's, or its Sublicensee's standard conversion methodology consistent with Accounting Standards.

10.3 **Taxes**.

10.3.1 **Withholding Taxes**. Where any sum due to be paid to Silence by Hansoh under this Agreement is subject to Enterprise Income Tax or where any sum due to be paid to Hansoh by Silence under this Agreement is subject to a similar withholding tax, the Parties shall use their commercially reasonable efforts to take all such actions, including but not limited to [***]. In particular, [***], to the extent legally able to do so. If and to the extent the Enterprise Income Tax or withholding tax cannot be fully eliminated, the paying Party shall [***]. If any Enterprise Income Tax or withholding taxes are refundable, creditable or otherwise recoverable, each Party will provide the other such assistance as is reasonably required to obtain a refund of the withheld taxes, obtain a credit with respect to such taxes paid, or otherwise recover such taxes. In the event that a government authority retroactively determines that a payment made by a Party to the other pursuant to this Agreement should have been subject to withholding (or to additional withholding) taxes, and such Party (the "**Withholding Party**") remits such withholding taxes to the government authority, the Withholding Party shall have the right (a) [***], (b) [***], or (c) [***].

10.3.2 **Other Taxes**. Except as set out in Section 10.3.1, all payments are exclusive of any tax, including value added taxes, sales taxes, consumption taxes, and other similar taxes (the "**Indirect Taxes**"). If any Indirect Taxes are chargeable in respect of any payments, the paying Party shall pay such Indirect Taxes at the applicable rate in respect of such payments following receipt, where applicable, of an Indirect Taxes invoice in the appropriate form issued by the receiving Party in respect of those payments. The Parties shall issue invoices for all amounts payable under this Agreement consistent with Indirect Tax requirements and irrespective of whether the sums may be netted

for settlement purposes. If the Indirect Taxes originally paid or otherwise borne by the paying Party are in whole or in part subsequently determined not to have been chargeable, all reasonably necessary steps will be taken by the receiving Party to receive a refund of such undue Indirect Taxes from the applicable governmental authority or other fiscal authority and any amount of undue Indirect Taxes repaid by such authority to the receiving Party will be transferred to the paying Party within [***] ([***]) days after receipt.

10.3.3 **Taxes Resulting from a Party's Action**. Notwithstanding the foregoing in this Section 10.3, if a Party takes any action of its own discretion (not required by the terms of this Agreement, Applicable Law, or a Regulatory Authority), including any assignment, sublicense, change of place of incorporation, or failure to comply with Applicable Laws or filing or record retention requirements, which results in an additional or increased withholding obligation with respect to payments to be made pursuant to this Agreement ("**Withholding Tax Action**"), then such Party shall bear the amount of such withholding to the extent associated with such Withholding Tax Action. For clarity, if Hansoh undertakes a Withholding Tax Action, then the sum payable by Hansoh (in respect of which such withholding is required to be made) shall be increased to the extent necessary to ensure that Silence receives a sum equal to the sum which it would have received had no such Withholding Tax Action occurred. For the avoidance of doubt, a change in Applicable Laws that results in a new or increased withholding or deduction obligation, absent either Party taking a Withholding Tax Action, shall not affect the withholding and deduction obligations provided in this Section 10.3.

10.3.4 Prevention of Facilitation of Tax Evasion.

(a) Each Party represents, warrants and undertakes that it and its Affiliates shall not commit a tax evasion facilitation offence under Applicable Law in connection with or attributable to this Agreement or the transactions contemplated hereby.

(b) Each Party shall promptly report to the other Party any apparent breach of Section 10.3.4(a) and shall (i) answer, in reasonable detail, any written or oral inquiry from the other Party related to its and its Affiliates compliance with Section 10.3.4(a), (ii) facilitate the interview of employees of such Party by the other Party (or any agent of such Party) at any reasonable time specified by the inquiring Party related to such Party's compliance with Section 10.3.4(a) and (iii) cooperate with the inquiring Party or any governmental authority in relation to any investigation relating to the matters referred to in Section 10.3.4(a), in all cases, as reasonably required to enable that other Party to comply with its undertaking in Section 10.3.4(a).

10.4 **Financial Records**. Hansoh shall, and shall cause its Affiliates and Sublicensees to, keep complete and accurate books and records pertaining to Gross Sales and Net Sales of Licensed Products in sufficient detail to calculate all amounts payable hereunder with respect thereto and to verify compliance with its obligations under this Agreement. Such books and records shall be retained by Hansoh and its Affiliates until [***] years after the end of the Year to which such books and records pertain.

10.5 **Audit**. At either Party's reasonable request, the other Party shall, and shall cause its Affiliates to, permit an independent public accounting firm of internationally recognized standing designated by the auditing Party and reasonably acceptable to the audited Party, at reasonable times during normal business hours, under supervision of the audited Party's personnel, and upon reasonable notice, to audit the books and records maintained pursuant to Section 10.4 to ensure the accuracy of all reports and payments made hereunder. Such examinations may not (a) be conducted for any Quarter more than [***] years after the end of such Year to which such books and records pertain, (b) be conducted more than once in any [***] month period (unless a previous audit during such [***]-month period revealed an underpayment with respect to such period), or (c) be repeated for any Quarter, unless as a component of an examination applicable to a Year that includes such Quarter. The accounting firm shall report to the Parties with reasons whether the reports are correct or not, and the specific details concerning any discrepancies. Except as provided below, the cost of this audit shall be borne by the auditing Party, unless the audit reveals a variance of more than [***] ([***]%) from the reported amounts, in which case the audited Party shall bear the cost of the audit. If such audit concludes that (x) additional amounts were owed by the audited Party, the audited Party shall pay the additional amounts within [***] ([***]) days, or (y) excess payments were made by the audited Party, the auditing Party shall reimburse such excess payments, in either case ((x) or (y)), within [***] ([***]) days after the date on which such audit is completed by the auditing Party.

10.6 **Confidentiality**. The receiving Party shall treat all information subject to review under this ARTICLE 10 in accordance with the confidentiality provisions of ARTICLE 12 and the Parties shall cause any independent public accounting firm appointed in accordance with Section 10.5, and the accounting firm, to enter into reasonably acceptable confidentiality agreements with the audited Party obligating such firm to retain all such

financial information in confidence pursuant to such confidentiality agreement. The independent public accounting firm shall disclose to the receiving Party only whether the payments made are correct and details concerning any discrepancies in sufficient detail such that the receiving Party is able to fully evaluate the methodology and conclusions of the audit, but no information not related to the relevant payments shall be disclosed to the receiving Party.

ARTICLE 11
INTELLECTUAL PROPERTY

11.1 Ownership of Intellectual Property.

11.1.1 United States Law. Inventorship of Information and inventions conceived, discovered, developed, or otherwise made under this Agreement shall be determined in accordance with Applicable Law in the United States of America as such law exists as of the Effective Date irrespective of where such conception, discovery, development or making occurs.

11.1.2 Silence Ownership. As between the Parties, Silence or an Affiliate designated by Silence shall own and retain all right, title, and interest in and to any and all Silence Background IP, Silence Research IP and Silence China Product Development IP.

11.1.3 Hansoh Ownership. As between the Parties, Hansoh or an Affiliate designated by Hansoh shall own and retain all right, title, and interest in and to any and all Hansoh Background IP, Hansoh Research IP and Hansoh China Product Development IP.

11.1.4 **Joint Ownership**. As between the Parties, the Parties shall each own an equal, undivided interest in any and to all Joint Research IP. At least once per Quarter (which the Parties expect would be at each JSC meeting unless the JSC has been disbanded) each Party shall disclose to the other Party in writing the development, making, conception, or reduction to practice of any Joint Research IP. Subject to the exclusive licenses granted by Silence to Hansoh to Joint Research IP under Section 6.1, each Party shall have the right to Exploit (including by way of granting licenses, assignments, mortgages or otherwise) the Joint Research IP without a duty of seeking consent or accounting to the other Party.

11.1.5 **Assignment Obligation**. Each Party shall cause all Persons who perform Development activities for such Party under this Agreement to be under an obligation to assign (or, if such Party is unable to cause such Person to agree to such assignment obligation despite such Party's using commercially reasonable efforts to negotiate such assignment obligation, provide a license under) their rights in any Information and inventions resulting therefrom to such Party to the extent that the foregoing relates specifically to a Licensed Product.

11.2 **Patent Working Group**. The JSC shall establish a working group to assist in the communication with respect to the prosecution and maintenance of Product Specific Patents and Joint Research Patents (the "**Patent Working Group**"), and each Party (through its representatives on the Patent Working Group) shall use its Commercially Reasonable Efforts to ensure that there are or will be a commercially reasonable set of Product Specific Patents directed to each Licensed Target and to Licensed Products directed to each such Licensed Target. The Patent Working Group shall meet as

necessary to perform its responsibilities or as otherwise directed by the JSC, and shall continue to exist only for so long as the Parties determine it is reasonably necessary.

11.3 Maintenance and Prosecution of Patents.

11.3.1 Silence Patents. Except as set out in Section 11.3.3, Silence shall have the sole right, but not the obligation, to prepare, file, prosecute, and maintain the Silence Background Patents, Silence Research Patents and Silence China Product Development Patents worldwide, at Silence's sole cost and expense. Silence shall consult with and keep Hansoh reasonably informed on all steps with regard to the preparation, filing, prosecution, and maintenance of the Silence Research Patents and the Silence China Product Development Patents. Silence shall provide Hansoh with a copy of material communications to and from the patent authorities regarding Silence Research Patents and Silence China Product Development Patents in the Hansoh Territory, including drafts of any material filings or responses to be made to such patent authorities sufficiently in advance of submitting such filings or responses so as to allow Hansoh a reasonable opportunity to review and comment thereon. Silence shall reasonably consider and reasonably incorporate Hansoh's requests and suggestions with respect to such drafts and with respect to strategies for filing and prosecuting the Silence Research Patents and Silence China Product Development Patents in the Hansoh Territory.

11.3.2 Hansoh Patents. Hansoh shall have the sole right, but not the obligation, to prepare, file, prosecute, and maintain the Hansoh Background Patents, the Hansoh Research Patents and Hansoh China Product Development Patents worldwide, at Hansoh's sole cost and expense. Hansoh shall consult with and

keep Silence reasonably informed on all steps with regard to the preparation, filing, prosecution, and maintenance of the Hansoh Research Patents and the Hansoh China Product Development Patents. Hansoh shall provide Silence with a copy of material communications to and from the patent authorities regarding Hansoh Research Patents and Hansoh China Product Development Patents in the Silence Territory, including drafts of any material filings or responses to be made to such patent authorities sufficiently in advance of submitting such filings or responses so as to allow Silence a reasonable opportunity to review and comment thereon. Hansoh shall reasonably consider and reasonably incorporate Silence's requests and suggestions with respect to such drafts and with respect to strategies for filing and prosecuting the Hansoh Research Patents and Hansoh China Product Development Patents in the Silence Territory.

11.3.3 **Product Specific Patents**. Silence shall have the first right, but not the obligation, to prepare, file, prosecute, and maintain the Product Specific Patents worldwide, at Silence's sole cost and expense. Silence shall consult with and keep Hansoh reasonably informed on all steps with regard to the preparation, filing, prosecution, and maintenance of the Product Specific Patents in the Hansoh Territory, and shall provide Hansoh with a copy of material communications to and from the patent authorities regarding such Product Specific Patents in the Hansoh Territory, including drafts of any material filings or responses to be made to such patent authorities sufficiently in advance of submitting such filings or responses so as to allow Hansoh a reasonable opportunity to review and comment thereon. Silence shall reasonably consider and reasonably incorporate Hansoh's requests and suggestions with respect to such drafts and with respect to strategies for filing

and prosecuting the Product Specific Patents in the Hansoh Territory. If Silence, after the exercise of the Option by Hansoh in respect of the Licensed Target to which the Licensed Compound or Licensed Product claimed by such Product Specific Patent relates, determines in its sole discretion to abandon or not maintain any such Product Specific Patents in the Hansoh Territory, then Silence shall provide Hansoh with prior written notice sufficiently in advance of any abandonment to enable Hansoh, [***], to maintain such Product Specific Patent [***] in the Hansoh Territory, at its sole cost and expense provided always that such costs shall be treated as a credit against the royalty payments due in respect of a Licensed Product Covered by such Product Specific Patent.

11.3.4 **Joint Research Patents**. [***] shall have the first right, but not the obligation, to prepare, file, prosecute, and maintain the Joint Research Patents worldwide, at [***]'s sole cost and expense. [***] shall keep [***] reasonably informed of all steps with regard to the preparation, filing, prosecution, and maintenance of the Joint Research Patents, and shall provide [***] with a copy of material communications to and from the patent authorities regarding such Joint Research Patents, including drafts of any material filings or responses to be made to such patent authorities sufficiently in advance of submitting such filings or responses so as to allow [***] a reasonable opportunity to review and comment thereon. [***] shall reasonably consider and reasonably incorporate [***]'s requests and suggestions with respect to such drafts and with respect to strategies for filing and prosecuting the Joint Research Patents. If [***], during the Term, determines in its sole discretion to abandon or not maintain any of the Joint Research Patents in the Hansoh Territory, then [***] shall provide [***] with

prior written notice sufficiently in advance of any abandonment to enable [***], [***] to maintain, [***] such Joint Research Patent, [***]. In such event, [***] shall keep [***] reasonably informed of all steps with regard to the preparation, filing, prosecution, and maintenance of the Joint Research Patents, and shall provide [***] with a copy of material communications to and from the patent authorities regarding such Joint Research Patents, including drafts of any material filings or responses to be made to such patent authorities sufficiently in advance of submitting such filings or responses so as to allow [***] a reasonable opportunity to review and comment thereon. In the event that [***] assumes the prosecution and maintenance of any Joint Research Patent, [***] shall have the first right to enforce such Joint Research Patent and [***] shall have the second right and the provisions of Section 11.4.5 shall be applied accordingly.

11.3.5 **Patent Term Extension and Supplementary Protection Certificate.** The Parties shall cooperate on decisions regarding patent term extensions, including supplementary protection certificates and any other extensions that are now or become available in the future, wherever applicable, for Product Specific Patents in the Hansoh Territory and Joint Research Patents in any country or other jurisdiction. [***] shall have the responsibility of applying for any extension or supplementary protection certificate with respect to such Patents in the [***]. Each Party shall keep the other fully informed of its efforts to obtain such extension or supplementary protection certificate. Each Party shall provide prompt and reasonable assistance, as requested by the other, including by taking such action as patent holder as is required under

any Applicable Law to obtain such patent extension or supplementary protection certificate.

11.3.6 **Cooperation.** Each Party shall assist and cooperate with the other Party as such other Party may reasonably request from time to time in connection with its activities set forth in this Section 11.3.

11.4 Enforcement of Patents.

11.4.1 **Notice**. Each Party shall promptly notify the other Party in writing of any alleged or threatened infringement of the Product Specific Patents or Joint Research Patents in any jurisdiction in the Hansoh Territory of which such Party becomes aware in connection with the Exploitation of any Licensed Product or any product that competes with a Licensed Product in the Hansoh Territory (an "**Infringement**").

11.4.2 **Silence Patents**. Except as set out in Section 11.4.4, Silence shall have the sole and exclusive right, but not the obligation, to enforce and defend worldwide under its control, at its own expense, the Silence Background Patents, Silence Research Patents and Silence China Product Development Patents.

11.4.3 **Hansoh Patents**. Hansoh shall have the sole right, but not the obligation, to enforce and defend worldwide under its control, and at its own expense, the Hansoh Background Patents, Hansoh Research Patents and Hansoh China Product Development Patents.

11.4.4 **Product Specific Patents**. After the exercise of the Option by Hansoh in respect of the Licensed Target to which the Licensed Compound or Licensed

Product claimed by such Product Specific Patent relates, Hansoh shall have the first right, but not the obligation, to enforce and defend worldwide under its control, [***], such Product Specific Patents in the Hansoh Territory. If Hansoh does not take commercially reasonable steps to enforce or defend any such Infringement with respect to such Product Specific Patents in the Hansoh Territory (a) within [***] ([***]) days following the first notice provided to it pursuant to this Section 11.4.4, or (b) if earlier, [***] ([***]) Business Days before the time limit, if any, set forth in appropriate laws and regulations for filing of such actions, then Silence may enforce such Product Specific Patents at its own expense.

11.4.5 **Joint Research Patents**. During the Term, except as set out in Sections 11.3.4 and 11.4.4, [***] shall have the first right, but not the obligation, to enforce and defend worldwide under its control, and at its own expense, the Joint Research Patents. If [***] does not take commercially reasonable steps to enforce or defend any such Infringement with respect to Joint Research Patents in the Hansoh Territory (a) within [***] ([***]) days following the first notice provided to it pursuant to this Section 11.4.5, or (b) if earlier, [***] ([***]) Business Days before the time limit, if any, set forth in appropriate laws and regulations for filing of such actions, then [***] may enforce such Joint Research Patent(s) at its own expense.

11.4.6 **Cooperation**. The Parties agree to cooperate fully in any Infringement action pursuant to this Section 11.4.6. Where a Party brings such an action, the other Party shall, where necessary, furnish a power of attorney solely for such purpose or shall join in, or be named as a necessary party to, such action. Unless otherwise set forth herein, the Party entitled to bring any Infringement

litigation in accordance with this Section 11.4.6 shall have the right to settle such claim; provided that no Party shall have the right to settle any Infringement litigation under this Section 11.4.6 in a manner that (a) would restrict the scope or admit the invalidity or unenforceability of a Patent Controlled (other than pursuant to this Agreement) by the other Party, (b) diminishes or has a material adverse effect on the rights or interest of the other Party, or (c) imposes any costs or liability on, or involves any admission by, the other Party, in each case (a) – (c) without the express written consent of such other Party, such consent not to be unreasonably withheld, conditioned, or delayed. The Party commencing the litigation shall provide the other Party with copies of all pleadings and other documents filed with the court and shall consider reasonable input from the other Party during the course of the proceedings.

11.4.7 **Recovery**. Except as otherwise agreed by the Parties in connection with a cost sharing arrangement, any recovery realized as a result of such litigation described in this Section 11.4.7 (whether by way of settlement or otherwise) shall be first allocated to reimburse the Parties for their costs and expenses in making such recovery (which amounts shall be allocated pro rata if insufficient to cover the totality of such expenses). Any remainder after such reimbursement is made shall be distributed to Silence or to Hansoh based on the relationship of the recovery to the Silence Territory or Hansoh Territory, as applicable; provided that to the extent that any award or settlement (whether by judgment or otherwise) is paid to Hansoh in respect of any of the Silence Background Patents, Silence Research Patents, Silence China Product Development Patents or Joint Research Patents (including Product Specific Patents), such amounts shall be treated as [***].

11.5 **Infringement Claims by Third Parties**. If the manufacture, sale, or use of a Licensed Product in the Hansoh Territory pursuant to this Agreement results in, or may result in, any claim, suit, or proceeding by a Third Party alleging patent infringement by Hansoh (or its Affiliates or Sublicensees), Hansoh shall have the first right, but not the obligation, to defend and control the defense of any such claim, suit, or proceeding [***]; provided, however, that the provisions of Section 11.4.2 shall govern the right of Hansoh to assert a counterclaim of infringement of any Silence Background Patent, Silence China Product Development IP or Silence Research Patent.

11.6 **Invalidity or Unenforceability Defenses or Actions**.

11.6.1 **Notice**. Each Party shall promptly notify the other Party in writing of any alleged or threatened assertion of invalidity or unenforceability of any of the Silence Background Patents, Silence Research IP, Silence China Product Development Patents, or Joint Research Patents by a Third Party, in each case in the Hansoh Territory and of which such Party becomes aware.

11.6.2 **Silence Patents**. Except as set out in Section 11.6.4, Silence shall have the sole right, but not the obligation, to defend and control the defense of the validity and enforceability of the Silence Background Patents, Silence China Product Development Patents and Silence Research Patents.

11.6.3 **Hansoh Patents**. Hansoh shall have the sole right, but not the obligation, to defend and control the defense of the validity and enforceability of the Hansoh Background Patents, Hansoh China Product Development Patents and Hansoh Research Patents.

11.6.4 **Product Specific Patents.** After the exercise of the Option by Hansoh in respect of the Licensed Target to which the Licensed Compound or Licensed

Product claimed by such Product Specific Patent relates, Hansoh shall have the first right, but not the obligation, to defend and control the defense of the validity and enforceability of such Product Specific Patents in the Hansoh Territory. Silence may participate in any such claim, suit, or proceeding in the Hansoh Territory related to such Product Specific Patents in the Hansoh Territory with counsel of its choice at its own expense; provided that Hansoh shall retain control of the defense in such claim, suit, or proceeding. If Hansoh elects not to defend or control the defense of any such Product Specific Patents in the Hansoh Territory, or otherwise fails to initiate and maintain the defense of any such claim, suit, or proceeding, then Silence may conduct and control the defense of any such claim, suit, or proceeding, at its own expense; provided, that Silence shall obtain the written consent of Hansoh prior to settling or compromising such defense**,** such consent not to be unreasonably withheld, conditioned, or delayed.

11.6.5 **Joint Research Patents**. Except as set out in Section 11.6.4, [***] shall have the first right, but not the obligation, to defend and control the defense of the validity and enforceability of the Joint Research Patents. [***] may participate in any such claim, suit, or proceeding in the Hansoh Territory related to such Joint Research Patents, in each case that claim or cover a Licensed Product with counsel of its choice at its own expense; provided that [***] shall retain control of the defense in such claim, suit, or proceeding. If [***] elects not to defend or control the defense of any such Joint Research Patents, in each case that Cover Licensed Product in a suit brought in the Hansoh Territory, or otherwise fails to initiate and maintain the defense of any such claim, suit, or proceeding, then [***] may conduct and control the defense of any such claim, suit, or proceeding, at its own expense; provided,

that [***] shall obtain the written consent of [***] prior to settling or compromising such defense, such consent not to be unreasonably withheld, conditioned, or delayed. To the extent that there is any claim, suit, or proceeding of any of the Joint Research Patents in the Hansoh Territory that is not covered by the process set forth above, then each Party shall have the right to defend and control the defense of the validity and enforceability of the Joint Research Patents subject to Applicable Law.

11.6.6 **Cooperation**. Each Party shall assist and cooperate with the other Party as such other Party may reasonably request from time to time in connection with its activities set forth in this Section 11.6, including by being joined as a party plaintiff in such action or proceeding, providing access to relevant documents and other evidence, and making its employees available at reasonable business hours. In connection with any such defense or claim or counterclaim related to Section 11.6.5, the controlling Party shall keep the other Party reasonably informed of any steps taken, and shall provide copies of all documents filed, in connection with such defense, claim, or counterclaim. In connection with the activities set forth in this Section 11.6, each Party shall consult with the other as to the strategy for the defense of the Product Specific Patents and Joint Research Patents.

ARTICLE 12
CONFIDENTIALITY AND NON-DISCLOSURE

12.1 **Confidentiality Obligations**. At all times during the Term and (i) following termination of this Agreement in its entirety, for a period of: (x) [***] ([***]) years for Restricted Information and (y) [***] ([***]) years for all other Confidential Information, or, (ii) following expiry of this Agreement in its entirety, for a period of [***] ([***]) years for

all Confidential Information (including Restricted Information), each Party shall, and each of the foregoing shall cause its or its Affiliates' respective officers, directors, employees, consultants, contractors, agents, partners (whether general or limited), financing sources or other representatives ("**Representatives**") to, keep confidential and not publish or otherwise disclose to a Third Party and not use, directly or indirectly, for any purpose, any Confidential Information furnished or otherwise made known to it, directly or indirectly, by the other Party, except to the extent such disclosure or use is expressly permitted by the terms of this Agreement. Notwithstanding the foregoing, to the extent the receiving Party can demonstrate by documentation or other competent proof, the confidentiality and non-use obligations under this Section 12.1 with respect to any Confidential Information shall not include any information that:

12.1.1 has been published by a Third Party or otherwise is or hereafter becomes part of the public domain through no fault on the part of the receiving Party;

12.1.2 have been in the receiving Party's or its Representatives' possession prior to disclosure by the disclosing Party without any obligation of confidentiality to the disclosing Party with respect to such information;

12.1.3 is subsequently received by the receiving Party or its Representatives from a Third Party and without breach of any agreement between such Third Party and the disclosing Party;

12.1.4 that is generally made available to Third Parties by the disclosing Party without restriction on disclosure; or

12.1.5 have been independently developed by or for the receiving Party or its Representatives without reference to or use of the disclosing Party's Confidential Information.

Specific aspects or details of Confidential Information shall not be deemed to be within the public domain or in the possession of the receiving Party merely because the Confidential Information is embraced by more general information in the public domain or in the possession of the receiving Party. Further, any combination of Confidential Information shall not be considered in the public domain or in the possession of the receiving Party merely because individual elements of such Confidential Information are in the public domain or in the possession of the receiving Party unless the combination and its principles are in the public domain or in the possession of the receiving Party.

12.2 **Permitted Disclosures**. Each Party may disclose Confidential Information of the other Party to the extent such disclosure is reasonably necessary in the following instances:

1.1.1 obtaining or maintaining Regulatory Approval of the Licensed Products;

1.1.2 complying with law, regulation or order of any Regulatory Authority, court of competent jurisdiction or rule of stock exchange;

1.1.3 disclosure to its Representatives, in each case on a need-to-know basis in connection with the Development, manufacture, or Commercialization of any Licensed Product in accordance with the terms of this Agreement, in each case under written obligations of confidentiality and non-use at least as stringent as those herein; and

1.1.4 disclosure to actual and bona fide potential investors, acquirors, licensees, sublicensees, and other financial or commercial partners for the purpose of evaluating or carrying out an actual or potential investment, acquisition, or collaboration, in each case under customary and industry standard written obligations of confidentiality and non-use; provided that, where the terms of this Agreement are being disclosed, the disclosing Party redacts the financial

terms and other provisions of this Agreement that are not reasonably required to be disclosed in connection with such potential investment, acquisition, or collaboration, which redaction shall be prepared in consultation with the other Party.

12.2.1 Notwithstanding the foregoing, in the event a Party is required to make a disclosure of the other Party's Confidential Information pursuant to Section 12.2.1 or 12.2.2, it will, except where impermissible or impracticable, give reasonable advance notice to the other Party of such disclosure and comply with all reasonable requests of the disclosing Party with respect to maintaining confidence in such Confidential Information and in any event shall use the same diligent efforts to secure confidential treatment of such Confidential Information as such Party would use to protect its own Confidential Information, but in no event less than reasonable efforts. In any event, the Parties agree to take reasonable action to avoid disclosure of Confidential Information. Any information disclosed pursuant to this Section 12.2 shall remain Confidential Information and subject to the restrictions set forth in this Agreement, including the foregoing provisions of this ARTICLE 12.

12.3 **Use of Name**. Except as expressly provided in this Agreement, neither Party shall use the name, logo, or trademark of the other Party or any of its Affiliates (or any abbreviation or adaptation thereof) in any publication, press release, marketing and promotional material, or other form of publicity without the prior written approval of such other Party in each instance, which approval shall not be unreasonably withheld, conditioned, or delayed. The restrictions imposed by this Section 12.3 shall not prohibit either Party from making any disclosure identifying the other Party that, in the reasonable opinion of

the disclosing Party's counsel, is required by Applicable Law; provided, that such Party shall submit the proposed disclosure identifying the other Party in writing to such other Party as far in advance as reasonably practicable (and in no event less than [***] ([***]) Business Days prior to the anticipated date of disclosure) so as to provide a reasonable opportunity to comment on such disclosure.

12.4 **Public Announcements**. The Parties have agreed the press releases set out as Schedule 12.4 shall be the press release announcing the transaction contemplated by this Agreement. Other than the relevant press release, neither Party shall issue any public announcement, press release, or other public disclosure regarding this Agreement or its subject matter without the other Party's prior written consent, except for any such disclosure that is, required by Applicable Law or the rules of a stock exchange on which the securities of the disclosing Party are listed (or to which an application for listing has been submitted). In the event a Party is, required by Applicable Law or the rules of a stock exchange on which its securities are listed (or to which an application for listing has been submitted) to make such a public disclosure, such Party shall submit the proposed disclosure in writing to the other Party as far in advance as reasonably practicable (and in no event less than [***] ([***]) Business Days prior to the anticipated date of disclosure) so as to provide a reasonable opportunity to comment thereon. Notwithstanding anything to the contrary herein, (i) following initial press release announcing this Agreement, each Party shall be free to disclose, without the other Party's prior written consent, the existence of this Agreement, and those terms of the Agreement which have already been publicly disclosed in accordance herewith, and (ii) in respect of a particular Licensed Target, Silence may disclose the identity of such Licensed Target and its stage of Development, provided always that in respect of the Global Licensed Target and the corresponding Global Licensed Compounds and Global Licensed Products, subject to Hansoh's prior written consent (such consent not to be unreasonably

withheld, delayed or conditioned). Except as expressly set forth to the contrary in the foregoing or this Agreement, Silence shall not disclose Hansoh's name in relation to a Licensed Target and the corresponding Licensed Compounds and Licensed Products without Hansoh's prior written consent (such consent not to be unreasonably withheld, delayed, or conditioned).

12.5 **Publications**. The Parties acknowledge that scientific publications must be strictly monitored to prevent any adverse effect from premature publication of results of the Development activities hereunder.

12.5.1 **During the Research Collaboration Term**. During the Research Collaboration Term:

(a) Silence shall have the right to make any publications, presentations, or public disclosures related to a Licensed Product subject to Hansoh's prior review and approval such approval not to be unreasonably withheld, delayed or conditioned;

(b) Without prejudice to the provisions of Section 12.4, Silence shall be entitled to disclose the progress of its Development activities related to Licensed Products directed to each Licensed Target without disclosing the identity of the Licensed Target unless disclosure of the identity of the Licensed Target mutually agreed to in writing provided always that such agreement shall not be unreasonably withheld, delayed or conditioned; and

(c) Hansoh may not make any publications, presentations, or public disclosures without Silence's prior written approval, except as otherwise specified in this Agreement.

12.5.2 **Following Option Exercise**. Following Hansoh's exercise of an Option in respect of a particular Licensed Target:

(a) Hansoh shall have the right to make any publications, presentations, or public disclosures related to Licensed Products directed to the Global Licensed Target subject to Silence's prior review and approval;

(b) Silence shall not make any publications, presentations, or public disclosures related to the Global Licensed Products without Hansoh's prior written approval; and

(c) Both Parties will cooperate to agree a mutual public disclosure strategy in relation to publications, presentations and public disclosures related to Licensed Products directed to a China Licensed Target. Notwithstanding the foregoing, each Party shall be entitled to disclose the progress of its Development activities related to Licensed Products directed to a China Licensed Target to the extent relating to the Silence Territory, for publications made by Silence, or to the Hansoh Territory, for publications made by Hansoh, without disclosing the Licensed Target(s) unless mutually agreed to in writing provided always that such agreement shall not be unreasonably withheld, delayed or conditioned.

12.5.3 **Review Process**. Before any paper is submitted for publication or an oral presentation is made for which review or approval rights are provided under Section 12.5, the publishing or presenting Party (the "**Publishing Party**") shall deliver a then-current copy of the paper or materials for oral presentation

to the non-publishing Party at least [***] ([***]) days prior to submitting the paper to a publisher or making the presentation. The non-publishing Party shall review any such paper and give its comments to such Publishing Party within [***] ([***]) days after the delivery of such paper to such other Party. The Publishing Party shall comply with the other Party's request to delete references to the other Party's Confidential Information in any such paper and will withhold publication of any such paper or any presentation of same for an additional [***] ([***]) days in order to permit the Parties to obtain Patent protection if such other Party deems it necessary.

12.6 **Return of Confidential Information**. Upon termination of this Agreement in its entirety, each Party shall promptly return to the other Party, or delete or destroy, all records and materials in such Party's possession or control containing Confidential Information of the other Party; provided that the other Party shall be permitted to retain one (1) copy of such Confidential Information for the sole purpose of performing any continuing obligations under this Agreement, as required by Applicable Law, or for legal archival purposes. If this Agreement is terminated with respect to one or more Licensed Target, but not in its entirety, each Party shall promptly return to the other Party, or delete or destroy, all records and materials in such Party's possession or control containing Confidential Information of the other Party that relates to the terminated Licensed Target. Notwithstanding the foregoing, such other Party also shall be permitted to retain such additional copies of or any computer records or files containing such Confidential Information that have been created solely by such Party's automatic archiving and back-up procedures, to the extent created and retained in a manner consistent with such other Party's standard archiving and back-up procedures, but not for any other use or purpose.

ARTICLE 13
REPRESENTATIONS AND WARRANTIES

13.1 **Mutual Warranties**. Each Party hereby represents and warrants, as of the Effective Date, as follows:

13.1.1 **Organization**. It is a company duly organized, validly existing, and in good standing under the laws of the jurisdiction of its organization, and has all requisite power and authority, corporate or otherwise, to execute, deliver, and perform this Agreement.

13.1.2 **Authorization**. The execution and delivery of this Agreement and the performance by such Party of the transactions contemplated hereby have been duly authorized by all necessary corporate action, and do not violate (a) such Party's charter documents, bylaws, or other organizational documents, (b) any agreement, instrument, or contractual obligation to which such Party is bound, (c) any requirement of any Applicable Law, or (d) any order, writ, judgment, injunction, decree, determination, or award of any court or governmental agency presently in effect applicable to such Party.

13.1.3 **Binding Agreement**. This Agreement is a legal, valid, and binding obligation of such Party enforceable against it in accordance with its terms, subject to the effects of bankruptcy, insolvency, or other laws of general application affecting the enforcement of creditor rights, judicial principles affecting the availability of specific performance, and general principles of equity (whether enforceability is considered a proceeding at law or equity).

13.1.4 **No Inconsistent Obligation**. It is not under any obligation, contractual or otherwise, to any Person that conflicts with or is inconsistent with the terms

of this Agreement, or that would impede the diligent and complete fulfilment of its obligations hereunder.

13.2 **Additional Warranties by Silence**. Silence hereby represents and warrants, as of the Effective Date, as follows:

13.2.1 it has the right to grant all rights and licenses it purports to grant to Hansoh with respect to the Licensed Know-How and Licensed Patents under this Agreement, free and clear of any rights therein granted to any Third Party, and it has not granted to any other Person any rights in the Licensed Know-How and Licensed Patents in any manner that would conflict with the rights granted to Hansoh under this Agreement;

13.2.2 the Licensed Know-How and the Licensed Patents are not subject to any encumbrance, lien or claim of ownership by any Third Party in any way that would conflict with the rights granted to Hansoh under this Agreement;

13.2.3 All of the Silence Background Patents that are issued patents are in full force and effect, and Silence has no knowledge that any issued patents that are part of the Silence Background Patents are invalid or unenforceable;

13.2.4 it is not the subject of any Patent proceeding in respect of any Silence Background Patent, and it is not aware of any pending or threatened action, suit, proceeding, or claim by a Third Party challenging Silence's ownership rights in, or the validity or scope of, such Silence Background Patents;

13.2.5 no claim or action has been brought or, to Silence's knowledge, threatened in writing, by any Third Party alleging that the use of the Silence Background IP or any of its activities relating to the Licensed Products infringes or

misappropriates, or would infringe or misappropriate, any intellectual property right of any Third Party; and

13.2.6 to Silence's knowledge, all applicable fees due to patent authorities with respect to the filing and prosecution of the Silence Background Patents existing as of the Effective Date have been paid on or before the due date for payment (as such due date may be extended in accordance with Applicable Law or patent authority rules and regulations).

13.3 **Mutual Covenants**. Each Party hereby covenants and agrees, in connection with the performance of its activities under this Agreement:

13.3.1 it shall not employ, contract with, or retain any person directly or indirectly to perform any of the activities under this Agreement if such person is under investigation by the FDA or NMPA or any other regulatory agency for debarment or is presently debarred by the FDA pursuant to the Generic Drug Enforcement Act of 1992, as amended (21 U.S.C. § 301, *et seq.*), or by NMPA pursuant to similar Applicable Law, or is subject to any debarment or similar sanction by any other Regulatory Authority;

13.3.2 all research conducted by or on behalf of it shall be performed in accordance with Applicable Laws, and applicable established internal policies and procedures (if any), including policies and procedures pertaining to research involving laboratory animals or hazardous agents and materials, as applicable. Each Party agrees that any animals used in the performance of studies under the Research Plan will be handled in accordance with established guidelines for the care and use of laboratory animals. Further, each Party covenants that all research conducted pursuant to this Agreement involving the use of

animals was, or will be, reviewed and approved by its or its animal care and use committee prior to commencement of the applicable research; and

13.3.3 in the performance of its obligations under this Agreement, such Party shall comply and shall cause its and its Affiliates' employees and contractors to comply with all Applicable Laws and, without limiting the generality of the foregoing, it shall not perform any actions that are prohibited by local or other anti-corruption laws (collectively, "**Anti-Corruption Laws**") that may be applicable to such Party. Without limiting the generality of the foregoing, (i) neither Party shall make any payments, or offer or transfer anything of value, to any government official or government employee, to any political party official or candidate for political office or to any other Third Party related to the transaction in a manner that would violate Anti-Corruption Laws, and (ii) to the extent that a Party is carrying out activities in the Hansoh Sole Region, each Party shall perform, and shall cause its Affiliates or other licensees or sublicensees to perform, its obligations and responsibilities under this Agreement in compliance with all applicable rules, regulations, or guidance issued by the Human Genetic Resources Administration of China ("**HGRAC**") when collecting, preserving, using, disclosing, or supplying any "human genetic resources", as such term is defined by the HGRAC, or related data.

13.4 **Additional Covenants of Silence**. Silence hereby covenants to Hansoh that it will not (a) license, sell, assign or otherwise transfer Silence Background IP, Silence Research IP or Silence China Product Development IP in a manner that conflicts with the rights granted to Hansoh hereunder, or (b) permit to exist or grant to any Third Party, with respect to any Silence Background IP, Silence Research IP or Silence China Product

Development IP, any lien, encumbrance, charge, security interest, mortgage, liability, or other restriction (including in connection with any indebtedness) (each a "**Third Party Restriction**") which materially conflicts with the rights granted to Hansoh hereunder, provided always that (x) nothing in parts (a) or (b) of this Section 13.4 shall prevent Silence from entering into any transaction that is subject to Hansoh's rights under this Agreement and (y) in the event that a Third Party Restriction which materially conflicts with the rights granted to Hansoh is imposed on Silence (as opposed to being granted by Silence) by operation of law or otherwise, Silence's sole obligation shall be to use such efforts as would be commercially reasonable (taking into account all relevant factors including the nature of the third party right, the consequences to Silence and Hansoh and the cost and benefit of such efforts) to have such Third Party Restriction removed.

13.5 **Additional Covenants of Hansoh**. Hansoh hereby covenants to Silence that it will not (a) license, sell, assign or otherwise transfer Hansoh Background IP, Hansoh Research IP or Hansoh China Product Development IP in a manner that conflicts with the rights granted to Silence hereunder, or (b) permit to exist or grant to any Third Party, with respect to any Hansoh Background IP, Hansoh Research IP or Hansoh China Product Development IP, any lien, encumbrance, charge, security interest, mortgage, liability, or other restriction (including in connection with any indebtedness) (each a "**Third Party Restriction**") which materially conflicts with the rights granted to Silence hereunder, provided always that (x) nothing in parts (a) or (b) of this Section 13.5 shall prevent Hansoh from entering into any transaction that is subject to Silence's rights under this Agreement and (y) in the event that a Third Party Restriction which materially conflicts with the rights granted to Silence is imposed on Hansoh (as opposed to being granted by Hansoh) by operation of law or otherwise, Hansoh's sole obligation shall be to use such efforts as would be commercially reasonable (taking into account all relevant factors

including the nature of the third party right, the consequences to Hansoh and Silence and the cost and benefit of such efforts) to have such Third Party Restriction removed.

13.6 **Disclaimer of Warranties**. Except for the express warranties set forth herein, neither Silence nor Hansoh nor any of their respective Affiliates makes any warranties, express or implied, either in fact or by operation of law, by statute, or otherwise, and each Party specifically disclaims any other warranties, whether written or oral, express or implied, including any warranty of quality, merchantability, or fitness for a particular use or purpose, [***].

ARTICLE 14
INDEMNITY

14.1 **Indemnification of Silence**. Hansoh shall indemnify, defend, and hold harmless Silence, its Affiliates, and their respective directors, officers, employees, and agents (collectively, the "**Silence Indemnitees**") from and against any and all losses, damages, liabilities, penalties, costs, and expenses (including reasonable attorneys' fees and expenses) (collectively, "**Losses**") in connection with any and all suits, investigations, claims, or demands of Third Parties (collectively, "**Claims**") incurred by or rendered against the Silence Indemnitees arising from or occurring as a result of:

14.1.1 the Exploitation of any Licensed Product by or on behalf of Hansoh or any of its Affiliates, Sublicensees, subcontractors, agents, or consultants; or

14.1.2 the breach by Hansoh of any warranty, representation, covenant, or agreement made by Hansoh in this Agreement;

except in each case to the extent of those Losses for which Silence, in whole or in part, has an obligation to indemnify Hansoh pursuant to Section 14.2.

14.2 **Indemnification of Hansoh**. Silence shall indemnify, defend, and hold harmless Hansoh, its Affiliates, and its and their respective directors, officers, employees, and agents (collectively, the "**Hansoh Indemnitees**"), from and against any and all Losses in connection with any and all Claims incurred by or rendered against the Hansoh Indemnitees arising from or occurring as a result of:

14.2.1 the Exploitation of any Licensed Compound or Licensed Product by or on behalf of Silence or any of its Affiliates, Sublicensees, subcontractors, agents, or consultants; or

14.2.2 the breach by Silence of any warranty, representation, covenant, or agreement made by Silence in this Agreement;

except to the extent of those Losses for which Hansoh, in whole or in part, has an obligation to indemnify Silence pursuant to Section 14.1.

14.3 **Indemnification Procedure**. A Party that intends to claim indemnification under this ARTICLE 14 (the "**Indemnitee**") shall promptly notify the indemnifying Party (the "**Indemnitor**") in writing of any Claim in respect of which the Indemnitee intends to claim such indemnification, and the Indemnitor shall have sole control of the defense or settlement of such Claim. The Indemnitee may participate at its expense in the Indemnitor's defense of and settlement negotiations for any Claim with counsel of the Indemnitee's own choice. The indemnity arrangement in this ARTICLE 14 shall not apply to amounts paid in settlement of any action with respect to a Claim if such settlement is effected without the consent of the Indemnitor, which consent shall not be unreasonably withheld, conditioned, or delayed. The failure to deliver written notice to the Indemnitor within a reasonable time after the commencement of any action with respect to a Claim shall only relieve the Indemnitor of its indemnification obligations

under this ARTICLE 14 if and to the extent the Indemnitor is actually prejudiced thereby. The Indemnitee shall cooperate fully with the Indemnitor and its legal representatives in the investigation of any action with respect to a Claim covered by this indemnification.

14.4 **Special, Indirect, and Other Losses**. Except for breach of confidentiality obligations under ARTICLE 12 or to the extent any such damages are required to be paid to a Third Party as part of a claim for which a Party provides indemnification under this ARTICLE 14, neither Party nor any of its Affiliates shall be liable for any loss of profits or business interruption or any indirect, incidental, special, exemplary, punitive, or consequential damages, including, however caused and on any theory of liability, whether in contract, tort, negligence, breach of statutory duty, or otherwise in connection with or arising in any way out of the terms of this agreement or the transactions contemplated hereby or the use of the Licensed Compound or Licensed Product, even if advised of the possibility of such damage. The foregoing limitation of liability shall not operate to limit or exclude either Party's liability for (a) death or personal injury, (b) fraud, or (c) any other liability which, pursuant to Applicable Law, cannot be limited or excluded.

14.5 **Insurance**. Each Party shall maintain, at its own expense, commercial general liability insurance and product liability and other appropriate insurance as required under Applicable Laws. Each Party shall maintain such insurance for the period commencing promptly after the Effective Date until expiry or termination of this Agreement. Each Party shall provide a certificate of insurance evidencing such coverage to the other Party upon request. It is understood that such insurance shall not be construed to create any limit of either Party's obligations or liabilities with respect to its indemnification obligations under this Agreement.

ARTICLE 15
TERM AND TERMINATION

15.1 **Term**. This Agreement shall commence on the Effective Date and, unless earlier terminated as provided herein, shall remain in effect, on a Licensed Product-by-Licensed Product, country-by-country and region-by-region basis, until the expiration of the Royalty Term for such Licensed Product in such country or region (the "**Term**"). Upon the expiration of the Royalty Term for a particular Licensed Product in a particular country or region, the licenses granted to Hansoh under Section 6.1 for such Licensed Product in such country or region shall become fully-paid, royalty-free, perpetual, irrevocable, and exclusive.

15.2 **Termination by Hansoh For Convenience**. Hansoh shall have the right to terminate this Agreement in its entirety, after the Option Exercise Date with respect to any Licensed Target in its entirety or on a country-by-country basis, for any or no reason, upon [***] ([***]) days' prior written notice to Silence which notice shall specify the relevant Licensed Target and the countries affected by such termination. Hansoh shall have the right to terminate this Agreement with respect to any Licensed Target in its entirety or on a country-by-country basis prior to the Option Exercise Date with respect to such Licensed Target, together with the associated Research Plan, or, in the case of termination of a Licensed Target in one or more, but not all, countries, the components of the associated Research Plan applicable solely to such terminated countries, for any or no reason, upon [***] ([***]) days' prior written notice to Silence (which notice shall specify the relevant Licensed Target and the countries affected by such termination) if no IND has been filed in respect of a Licensed Product directed to the relevant Licensed Target and on [***] ([***]) days' written notice to Silence if an IND has been filed.

15.3 **Termination for Material Breach**. Each Party shall have the right to terminate this Agreement with respect to any Licensed Target, (including all Licensed Compounds and Licensed Products directed thereto), in the event that the other Party materially breaches this Agreement with respect to such Licensed Target, and such breach shall have continued for [***] ([***]) days (or [***] ([***]) days with respect to any payment breach) after receipt from the non-breaching Party of written notice specifying the breach and requesting its cure. For clarity, in the event of any uncured payment breach relating to payment obligations arising prior to Option exercise, or that a material breach relates to all Licensed Targets, then this Agreement may be terminated in its entirety. On receipt of a notice by the alleged breaching Party pursuant to this Section, the non-breaching Party shall immediately make its Alliance Manager available for discussion at the request of the alleged breaching Party.

15.4 **Termination by Silence for Patent Challenge**. Silence shall have the right to terminate this Agreement in full, or on a Licensed Target-by-Licensed Target basis, upon written notice to Hansoh in the event that Hansoh or any of its Affiliates or Sublicensees directly asserts in its own respective name, or directs a Third Party to assert, a Patent Challenge; provided that with respect to any such Patent Challenge by any Sublicensee, Silence will not have the right to terminate under this Section 15.4 if, within [***] ([***]) days of Silence's notice to Hansoh under this Section 15.4, Hansoh (a) causes such Patent Challenge to be terminated or dismissed or (b) terminates the sublicense granted to such Sublicensee. For purposes of this Section, "**Patent Challenge**" means any challenge in a legal or administrative proceeding to the patentability, validity, ownership or enforceability of any of the Silence Background Patents, Silence Research Patents, Silence China Product Development Patents or Joint Research Patents (or any claim thereof), including by: (x) filing or pursuing a declaratory judgment action in which any of the Silence Background Patents, Silence Research Patents, Silence China Product

Development Patents or Joint Research Patents is alleged to be invalid or unenforceable; (y) citing prior art against any of the Silence Background Patents, Silence Research Patents, Silence China Product Development Patents or Joint Research Patents (other than art required to be cited by Applicable Law, including under a duty of candor to a patent office), filing a request for or pursuing a re-examination of any of the Silence Background Patents, Silence Research Patents, Silence China Product Development Patents or Joint Research Patents (other than with Silence's written agreement), or becoming a party to or pursuing an interference; or (z) filing or pursuing any opposition, cancellation, nullity, or other like proceedings against any of the Silence Background Patents, Silence Research Patents, Silence China Product Development Patents or Joint Research Patents; but excluding any challenge raised as a defense against a claim, action, or proceeding asserted by Silence, its Affiliates or its or their designated Third Party against Hansoh or its Affiliates or Sublicensees.

15.5 **Termination for Insolvency**. In the event that a Party (a) files or resolves to file for protection under (i) bankruptcy, (ii) insolvency, (iii) reorganization (save in the case of a solvent reorganization), (iv) restructuring (save in the case of a solvent restructuring), or (v) business rescue laws applicable to that Party in any jurisdiction; (b) makes an assignment for the benefit of creditors; (c) appoints or suffers appointment of a receiver, administrative receiver, bailiff or trustee or analogous appointment over substantially all of its property; (d) proposes or implements a scheme of arrangement, company voluntary arrangement or other agreement of composition, compromise or extension of its debts (other than in circumstances where such scheme, arrangement or agreement would have no adverse impact on the rights of any other Party to this Agreement); (e) proposes or is a party to any dissolution or liquidation or ceases continuation of substantially all of its business; (f) is subject to any filing of an application or a petition under any (i) bankruptcy, (ii) insolvency, (iii) reorganization (save in the case of a solvent

reorganization), (iv) restructuring (save in the case of a solvent restructuring), or (v) business rescue laws or has any such application or petition filed against it that, in any such case, is not discharged within [***] ([***]) days of the filing thereof; or (g) admits in writing its inability generally to meet its obligations as they fall due in the general course (providing always that a request for fulfilment of a specific obligation to be postponed for a specified time shall not amount to an admission that the Party is generally unable to meet its obligations as they fall due), then the other Party may terminate this Agreement in its entirety effective immediately upon written notice to such Party.

1.1 **Effects of Termination**.

1.1.1 **License Grant to Silence**

(a) If this Agreement is terminated with respect to a particular Licensed Target (and, in the event that this Agreement is terminated in its entirety, to all Licensed Targets); or

(b) If any Licensed Target becomes an Expired Target pursuant to Section 5.3,

(collectively the "**Returned Targets**"),

then, in each case, as of the date that any Licensed Target first becomes a Returned Target: (a) following a written notice from Silence to Hansoh requesting the same, Hansoh shall, subject to the provisions of Section 15.6.7, transfer to Silence any Regulatory Approval held by Hansoh in respect of any Returned Target or the relevant Licensed Compounds or Products and to the extent that such Regulatory Approval is not transferable, hold the foregoing on trust for Silence and grant Silence a right of reference to such Regulatory

Approval in order for Silence to obtain an equivalent Regulatory Approval in the relevant country; and (b) Hansoh hereby grants to Silence (without any further action required on the part of Hansoh) (i) an exclusive, royalty-free and fully paid-up, irrevocable and perpetual license, with the right to grant sublicenses, under any Joint Research Patents, Hansoh Research IP and Hansoh China Product Development IP, and (ii) a non-exclusive, royalty-free and fully paid-up, irrevocable and perpetual license, with the right to grant sublicenses, under any Hansoh Background IP, in each case (i) and (ii) solely to Exploit Licensed Compounds and Licensed Products directed to such Returned Target in the Field throughout the territories that were the subject of the relevant termination. In respect of each of the Joint Research Patents, Hansoh Research Patents and Hansoh China Product Development Patents licensed to Silence pursuant to this Section 15.6.1, Silence shall benefit from equivalent rights with respect to the maintenance, prosecution, enforcement and defense of such Patents as if such Patents were Joint Research Patents, and not Product Specific Patents, for the purposes of ARTICLE 11. For clarity, the license set out in this Section shall survive any expiration or termination of this Agreement.

1.1.2 **License Termination.** Upon any termination of this Agreement with respect to a Licensed Target, all rights and licenses granted with respect to such Licensed Target under Section 6.1 shall terminate and be of no further force or effect.

1.1.3 **Development Wind-Down or Transition**.

(a) **Clinical Studies**. Hansoh shall, at its option, be responsible for completing (in accordance with the established protocols) or the

orderly wind-down of any Clinical Studies that were Initiated by or on behalf of it prior to the termination of this Agreement (whether terminated in its entirety or with respect to a Licensed Target) provided always that if Hansoh decides to wind-down any Clinical Studies it shall notify Silence and the Parties shall, on Silence's reasonable request, enter into good faith discussions about the transfer of such Clinical Studies to Silence pursuant to Section 15.6.3(b); provided that such transfer will be effected at Silence's sole cost and expense. Notwithstanding anything to the contrary in this Agreement, Hansoh shall not, and shall not be obligated to, commence any Clinical Studies with respect to any Licensed Product directed to a terminated Licensed Target at any time after it has given or received a notice of termination pursuant to this ARTICLE 15 in respect of such Licensed Target. If the Parties agree in writing (including as to the meeting of the ongoing costs of such Clinical Studies), the sponsorship of any such ongoing Clinical Studies shall be transitioned to Silence.

(b) **Cooperation**. Hansoh shall effect a reasonable, orderly, and prompt transition of the Development activities relating to any terminated Licensed Target and corresponding terminated Licensed Products to Silence and/or its designee(s) following delivery of notice of termination so that Silence is able to assume responsibility for same as of the effective date of termination. Where the same cannot be fully achieved prior to the effective date of termination, Hansoh shall continue to provide such reasonable cooperation to Silence and its designee(s) until such transition has been completed. Without

limiting the generality of the foregoing, Hansoh shall, [***], provide consultation and assistance for a period of no more than [***] ([***]) days after termination for the purpose of transferring or transitioning to Silence [***] not already in Silence's possession in each case, to the extent [***] solely for Silence to continue the Development and/or Commercialization of the Licensed Products directed to the terminated Licensed Target in the Field in the Hansoh Territory.

1.1.4 **Commercial Wind-Down.** Hansoh, its Affiliates and Sublicensees shall be entitled to continue to sell (but not to actively promote after the effective date of termination) any existing inventory of Licensed Products directed to a Licensed Target in respect of which this Agreement has been terminated, and for which Regulatory Approval therefor has been obtained, in accordance with the terms and conditions of this Agreement, for a period of [***] ([***]) months after the effective date of such termination. Silence shall have the right, at its discretion, to purchase from Hansoh any or all of the inventory of Licensed Products and Licensed Compounds held by or on behalf of Hansoh at the date of termination at a price equal to Hansoh's Manufacturing cost with a reasonable, mutually agreed upon mark-up (not to exceed [***] ([***%])) to cover administrative, shipping and other costs; provided that Hansoh shall be able to retain a sufficient amount of inventory to complete the termination of its commercialisation activities. Silence shall notify Hansoh within [***] ([***]) days of the effective date of termination whether Silence elects to exercise such right.

1.1.5 **Contract Transfer**. At Silence's request, Hansoh shall use Commercially Reasonable Efforts to transfer or transition to Silence or its designee all then-existing commercial arrangements relating to Licensed Products directed to terminated Licensed Targets to the extent [***] for Silence to continue the Development and/or Commercialization of such Licensed Products in the Hansoh Territory. If any such contract between Hansoh and a Third Party is not assignable to Silence or its designee (whether by such contract's terms or because such contract does not relate specifically to the Licensed Products) but is otherwise [***] for Silence to continue the Development and/or Commercialization of the Licensed Products in the Hansoh Territory, or if Hansoh is performing such work for the Licensed Product itself (and thus there is no contract to assign), then Hansoh shall reasonably cooperate with Silence to negotiate for the continuation of such services for Silence from such entity.

1.1.6 **Assignment in respect of terminated Licensed Targets.** Subject to Sections 15.6.3 and 15.6.4, if this Agreement is terminated with respect to a particular Licensed Target (and, in the event that this Agreement is terminated in its entirety, to all Licensed Targets) Hansoh will deliver to Silence all its right, title and interest in and to all Licensed Compounds and Licensed Products Developed pursuant to this Agreement and which are directed to such terminated Licensed Target, and Silence will be free to Exploit such terminated Licensed Target, together with such Licensed Compounds and Licensed Products directed to such terminated Licensed Target as Silence, in its sole discretion, deems appropriate.

1.1.7 If Hansoh is entitled to terminate this Agreement pursuant to Section 15.3 or Section 15.5, Hansoh may elect to terminate this Agreement, or to continue this Agreement subject to the provisions set forth as follow:

(a) If Hansoh terminates this Agreement under Section 15.3 or Section 15.5, notwithstanding anything set forth to the contrary in this Section 15.6, Silence shall fully compensate Hansoh for reasonable costs or expenses incurred by it or its Affiliates in connection with the transfer of any relevant activities (including Development Activities, Clinical Studies, and Regulatory Approvals) from Hansoh to Silence pursuant to Sections 15.6.1, and 15.6.3 through 15.6.6.

(b) If Hansoh terminates this Agreement under Section 15.3 and Silence may by itself or its Affiliates, or grant any Third Party the license to, develop, use, import, export, offer for sale, sell, and otherwise commercialize the Licensed Products for the Field in and outside the Hansoh Territory ("**Re-Commercialization**") then, subject to Hansoh's satisfactory performance of the transfer activities as set out in Sections 15.6.3 through 15.6.6, in the event that Silence requests the transfer of any of the Regulatory Approvals obtained by Hansoh for the Commercialization of the relevant Licensed Compound or Licensed Product in the Hansoh Territory to Silence, then, to the extent that such Regulatory Approvals are transferred to Silence, Silence shall pay royalties (at [***]) and subject to the provisions of ARTICLE 10, calculated as if all the sales by Silence or its Affiliates or licensees (including sublicensees) were sales by

Hansoh), on sales of any Licensed Product that was the subject of such transferred Regulatory Approval in the countries where such transferred Regulatory Approvals were granted until the Re-Commercialization Cap has been reached where the Re-Commercialization Cap shall be [***].

(c) If Hansoh has the right to terminate this Agreement under Section 15.3, but elects to continue this Agreement, this Agreement shall continue in full force and effect, without prejudice to Hansoh's right to seek damages for the applicable breach by Silence in accordance with the remedies available to it under the Agreement or Applicable Law.

1.1.8 **Exclusivity**. Upon any termination of this Agreement with respect to a Licensed Target, each Party's obligations under ARTICLE 4 with respect to such Licensed Target shall terminate.

1.1.9 **Patent Prosecution.** Upon any termination of this Agreement with respect to a Licensed Target in any or all countries, Hansoh's rights in respect of the prosecution and enforcement of any Silence Background Patents, Silence Research Patents, Joint Research Patents and Product Specific Patents which relate to such Licensed Target in such terminated countries (and no continuing Licensed Target) shall terminate. If Hansoh has assumed the prosecution of any Patents pursuant to Section 11.3.3, and such Patent does not relate to any Licensed Target to which Hansoh has any continuing rights, then Hansoh shall ensure that the prosecution of such Patents is transferred to Silence in a prompt and orderly fashion such that no deadline is missed in respect of such

prosecution and/or enforcement and that the scope of such Patents is not limited or restricted as a consequence of such transfer.

1.1.10 **Confidential Information**. Upon any termination of this Agreement with respect to a Licensed Target, each Party shall return or cause to be returned to the other Party all Confidential Information of the other Party relating to such Licensed Target as provided in Section 12.6. Upon any termination of this Agreement in its entirety, each Party shall return or cause to be returned to the other Party all Confidential Information of the other Party as provided in Section 12.6. For the avoidance of doubt, the provision above shall not apply to: (i) Confidential Information which the receiving Party or its Representatives are required to retain by law, pursuant to a subpoena or order or requirement or an official request issued by any court of competent jurisdiction or by any other rule or regulation of any stock exchange or by any other governmental, administrative or regulatory body to which they are subject or the internal archive purpose; (ii) notes, reports, analyses, computations, studies or other documents in any format which contain, reflect or which are generated from Confidential Information and which are generated by the receiving Party or on its behalf by its Representatives; or (iii) Confidential Information which is stored electronically by the receiving Party's or its Representatives' automatic archiving or back-up systems, to the extent that such deletion would be technologically impracticable.

15.6 **Remedies**. Except as otherwise expressly provided herein, termination of this Agreement in accordance with the provisions hereof shall not limit remedies that may otherwise be available in law or equity.

15.7 **Accrued Rights; Surviving Obligations**. Termination or expiration of this Agreement

for any reason shall be without prejudice to any rights that shall have accrued to the benefit of a Party prior to such termination or expiration. Such termination or expiration shall not relieve a Party from obligations that are expressly indicated to survive the termination or expiration of this Agreement. Without limiting the foregoing, the following Sections shall survive any such termination or expiration: Articles 1 (Definitions) and 14 (Indemnity); the license granted by Hansoh to Silence in Section 3.7; Sections 5.3 (Non-Exercise of the Option), 6.3 (Sublicenses) (solely to the extent any license grants under this Agreement survive such termination or expiration), 6.7 (Confirmatory Patent License) (solely to the extent any license grants under this Agreement survive such termination or expiration), and 7.4.11 (Records); Sections 10.1 (Royalty Payments and Reports), 10.2 (Mode of Payment), and 10.3 (Taxes) (to the extent either Party has any outstanding payment obligations as at the effective date of such termination or expiration); and Sections 10.4 (Financial Records), 10.5 (Audit), 10.6 (Confidentiality), 11.1.5 (Assignment Obligation), 12.1 (Confidentiality Obligations), 12.2 (Permitted Disclosures), 12.3 (Use of Name), 12.4 (Public Announcements), 12.6 (Return of Confidential Information), 13.6 (Disclaimer of Warranties), 15.1 (Term), 15.6 (Effects of Termination), 15.8 (Accrued Rights; Surviving Obligations), 16.5 (Severability), 16.6 (Governing Law), 16.7 (Dispute Resolution), 16.8 (Notices), 16.9 (Entire Agreement; Amendments), 16.10 (English Language), 16.11 (Waiver and Non-Exclusion of Remedies), 16.12 (No Benefit to Third Parties), 16.13 (Further Assurance); 16.14 (Relationship of the Parties), 16.15 (Joint and Several Liability), and 16.18 (Use of Affiliates).

ARTICLE 16
MISCELLANEOUS

16.1 **Force Majeure**. Neither Party shall be held liable or responsible to the other Party or be deemed to have defaulted under or breached this Agreement for failure or delay in fulfilling or performing any term of this Agreement solely to the extent, and for so long as, such failure or delay is caused by or results from events beyond the reasonable control of the non-performing Party, including fires, floods, earthquakes, hurricanes, embargoes, shortages, epidemics, quarantines, war, acts of war (whether war be declared or not), terrorist acts, insurrections, riots, civil commotion, strikes, lockouts, or other labor disturbances (whether involving the workforce of the non-performing Party or of any other Person), acts of God or acts, omissions or delays in acting by any governmental authority (except to the extent such delay results from the breach by the non-performing Party or any of its Affiliates of any term or condition of this Agreement). The non-performing Party shall notify the other Party of such force majeure within [***] ([***]) days after such occurrence by giving written notice to the other Party stating the nature of the event, its anticipated duration, and any action being taken to avoid or minimize its effect. The suspension of performance shall be of no greater scope and no longer duration than is necessary and the non-performing Party shall use commercially reasonable efforts to remedy its inability to perform. If any such event continues for more than [***] ([***]) days, then such other Party shall have the right to terminate this Agreement upon [***] ([***]) days prior written notice to the non-performing Party.

16.2 **Export Control**. Neither Party shall export, directly or indirectly, any technical information acquired from the other Party under this Agreement or any products using such technical information to a location or in a manner that at the time of export requires an export license or other governmental approval, without first obtaining the written

consent to do so from the appropriate agency or other governmental entity in accordance with Applicable Law.

16.3 **Assignment**. Except as expressly provided hereunder, neither this Agreement nor any rights or obligations hereunder may be assigned or otherwise transferred by either Party without the prior written consent of the other Party (which consent shall not be unreasonably withheld, conditioned, or delayed); provided, however, that either Party may assign or otherwise transfer this Agreement and its rights and obligations hereunder without the other Party's consent:

16.3.1 in connection with the transfer or sale of all or substantially all of the business or assets of such Party relating to this Agreement to a Third Party, whether by merger, consolidation, divesture, restructure, sale of stock, sale of assets, or otherwise; provided that in the event of any such transaction (whether this Agreement is actually assigned or is assumed by the acquiring Party by operation of law (e.g., in the context of a reverse triangular merger)), (a) the Know-How, Patents, and other intellectual property rights of the acquiring party to such transaction (if other than one of the Parties to this Agreement) shall not be included in the technology for which rights have been granted under this Agreement, and (b) notice is provided to the other Party; or

16.3.2 to an Affiliate.

The rights and obligations of the Parties under this Agreement shall be binding upon and inure to the benefit of the successors and permitted assigns of the Parties, and the name of a Party appearing herein will be deemed to include the name of such Party's successors and permitted assigns to the extent necessary to carry out the intent of this Section 16.3. Any assignment not in accordance with this Section 16.3 shall be null and void.

16.4 **Acquisition of Silence.** Notwithstanding any other provision of this Agreement, except as set forth in this Section 16.4, in the event of an Acquisition of Silence or a Holding Company of Silence, no intellectual property or other subject matter owned or controlled by the acquiring entity or any of its Affiliates prior to such Acquisition, or developed or acquired by such acquiring entity after such Acquisition (or by any Affiliate of the acquiring entity that was not an Affiliate of Silence prior to such Acquisition), shall be included as, Silence Background IP, Silence Research IP, or Silence China Product Development IP hereunder, so long as such intellectual property and other subject matter were developed independently of this Agreement and without access to or use of any Hansoh Confidential Information, the Silence Background IP, Silence Research IP, or Silence China Product Development IP or any Joint Research IP, and are not used by or on behalf of Silence or such acquiring entity or any of its Affiliates in connection with any efforts related to this Agreement.

In addition, in the event that any acquiring entity of Silence or a Holding Company of Silence, or any of its Affiliates, is conducting any research, development or commercialisation activities in respect of any Licensed Targets, or does so in the future (a "**Competing Program**") then Silence will establish and implement appropriate firewall procedures to segregate all activities (and the personnel conducting such activities) in such Competing Program from the activities performed by or on behalf of Silence pursuant to this Agreement, including ensuring that personnel involved in working in such Competing Program shall not have access to any Confidential Information of either Party with respect to activities under this Agreement, provided that such firewall procedures and obligation to segregate shall not extend to any accounts, financial or administrative personnel and that the directors of the applicable acquiring entity may receive general updates on progress and all financial information with respect to both the Competing Program and the activities performed under this Agreement.

Provided that Silence has complied with this obligation, Silence shall not be in breach of Section 4.1 by reason of such Acquisition or by reason of the acquiring entity or its Affiliates having, initiating or performing a Competing Program.

16.5 **Severability**. If, for any reason, any part of this Agreement is adjudicated invalid, unenforceable, or illegal by a court of competent jurisdiction, such adjudication shall not, to the extent feasible, affect or impair, in whole or in part, the validity, enforceability, or legality of any remaining portions of this Agreement. All remaining portions shall remain in full force and effect as if the original Agreement had been executed without the invalidated, unenforceable, or illegal part. In such event, the Parties shall negotiate promptly in good faith to replace such invalid, unenforceable, or illegal part with a valid, enforceable, and legal provision which most closely effectuates the Parties' original intent.

16.6 **Governing Law**. This Agreement or the performance, breach, or termination hereof shall be interpreted, governed by, and construed in accordance with the laws of the [***], excluding any conflicts or choice of law rule or principle that might otherwise refer construction or interpretation of this Agreement to the substantive law of another jurisdiction; provided, that all questions concerning (a) inventorship of Patents under this Agreement shall be determined in accordance with Section 11.1.1 and (b) the construction or effect of Patents shall be determined in accordance with the laws of the country or other jurisdiction in which the particular Patent has been filed or granted, as the case may be, and the Parties consent to the exclusive jurisdiction of the courts of such country or jurisdiction. The Parties agree to exclude the application to this Agreement of the United Nations Convention on Contracts for the International Sale of Goods.

16.7 **Dispute Resolution**. Except for disputes resolved by the procedures set forth in Section 2.7.2, if a dispute arises between the Parties in connection with or relating to this

Agreement or any document or instrument delivered in connection herewith (a "**Dispute**"), it shall be resolved pursuant to this Section 16.7.

16.7.1 **General**. Any Dispute shall first be referred to the Senior Officers of the Parties, who shall confer in good faith on the resolution of the issue. Any final decision mutually agreed to by the Senior Officers shall be conclusive and binding on the Parties. If the Senior Officers are not able to agree on the resolution of any such issue within [***] ([***]) days (or such other period of time as mutually agreed by the Senior Officers) after such issue was first referred to them, then, except as otherwise set forth in Section 16.7.2, if a Party wishes to pursue further resolution of such Dispute, such Dispute shall be referred to and finally resolved by arbitration pursuant to the procedures set forth in Section 16.7.3 for purposes of having the matter finally settled.

16.7.2 Intellectual Property Disputes. In the event that a Dispute arises with respect to the validity, scope, enforceability, or inventorship of any Patent, trademark or other intellectual property rights, and such Dispute cannot be resolved in accordance with Section 16.7.1, unless otherwise agreed by the Parties in writing, such Dispute shall not be submitted to arbitration in accordance with Section 16.7.3 and instead, either Party may initiate litigation in a court of competent jurisdiction, notwithstanding Section 16.6, in any country or other jurisdiction in which such intellectual property rights apply.

16.7.3 Arbitration. If the Parties mutually agree to resolve a dispute by binding arbitration, then the Parties shall submit such dispute for resolution by binding arbitration before a tribunal of three (3) arbitrators in accordance with the Arbitration Rules of the [***], as then in effect. The seat, or legal place, of the arbitration shall be [***]. Each Party shall nominate one arbitrator and

the third arbitrator shall be nominated by the two Party-nominated arbitrators within [***] ([***]) days after the second arbitrator's appointment. If a Party does not nominate its arbitrator within [***] ([***]) days following the expiry of the allotted period, then such arbitrator shall be appointed by the [***] in accordance with its rules. Any arbitrator appointed by the [***] shall have substantial experience in the pharmaceutical industry. The arbitration shall be conducted, and all documents submitted to the arbitrators shall be, in English. Each Party shall bear its own legal costs for its counsel and other expenses, and the Parties shall equally share the fees of the arbitration; provided that the arbitrators shall have the discretion to provide that the losing Party is responsible for all or a portion of such costs and fees and in such case the arbitral award will so provide. The arbitrators shall have no power to award punitive, special, incidental, or consequential damages. In no event shall the arbitrators assign a value to any issue greater than the greatest value for such issue claimed by either Party or less than the smallest value for such issue for such item claimed by either Party. The award shall be final and binding upon the Parties and the Parties undertake to carry out any award without delay. Judgment on the award rendered by arbitration may be entered in any court of competent jurisdiction. Except to the extent necessary to confirm, enforce, or challenge an award of the arbitration, to protect or pursue a legal right, or as otherwise required by Applicable Law or regulation or securities exchange, neither Party nor any arbitrator may disclose the existence, content, or results of any arbitration hereunder without the prior written consent of both Parties. Notwithstanding anything to the contrary in the foregoing, in no event shall an arbitration be initiated after the date when commencement of a legal or equitable proceeding based on the dispute, controversy, or claim would be barred by the applicable New York statute of

limitations. Any disputes concerning the propriety of the commencement of the arbitration shall be finally settled by the arbitral tribunal.

16.7.4 **Interim Relief**. Notwithstanding anything herein to the contrary, nothing in this Section 16.7 shall preclude either Party from seeking interim or provisional relief, including a temporary restraining order, preliminary injunction, or other interim equitable relief concerning a Dispute following the arbitration procedures set forth in Section 16.7.3, if necessary to protect the interests of such Party. This Section shall be specifically enforceable.

16.8 **Notices**. Any notice or other communication required under this Agreement shall be in writing, shall be in the English language, shall refer specifically to this Agreement, and shall be deemed given only if (a) delivered by hand or (b) sent by internationally recognized overnight delivery service addressed to the Parties at their respective addresses specified below or to such other address as a Party may specify in accordance with this Section 16.8 and, in either case, an email copy of such notice or other communication is also provided. Such notice shall be deemed to have been given as of the date delivered by hand or on the [***] Business Day (at the place of delivery) after deposit with an internationally recognized overnight delivery service. This Section 16.8 is not intended to govern the day-to-day business communications necessary between the Parties in performing their obligations under the terms of this Agreement.

If to Hansoh, to:

Hansoh Bio LLC
9900 Medical Center Dr, Ste 200
Rockville, MD 20850
Attention: [***]
Email: [***]; [***]

If to Silence, to:

Silence Therapeutics Plc
72 Hammersmith Road
London W14 8TH
United Kingdom
Attention: [***]

With a copy to:

[***];

[***]; and

[***]

16.9 **Entire Agreement; Amendments**. This Agreement, together with the Schedules attached hereto, sets forth and constitutes the entire agreement and understanding between the Parties with respect to the subject matter hereof and all prior agreements, understandings, promises, and representations, whether written or oral, with respect thereto are superseded hereby ([***]). Each Party confirms that it is not relying on any representations or warranties of the other Party except as specifically set forth in this Agreement. No amendment, modification, release, or discharge shall be binding upon the Parties unless in writing and duly executed by authorized representatives of both Parties.

16.10 **English Language**. This Agreement has been written and executed in, and all notices and reports required or permitted to be given hereunder, and all written, electronic, oral or other communications between the Parties under or in connection with this Agreement shall be in, the English language, and the English language will control the interpretation of this Agreement. Any translation into any other language shall not be an official version thereof, and in the event of any conflict in interpretation between the English version and such translation, the English version shall control.

16.11 **Waiver and Non-Exclusion of Remedies**. Any term or condition of this Agreement may be waived at any time by the Party that is entitled to the benefit thereof, but no such waiver shall be effective unless set forth in a written instrument duly executed by the Party waiving such term or condition. The waiver by either Party of any right or of the failure to perform or of a breach by the other Party shall not be deemed a waiver of any other right or of any other breach or failure by such other Party whether of a similar nature or otherwise. The rights and remedies provided herein are cumulative and do not exclude any other right or remedy provided by Applicable Law or otherwise available except as expressly set forth herein.

16.12 **No Benefit to Third Parties**. Except as provided in ARTICLE 14, covenants and agreements set forth in this Agreement are for the sole benefit of the Parties hereto and their successors and permitted assigns, and they shall not be construed as conferring any rights on any other Persons.

16.13 **Further Assurance**. Each Party shall duly execute and deliver, or cause to be duly executed and delivered, such further instruments and do and cause to be done such further acts and things, including the filing of such assignments, agreements, documents, and instruments, as may be necessary or as the other Party may reasonably request in connection with this Agreement or to carry out more effectively the provisions and

purposes hereof, or to better assure and confirm unto such other Party its rights and remedies under this Agreement.

16.14 **Relationship of the Parties**. Silence and Hansoh are independent contractors and the relationship between the Parties shall not constitute a partnership, joint venture, or agency, including for tax purposes. Neither Party shall have the authority to make any statements, representations, or commitments of any kind, or to take any action, which shall be binding on the other Party, without the prior written consent of such other Party. All persons employed by a Party shall be employees of such Party and not of the other Party and all costs and obligations incurred by reason of any such employment shall be for the account and expense of such Party.

16.15 **Joint and Several Liability.** Each of the Hansoh Parties shall be jointly and severally responsible for all of the Hansoh obligations under this Agreement. In the event that there is a breach of any of the Hansoh obligations under this Agreement, Silence shall have no obligation ascertain or enquire as to which of the Hansoh Parties is in breach and shall be entitled to enforce this Agreement against one or both Hansoh Parties without reference to which Hansoh Party is in breach and each Hansoh Party shall be fully liable for any breach of this Agreement by itself and/or the other Hansoh Party.

16.16 **No Obligation to Disclose**. Notwithstanding anything to the contrary contained herein, nothing in this Agreement will require a Party (the "**Restricted Party**") to provide the other Party with access to Information the disclosure of which, in the Restricted Party's reasonable good faith opinion (a) would conflict with confidentiality obligations to which such Restricted Party or any of its Affiliates is bound, (b) would reasonably be expected to result in the forfeiture or waiver of any attorney-client or similar privilege, or (c) would violate Applicable Law, provided that, in the case of each of clause (a), (b) and (c), the Restricted Party will use Commercially Reasonable Efforts to provide the other Party, to

the extent possible, with access to the relevant Information in a manner that would not reasonably be expected to conflict with confidentiality obligations, result in the forfeiture or waiver of any such attorney-client or similar privilege, or violate Applicable Law. In the event that a Party relies upon this Section 16.16 in not providing the other Party with any Information requested, such Restricted Party shall be required to promptly notify the other Party that it has determined to not provide Information pursuant to this Section 16.16.

16.17 **Counterparts; Facsimile Execution**. This Agreement may be executed in two (2) or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one (1) and the same instrument. This Agreement may be executed by facsimile or electronically transmitted signatures and such signatures shall be deemed to bind each party hereto as if they were original signatures.

16.18 **Use of Affiliates.** Each Party acknowledges and agrees that any Affiliates of a Party may exercise any of the rights granted to such Party in this Agreement or perform any of such Party's obligations in this Agreement *provided* that such Party shall be responsible for the performance of any of its obligations that are performed by its Affiliates.

{SIGNATURE PAGE FOLLOWS}

THIS RESEARCH COLLABORATION, OPTION AND LICENSE AGREEMENT IS EXECUTED by the authorized representatives of the Parties as of the Effective Date.

SILENCE THERAPEUTICS PLC

By: /s/ Mark Rothera

Name: Mark Rothera

Title: CEO

HANSOH (SHANGHAI) HEALTHTECH CO., LTD.

By: /s/ Yuan Sun

Name: Yuan Sun

Title: Authorized Representative

JIANGSU HANSOH PHARMACEUTICAL GROUP COMPANY LIMITED

By: /s/ Yuan Sun

Name: Yuan Sun

Title: Authorized Representative

Schedule 1.68

Joint Development Plan Template

Phase	Study design	Countries	Start Month	Duration (months)	End Month	Responsibility
[***]	[***]	[***]				[***]
[***]	[***]	[***]				[***]
[***]	[***]	[***]				[***]
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Schedule 1.78

Licensed Targets

Section 1. China Licensed Targets

[***]

[***]

Section 2. Global Licensed Target

[***]

[***]

Schedule 1.95

Preliminary Targets

[***]

[***]

[***]

Schedule 1.105

Research Plan Template

Function	Activity	Start Month	Duration (months)	End Month	Direct Cost (USD 000's)	Total FTE Resource *
[***]	[***]	[***]	[***]	[***]		[***]
[***]	[***]	[***]	[***]	[***]		[***]
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Function	Activity	Start Month	Duration (months)	End Month	Direct Cost (USD 000's)	Total FTE Resource *
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Function	Activity	Start Month	Duration (months)	End Month	Direct Cost (USD 000's)	Total FTE Resource *
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Function	Activity	Start Month	Duration (months)	End Month	Direct Cost (USD 000's)	Total FTE Resource *
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Function	Activity	Start Month	Duration (months)	End Month	Direct Cost (USD 000's)	Total FTE Resource *
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Function	Activity	Start Month	Duration (months)	End Month	Direct Cost (USD 000's)	Total FTE Resource *
[***]	[***]	[***]				

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** [***].

Schedule 12.4

Form of Press Release.

1. SILENCE PRESS RELEASE

Silence Therapeutics and Hansoh Pharma Announce Collaboration to Develop Therapeutics Leveraging Silence's mRNAi GOLD™ Platform

Hansoh will make a $16 million upfront cash payment and Silence has the potential to receive up to $1.3 billion in milestones

Silence gains exclusive rights to two targets in all territories except the China region; Hansoh has rights to those two targets in the China region and global rights to a third target

15 October 2021

LONDON and SHANGHAI, Silence Therapeutics plc (AIM: SLN and Nasdaq: SLN), a leader in the discovery, development and delivery of novel short interfering ribonucleic acid (siRNA) therapeutics for the treatment of diseases with significant unmet medical need, and Hansoh Pharmaceutical Group Company Limited ("Hansoh Pharma", 3692.HK), one of the leading biopharmaceutical companies in China, today announced a collaboration to develop siRNAs for three undisclosed targets leveraging Silence's proprietary mRNAi GOLD™ platform.

Under the terms of the agreement, Hansoh will have the exclusive option to license rights to the first two targets in Greater China, Hong Kong, Macau and Taiwan following the completion of phase 1 studies. Silence will retain exclusive rights for those two targets in all other territories. Silence will be responsible for all activities up to option exercise and will retain responsibility for development outside the China region post phase 1 studies.

Hansoh will also have the exclusive option to license global rights to a third target at the point of IND filing. Hansoh will be responsible for all development activities post option exercise for the third target.

Hansoh will make a $16 million upfront payment and Silence is eligible to receive up to $1.3 billion in additional development, regulatory and commercial milestones. Silence will also receive royalties tiered from low double-digit to mid-teens on Hansoh net product sales.

Mark Rothera, President and Chief Executive Officer of Silence Therapeutics, said: "We believe Hansoh's extensive clinical development and commercialization experience in China make them an ideal partner. This collaboration is a good example of our hybrid model in action, balancing proprietary and partnered programs to maximize the substantial opportunity of our mRNAi GOLD™ platform for targeting disease associated genes in the liver. The Hansoh partnership enables us to move two new proprietary programs forward subsidized by non-dilutive capital while also gaining access to the second largest pharmaceutical market globally. We look forward to discussing this deal and our broader pipeline in more detail at our upcoming R&D Day on October 21st in New York City."

Eliza Sun, Executive Director of the Board of Hansoh Pharma, said: "We are excited to partner with Silence, a pioneer in siRNA therapeutic development with decades of scientific and technical experience. As one of the largest biopharma in China, Hansoh strives to partner with innovative companies globally to build out and advance our robust pipeline spanning across multiple therapeutic areas. We see substantial opportunity in Silence's mRNAi GOLD™ platform to develop and bring better precision-based medicines to patients across China and worldwide."

Enquiries:

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ir@silence-therapeutics.com

Investec Bank plc (Nominated Adviser and Broker) Tel: +44 (0) 20 7597 5970
Daniel Adams/Gary Clarence

European PR Tel: +44 (0) 20 3709 5700
Consilium Strategic Communications
Mary-Jane Elliott/Chris Welsh/Angela Gray
silencetherapeutics@consilium-comms.com

Hansoh Pharma
Dr. Sophia Dong, Director of Investor Relations
IR@hspharm.com

About Hansoh Pharma

Hansoh Pharma (3692.HK), one of the largest biopharmaceutical companies in Greater China and in Asia, is committed to discovering and developing life-changing medicines to help patients conquer serious diseases and disorders. Hansoh Pharma is supported by over 12,000 dedicated employees in China and the United States. Founded in 1995, Hansoh has fully integrated research and development, manufacturing, and commercial capabilities, supporting leading positions across a broad range of therapeutic areas, including oncology, central nervous system (CNS) disorders, infectious diseases, cardiovascular disease, diabetes, and autoimmune diseases. With the support of over 1,600 highly skilled R&D professionals, Hansoh has successfully developed multiple internally discovered drug candidates into NMPA-approved innovative medicines, including aumolertinib (阿 美乐®), a third-generation EGFR inhibitor for the treatment of NSCLC with EGFR mutations, flumatinib (昕福®), a second-generation BCR-ABL inhibitor for frontline treatment of chronic myeloid leukemia (CML), PEG-loxenatide (孚来 美®), the first once-weekly long-acting GLP-1 analogue discovered and developed in China for the treatment of diabetes, morinidazole (迈灵达®), a third-generation nitroimidazole antibiotic and tenofovir amibufenamide (恒 沐®), the first second-generation oral anti-HBV drug developed in China. For more information, please visit www.hspharm.com.

About Silence Therapeutics

Silence Therapeutics is developing a new generation of medicines by harnessing the body's natural mechanism of RNA interference, or RNAi, to inhibit the expression of specific target genes thought to play a role in the pathology of diseases with significant unmet need. Silence's proprietary mRNAi GOLD™ platform can be used to create siRNAs (short interfering RNAs) that precisely target and silence disease-associated genes in the liver, which represents a substantial opportunity. Silence's wholly owned product candidates include SLN360 designed to address the high and prevalent unmet medical need in reducing cardiovascular risk in people born with high levels of lipoprotein(a) and SLN124 designed to address iron-loading anemia conditions. Silence also maintains ongoing research and development collaborations with AstraZeneca, Mallinckrodt Pharmaceuticals, and Takeda, among others. For more information, please visit https://www.silence-therapeutics.com/.

Forward-Looking Statements

Certain statements made in this announcement are forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995 and other securities laws, including with respect to the Company’s clinical and commercial prospects and the anticipated timing of data reports from the Company’s clinical trials. These forward-looking statements are not historical facts but rather are based on the Company's current expectations, estimates, and projections about its industry; its beliefs; and assumptions. Words such as 'anticipates,' 'expects,' 'intends,' 'plans,' 'believes,' 'seeks,' 'estimates,' and similar expressions are intended to identify forward-looking statements. These statements are not guarantees of future performance and are

subject to known and unknown risks, uncertainties, and other factors, some of which are beyond the Company's control, are difficult to predict, and could cause actual results to differ materially from those expressed or forecasted in the forward-looking statements, including those risks identified in the Company's most recent Admission Document and its amended Annual Report on Form 20-F filed with the U.S. Securities and Exchange Commission on April 29, 2021. The Company cautions security holders and prospective security holders not to place undue reliance on these forward-looking statements, which reflect the view of the Company only as of the date of this announcement. The forward-looking statements made in this announcement relate only to events as of the date on which the statements are made. The Company will not undertake any obligation to release publicly any revisions or updates to these forward-looking statements to reflect events, circumstances, or unanticipated events occurring after the date of this announcement except as required by law or by any appropriate regulatory authority.

2. HANSOH PRESS RELEASE

Hansoh Pharma and Silence Therapeutics Announce Collaboration to Develop Therapeutics Leveraging Silence's mRNAi GOLD™ Platform

Hansoh will make a $16 million upfront cash payment and Silence has the potential to receive up to $1.3 billion in milestones

Hansoh has rights to two targets in the China region and global rights to a third target;

Silence gains exclusive rights to those two targets in all territories except the China region

15 October 2021

SHANGHAI and LONDON, Hansoh Pharmaceutical Group Company Limited ("Hansoh Pharma", 3692.HK), one of the leading biopharmaceutical companies in China and Silence Therapeutics plc (AIM:SLN and Nasdaq: SLN), a leader in the discovery, development and delivery of novel short interfering ribonucleic acid (siRNA) therapeutics for the treatment of diseases with significant unmet medical need, today announced a collaboration to develop siRNAs for three undisclosed targets leveraging Silence's proprietary mRNAi GOLD™ platform.

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a broad range of therapeutic areas, including oncology, central nervous system (CNS) disorders, infectious diseases, cardiovascular disease, diabetes, and autoimmune diseases. With the support of over 1,600 highly skilled R&D professionals, Hansoh has successfully developed multiple internally discovered drug candidates into NMPA-approved innovative medicines, including aumolertinib (阿 美乐®), a third-generation EGFR inhibitor for the treatment of NSCLC with EGFR mutations, flumatinib (昕福®), a second-generation BCR-ABL inhibitor for frontline treatment of chronic myeloid leukemia (CML), PEG-loxenatide (孚来 美®), the first once-weekly long-acting GLP-1 analogue discovered and developed in China for the treatment of diabetes, morinidazole (迈灵达®), a third-generation nitroimidazole antibiotic and tenofovir amibufenamide (恒 沐®), the first second-generation oral anti-HBV drug developed in China. For more information, please visit www.hspharm.com.

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Company cautions security holders and prospective security holders not to place undue reliance on these forward-looking statements, which reflect the view of the Company only as of the date of this announcement. The forward-looking statements made in this announcement relate only to events as of the date on which the statements are made. The Company will not undertake any obligation to release publicly any revisions or updates to these forward-looking statements to reflect events, circumstances, or unanticipated events occurring after the date of this announcement except as required by law or by any appropriate regulatory authority.

翰森制药和Silence Therapeutics宣布利用Silence mRNAi GOLD™ 平台合作开发治疗药物

翰森制药将现金支付1,600万美元首付款，Silence有望收到最高超过13亿美元潜在里程碑付款

翰森制药在中国地区拥有这两个靶点的权利和第三个靶点的全球权利;

Silence在除中国地区以外的所有地区获得两个靶点的排他权益

10月 15 2021

上海及伦敦，翰森制药集团有限公司（翰森制药,3692.HK），中国顶尖的生物制药企业，Silence Therapeutics (AIM: SLN及Nasdaq: SLN), siRNA治疗领域的领先的创新企业，致力于发现、开发和提供新型短干扰核糖核酸(siRNA)疗法，用于治疗具有显著未满足医疗需求的疾病，今日宣布利用Silence独有的mRNAi GOLD™平台合作开发针对3个未披露靶点的siRNA药物。

根据协议条款，在完成1期临床研究后，翰森制药将拥有两个靶点在中国的独家许可权。Silence将保留这两个靶点在所有其他地区的权益。Silence将负责执行期权之前的所有开发活动，并将保留在1期临床研究结束后中国地区以外的开发责任。

翰森制药还将在第三个靶点提交IND时拥有全球独家权益，并将负责第三个靶点期权行使后的所有开发活动。

翰森制药将支付1,600万美元首付款，Silence有望收到包含研发、注册及商业化里程碑在内的最高超过13亿美元潜在里程碑付款。Silence还将获得基于产品净销售额的低双位数至中位百分之十几的销售提成。

翰森制药集团执行董事孙远女士表示: “我们很高兴与Silence合作，Silence 是siRNA治疗领域的研发先驱，拥有数十年的科学和技术经验。作为中国最大的制药企业之一，翰森制药努力与全球创新公司合作，以建立和推进我们跨越多个治疗领域的强大研发管线。我们认为Silence的mRNAi GOLD™ 平台中有非常大的潜力，可以为中国和全球患者开发和提供更好的精准治疗药物。”

Silence Therapeutics总裁兼首席执行官Mark Rothera表示: “翰森制药在中国有丰富的临床开发和商业化经验，我们相信会是我们理想的合作伙伴。此次合作是我们多元化合作模式的范例，可以很好地平衡独立研发和合作项目，最大限度地利用我们mRNAi GOLD™ 平台，针对肝脏疾病相关基因靶向开发药物。与翰森制药的合作使我们能够推进两个新的非稀释资本补贴的专有项目，同时还可以进入全球第二大医药市场。我们期待在即将于10月21日在纽约市举行的研发开放日更详细地讨论这笔交易和我们丰富的研发管线布局。”

联系方式:

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关于翰森制药集团
翰森制药(3692.HK)，中国及亚洲最大的制药公司之一, 致力于发现和开发提升生命质量的药物，以帮助患者克服严重的疾病和障碍。翰森制药目前在中国及美国拥有超过12,000名员工。翰森制药成立于1995年，翰森制药拥有药物研发、制造和商业化能力，在多个治疗领域中处于领先地位，包括抗肿瘤、中枢神经系统（CNS）、抗感染、心血管疾病、糖尿病及自身免疫疾病等。翰森制药拥有超过1,600名专业研发人员，已经在中国成功上市了5个自主研发的创新药,包括**阿美乐®**，用于EGFR突变的NSCLC治疗的三代EGFR抑制剂；**昕福®**，用于一线慢性粒细胞白血病（CML）治疗的二代BCR-ABL抑制剂；**孚来美®**，用于糖尿病治疗的首款获批上市的国产长效GLP-1周制剂；**迈灵达®**，三代硝基咪唑类抗生素；**恒沐®，**首个中国原研的二代口服抗乙肝病毒（HBV）药物。

更多信息详见：www.hspharm.com

关于Silence Therapeutics
Silence Therapeutics通过利用人体天然的RNA干扰或RNAi机制来抑制特定靶基因的表达，开发新一代药物。这些靶基因在多种疾病的病理学中发挥作用，具有显著未满足的临床需求。Silence专有的mRNAi GOLD™ 平台可用于创建siRNA（短干扰RNA），以精确靶向和沉默肝脏中的相关疾病基因，具有非常大的潜力。Silence的候选药物包括SLN360，旨在解决脂蛋白(a)高表达，降低出生时伴随脂蛋白(a)高表达人群的心血管病风险，具有广泛的未被满足的医疗需求；SLN124旨在解决铁负荷性贫血。Silence还拥有多项在研项目并与阿斯利康、Mallinckrodt Pharmaceuticals和武田等多家企业有研发合作。

更多信息详见：https://www.silence-therapeutics.com/.

Exhibit 12.1

CERTIFICATION REQUIRED BY RULE 13A-14(A) OR 15D-14(A)
UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO
SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Craig Tooman, certify that:

1. I have reviewed this annual report on Form 20-F of Silence Therapeutics 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 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 15, 2023
By: /s/ Craig Tooman
Craig Tooman
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 12.2

CERTIFICATION REQUIRED BY RULE 13A-14(A) OR 15D-14(A)
UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO
SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Rhonda Hellums, certify that:

1. I have reviewed this annual report on Form 20-F of Silence Therapeutics 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 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 15, 2023
By: /s/ Rhonda Hellums
Rhonda Hellums
Chief Financial Officer
(Principal Financial Officer)

Exhibit 13.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

I, Craig Tooman, President and Chief Executive Officer of Silence Therapeutics plc (the "Company"), hereby certify, pursuant to 18 U.S.C. §1350, as adopted pursuant to §906 of the Sarbanes-Oxley Act of 2002, that, to the best of my knowledge:

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

2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 15, 2023

/s/ Craig Tooman
Craig Tooman
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 13.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

I, Rhonda Hellums, Chief Financial Officer of Silence Therapeutics plc (the "Company"), hereby certify, pursuant to 18 U.S.C. §1350, as adopted pursuant to §906 of the Sarbanes-Oxley Act of 2002, that, to the best of my knowledge:

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

2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 15, 2023

/s/ Rhonda Hellums
Rhonda Hellums
Chief Financial Officer
(Principal Financial Officer)

Exhibit 15.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Form F-3 (No. 333-260265) and Form S-8 (No. 333-248682) of Silence Therapeutics plc of our report dated March 15, 2023 relating to the financial statements, which appears in this Form 20-F.

/s/ PricewaterhouseCoopers LLP

Reading, United Kingdom

March 15, 2023