

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549
FORM 10-K**

(Mark One)

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

For the fiscal year ended December 31, 2025

or

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

For the transition period from _____ to _____

Commission File Number 001-39487

Silence Therapeutics plc

(Exact name of registrant as specified in its charter)

England and Wales

(State or other jurisdiction of incorporation or organization)

Not Applicable

(I.R.S. Employer Identification No.)

12 Hammersmith Grove

London, United Kingdom

(Address of principal executive offices)

W6 7AP

(Zip code)

Tel: +44 20 3457 6900

(Registrant's telephone number, including area code)

Securities 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 three ordinary shares, nominal value £0.05 per share	SLN	The Nasdaq Stock Market LLC
Ordinary share, nominal value £0.05 per share*	*	The Nasdaq Stock Market LLC*

**Not for trading, but only in connection with the listing of the American Depositary Shares on The Nasdaq Stock Market LLC.*

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

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

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. 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, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer

Accelerated filer

Non-accelerated filer

Smaller reporting company

Emerging growth company

If an emerging growth company, 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.

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 whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes No

The aggregate market value of the ordinary shares held by non-affiliates of the registrant, based upon \$5.80, the closing price of the registrant's American Depositary Shares on the Nasdaq Global Market on June 30, 2025 (the last business day of the registrant's most recently completed second fiscal quarter) was approximately \$206.2 million.

As of January 31, 2026, the registrant had 141,701,848 ordinary shares (including ordinary shares in the form of American Depositary Shares) outstanding, nominal value £0.05 per share.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's proxy statement to be filed with the Securities and Exchange Commission pursuant to Regulation 14A in connection with the registrant's 2026 Annual General Meeting of Shareholders are incorporated by reference into Part III of this Annual Report on Form 10-K. Such proxy statement will be filed with the Securities and Exchange Commission not later than 120 days following the end of the registrant's fiscal year ended December 31, 2025.

TABLE OF CONTENTS

PART I	4
Item 1. Business.....	4
Item 1A. Risk Factors.....	34
Item 1B. Unresolved Staff Comments.....	73
Item 1C. Cybersecurity.....	73
Item 2. Properties.....	74
Item 3. Legal Proceedings.....	74
Item 4. Mine Safety Disclosures.....	74
PART II	75
Item 5. Market for Registrant’s Common Equity, Related Stockholder Matters, and Issuer Purchases of Equity Securities.....	75
Item 6. Reserved.....	75
Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations.....	76
Item 7A. Quantitative and Qualitative Disclosures About Market Risk.....	90
Item 8. Financial Statements and Supplementary Data.....	90
Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure.....	90
Item 9A. Controls and Procedures.....	90
Item 9B. Other Information.....	91
Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections.....	91
PART III	92
Item 10. Directors, Executive Officers and Corporate Governance.....	92
Item 11. Executive Compensation.....	92
Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.....	92
Item 13. Certain Relationships and Related Transactions, and Director Independence.....	92
Item 14. Principal Accountant Fees and Services.....	92
PART IV	93
Item 15. Exhibits and Financial Statement Schedules.....	93
Item 16. Form 10-K Summary.....	95

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, or the 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, but are not limited to, 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 future anticipated milestone payments from our existing collaborations will be sufficient to fund our operating expenses and capital expenditure requirements into 2028; and
- regulatory developments in the United States, United Kingdom, European Union, or EU, and other jurisdictions.

You should refer to the section titled “Risk Factors” in Part I, Item 1A. of this Annual Report 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, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this Annual Report.

GENERAL INFORMATION

Unless context otherwise requires, all references in this Annual Report on Form 10-K, or Annual Report, to “Silence,” “Silence Therapeutics,” “Silence Therapeutics plc,” “the Company,” “we,” “us” and “our” refer to Silence Therapeutics plc and, where appropriate, its consolidated subsidiaries.

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 Annual 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.

RISK FACTORS SUMMARY

Our business is subject to a number of risks and uncertainties. If any of the following risks are realized, our business, financial condition and results of operations could be materially and adversely affected. You should carefully review and consider the full discussion of our risk factors in the section titled “Risk Factors” in Part I, Item 1A. of this Annual Report. Set forth below is a summary list of the principal risk factors as of the date of the filing this Annual Report:

- We have a history of net losses, and we anticipate that we will continue to incur significant losses for the foreseeable future.
- We have never generated any revenue from product sales and may never be profitable.
- We will require additional financial resources to continue the 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.
- Raising additional capital may cause dilution to our holders, including holders of our American Depositary Shares representing our ordinary shares, or ADSs, restrict our operations or require us to relinquish rights to our technologies or product candidates.
- The approach we are taking to discover and develop drugs is novel and may never lead to marketable 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.
- 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.
- 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.
- 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.
- 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 face potential product liability and other claims, and, if successful claims are brought against us, we may incur substantial liability and costs.

- Cybersecurity risks and the failure to maintain the confidentiality, integrity, and availability of our computer hardware, software, data and internet applications and related tools and functions, or those of third parties with whom we work, could result in damage to our reputation and/or subject us to costs, fines or lawsuits.
- We and the third parties with whom we work are subject to stringent and evolving U.S. and foreign data privacy and security laws, regulations contractual obligations, industry standards, policies, and other obligations, and our (or the third parties with whom we work) actual or perceived failure to comply with such obligations could lead to regulatory investigations or actions; litigation (including class actions); fines and penalties; disruptions of our business operations; reputational harm; loss of revenue or profits; and other adverse business consequences.
- 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 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.
- We have incurred and will continue to incur increased costs as a result of operating as a public company, and our management has devoted and will continue to be required to devote substantial time to new compliance initiatives and corporate governance practices.
- The trading price of our ADSs may be volatile, and you could lose all or part of your investment.
- Future sales, or the possibility of future sales, of a substantial number of our ADSs could adversely affect the price of such securities.
- We may identify material weaknesses in our internal control over financial reporting. If we experience material weaknesses or significant 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.
- Holders of our ADSs have fewer rights than our shareholders and must act through the depositary to exercise their rights.
- 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.
- Claims of U.S. civil liabilities may not be enforceable against us.
- 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.

PART I

Item 1. 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 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™ (GalNAc Oligonucleotide Discovery) platform consists of siRNA product candidates designed to precisely target and 'silence' specific disease-associated genes in the liver. Using our mRNAi GOLD platform, we have generated siRNA product candidates targeting areas of high unmet need across rare and common diseases where treatments are limited or inadequate.

Rare Diseases

Divesiran (SLN124) is our potential first-in-class siRNA in Phase 2 development for polycythemia vera, or PV. PV is a rare myeloproliferative neoplasm characterized by the overproduction of red blood cells, or RBCs. Elevated hematocrit, or HCT, - an index of RBC mass - is a hallmark of the disease and HCT levels above 45% increases the risk of thrombotic and cardiovascular events. Divesiran works by "silencing" the TMPRSS6 gene, lifting the natural brake on hepcidin - the body's master iron regulator. When TMPRSS6 is turned down in people living with PV, hepcidin levels rise, reducing iron availability to the bone marrow. With less iron available, the overproduction of RBCs seen in PV is reduced. This helps keep HCT levels in a safer range and can reduce or eliminate the need for phlebotomies. Additionally, siRNA therapies have a highly potent and durable effect - enabling less frequent and more convenient dosing. In the Phase 1 part of the SANRECO clinical trial evaluating divesiran treatment in 21 PV patients, divesiran produced durable HCT control and substantially reduced phlebotomy use following infrequent dosing (Q6W). Based on the strong durability observed in the Phase 1 trial, the ongoing Phase 2 part of the SANRECO trial is evaluating both a Q6W and Q12W dosing interval. The SANRECO Phase 2 trial is fully enrolled, and topline results are anticipated in the third quarter of 2026. The U.S. Food and Drug Administration, or FDA, has granted divesiran Fast Track and orphan drug designations for PV. Divesiran has also been granted orphan drug designation by the European Commission for PV in Europe. While our initial focus is on PV, divesiran has shown the potential in preclinical studies to address multiple hematological conditions through the unifying mechanism of elevating hepcidin in conditions with dysregulation of iron homeostasis.

SLN548 is our Phase 1 ready siRNA product candidate that works by "silencing" the complement factor B, or CFB, gene, potentially playing a therapeutic role in conditions associated with over activation of this pathway, including complement-mediated renal diseases, among others. SLN548 has demonstrated positive preclinical results and we are seeking a third-party partner to initiate clinical development.

Cardiometabolic Diseases

Zerlasiran (SLN360) is our Phase 3 ready siRNA product candidate for cardiovascular disease that works by "silencing" the LPA gene, lowering production of apolipoprotein(a), a key component of lipoprotein(a), or Lp(a), that has been associated with an increased risk of cardiovascular events. High Lp(a), defined as 125nmol/L or higher, is a genetically determined cardiovascular risk factor affecting at least 20% of the world's population and is associated with a high risk of heart attack, stroke and aortic stenosis. Unlike low-density lipoprotein, or LDL, Lp(a) levels are predominantly genetically determined, typically by age five, and unaffected by diet or lifestyle. There are currently no approved medicines that selectively lower Lp(a). Guidelines from the European Atherosclerosis Society, or EAS, Canadian Cardiovascular Society, or CCS, and the National Lipid Association, or NLA, suggest at least one test in an adult lifetime. The American College of Cardiology, or ACC, and American Heart Association, or AHA, recommend testing for those with a family history of premature atherosclerotic cardiovascular disease, or ASCVD, or personal history of ASCVD. In Phase 1 and Phase 2 clinical trials, zerlasiran showed the potential to

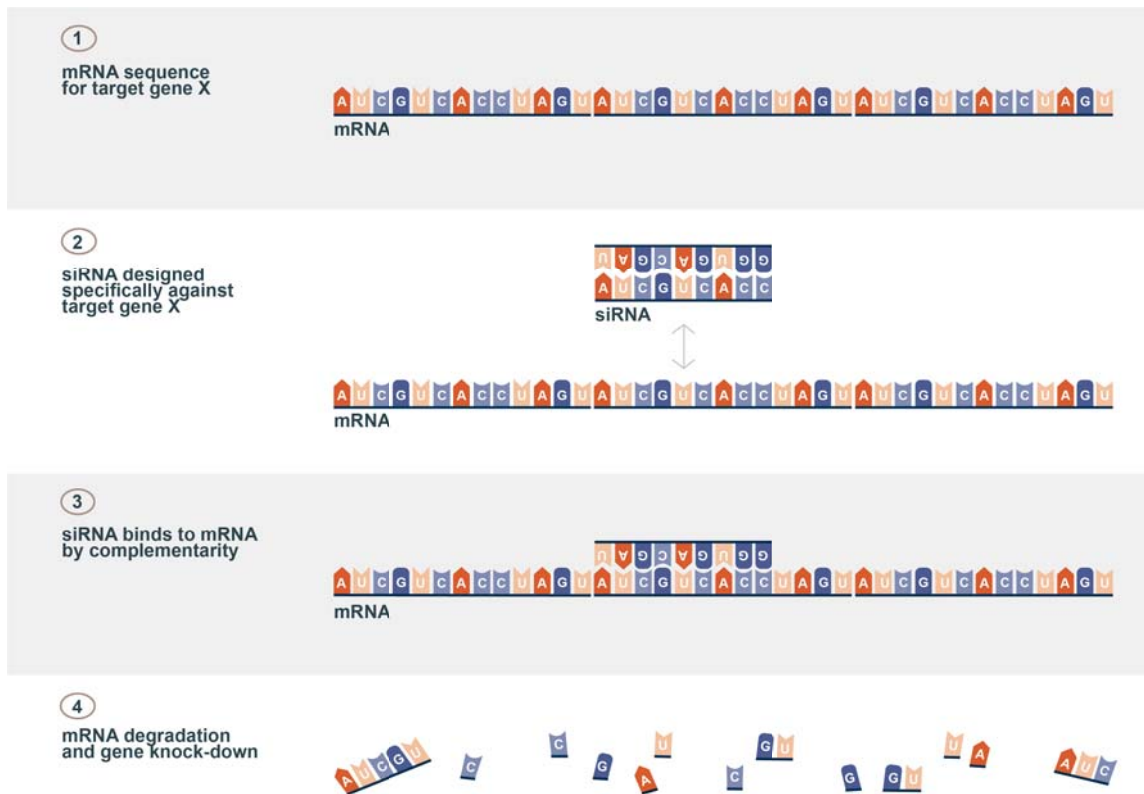
substantially lower Lp(a) levels in ASCVD patients with persisting effects following infrequent dosing and was well tolerated with no major safety concerns. We have received positive regulatory feedback from the FDA and European Medicines Agency, or EMA, on the Phase 3 cardiovascular outcomes trial design for zerlasiran in patients with high Lp(a). In 2025, we completed core Phase 3 readiness activities, including manufacturing and supply scale up. Zerlasiran is Phase 3 ready and we are seeking a third-party partner for potential Phase 3 development as well as potential future commercialization.

SLN312 is our siRNA product candidate under our collaboration with AstraZeneca that works by "silencing" ANGPTL3, an important modulator of lipid metabolism. Inhibition of ANGPTL3 has emerged as a promising new therapeutic approach to reduce triglycerides (TG) and LDL-C levels, the latter independent of the LDL-C receptor function. Since ANGPTL3 suppresses lipoprotein lipase, or LPL, and endothelial lipase, or EL, activity, its inhibition facilitates the clearance of very low-density lipoprotein cholesterol, decreasing both LDL-C and TG levels. AstraZeneca shared interim results from its Phase 1 randomized, single-blind, placebo-controlled trial assessing SLN312 in 98 patients with dyslipidemia. Interim results showed SLN312 produced durable dose-dependent reductions in ANGPTL3, triglycerides and atherogenic lipoproteins after single and multiple doses. The strong duration of effect observed supports potential for infrequent dosing. SLN312 was well tolerated with no safety concerns identified. Phase 1 data presentations are planned for medical and research congresses in 2026. On March 4, 2026, AstraZeneca notified Silence that they will not pursue further development beyond Phase 1. We will re-gain full development, manufacturing and commercialization rights globally to this clinical asset following Phase 1 and are evaluating plans for further clinical development.

SLN365 is our potential first-in-class siRNA product candidate that works by "silencing" GPR146, a novel mechanism of action for the management of cholesterol levels in patients, independent of LDLR function. Hypercholesterolemia is a highly prevalent indication with an estimated 1 in 300 individuals worldwide living with the familial form HeFH (heterozygous) and around 1 in 300,000 individuals suffering from the form HoFH (homozygous) globally. SLN365 has demonstrated promising preclinical results in non-human primates and we anticipate additional preclinical data in the second quarter of 2026.

SLN098 is our siRNA product candidate that works by "silencing" INHBE, a novel target for obesity supported by human genetics, strong preclinical data and emerging third-party clinical data demonstrating early efficacy and safety. Despite recent advances in obesity treatment, limitations of current standards of care leave millions at risk of further complications. Around one billion patients worldwide are affected by obesity and associated co-morbidities. Current obesity treatments offer weight loss around 15-20% which plateaus after 12-24 months and are associated with up to 40% lean muscle mass loss. More than two thirds of weight loss is regained within the first year after discontinuation of treatment. There is also poor tolerability and compliance with up to 30% of patients discontinuing GLP/GIP agonists treatment. SLN098 has the opportunity to address unmet needs including increasing fat loss, preventing muscle mass loss and slowing weight regain. SLN098 has demonstrated deep and durable knockdown in nonhuman primates and we anticipate additional disease model data in the second quarter of 2026 to further validate the mechanism of action. We believe there is an opportunity to develop SLN098 either as a monotherapy or add-on to GLP/GIP agonists or as a weight maintenance treatment.

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 and clinical studies, we have observed a durable, dose-dependent silencing effect with our product candidates following subcutaneous injection. 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 zerlasiran. In preclinical and clinical studies,

zerlasiran 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 and clinical studies, divesiran 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 reaches 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 human genetics evidence, 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.

We have built a promising pipeline of siRNA product candidates based on our mRNAi GOLD™ platform for rare and common diseases with high unmet need.

Our siRNA Product Candidates

Divesiran (SLN124)

Overview

Divesiran is our potential first-in-class siRNA product candidate in Phase 2 development for PV. PV is a rare myeloproliferative neoplasm characterized by the overproduction of RBCs and affects approximately 3.5 million individuals worldwide. Elevated HCT - an index of RBC mass - is a hallmark of the disease. Elevated HCT levels above 45% is associated with a four-times higher rate of death from cardiovascular or thrombotic events. PV is associated with a range of burdensome symptoms including fatigue, cognitive disturbance and pruritis and additionally, longer term can transform to myelofibrosis and Acute Myeloid Leukemia, or AML. The aim of treatment is to maintain HCT less than 45%, a level that is associated with a reduced incidence of thrombosis and cardiovascular-associated death. The current standard of care includes repeated phlebotomies to reduce HCT and/or cytoreductive agents to reduce red blood cell production. There are currently no approved therapies that specifically target RBCs and HCT.

Divesiran is administered subcutaneously and works by specifically binding to and inducing RNAi-mediated degradation of mRNAs made from the Tmprss6 gene. Tmprss6 is a negative regulator of hepcidin, which is the main hormone controlling iron homeostasis in the body. While our initial focus is on PV, divesiran has shown the potential in preclinical studies to address multiple hematological conditions through this central mechanism. By silencing Tmprss6 in PV patients, divesiran aims to increase hepcidin production and release by liver hepatocytes, reducing iron availability to the bone marrow. With less iron available, the overproduction of red blood cells seen in PV is reduced. This helps keep HCT levels in a safer range and can reduce or eliminate the need for phlebotomies. Additionally, siRNA therapies have a highly potent and durable effect - enabling less frequent and more convenient dosing.

In the SANRECO Phase 1 clinical trial evaluating divesiran treatment in 21 PV patients, divesiran produced durable HCT control and substantially reduced phlebotomy use following infrequent dosing (Q6W). Based on the strong durability observed in the Phase 1 trial, the ongoing SANRECO Phase 2 trial is designed to evaluate both a Q6W and Q12W dosing interval. The SANRECO Phase 2 trial is fully enrolled and topline results are anticipated in the third quarter of 2026. The FDA has granted divesiran Fast Track and orphan drug designations for PV. Divesiran has also been granted orphan drug designation by the European Commission for PV in Europe.

Disadvantages of existing treatment options

The primary treatment goal in PV is to reduce the risk of thrombotic events by reducing hematocrit (the percent volume of red blood cells in the blood) 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, divesiran elevates endogenous hepcidin produced and secreted by the liver, avoiding high local concentrations of hepcidin at the injection site. Based on results from the Phase 1 portion of the SANRECO clinical trial, divesiran has shown the potential to maintain durable HCT control and substantially reduce phlebotomy requirements with infrequent dosing in a broad range of PV patients. Importantly, divesiran has also shown to be well tolerated to-date with no dose-limiting toxicities.

GEMINI Trial

The GEMINI trial was a randomized, double-blind, placebo controlled, single-ascending dose trial to investigate the safety, tolerability, PK and PD response of divesiran (1.0, 3.0 and 4.5 mg/kg doses) administered subcutaneously in 24 healthy volunteers. 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 two months.
- Divesiran 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. Divesiran plasma concentrations increased in a greater than dose-linear fashion between dosing groups.
- All divesiran 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.

SANRECO Phase 1/2 Program

Our SANRECO clinical trial is a Phase 1/2 clinical trial with an open-label dose escalation phase followed by a randomized placebo controlled and double-blind phase of divesiran in PV patients.

The Phase 1 portion of the SANRECO clinical trial completed in February 2025 and was a 34-week, open-label trial that evaluated divesiran (3 mg/kg, 6 mg/kg and 9 mg/kg) administered subcutaneously every six weeks for four doses, with a 16-week follow-up period following the date of the last administered dose in 21 PV patients. Key inclusion criteria for the trial included a PV diagnosis and a history of requiring at least three phlebotomies in the last six months or five phlebotomies in the last year prior to screening. Patients were allowed to be on stable doses of cytoreductive agents. Given the exploratory nature of this Phase 1 clinical trial, both well-controlled patients (defined as those with baseline HCT levels at 45% or less) and uncontrolled patients (defined as those with baseline HCT levels greater than 45%) were enrolled.

Results from the SANRECO Phase 1 trial showed divesiran's potential to maintain durable HCT control to target levels with infrequent dosing (Q6W) without the need for phlebotomies in the target population. A summary of the results can be found below.

- Results included 21 phlebotomy-dependent PV patients with a combined history of 79 phlebotomies prior to dosing. Therapeutic phlebotomies were essentially eliminated in the target population and mean HCT levels were lowered and maintained to 45% for all cohorts regardless of baseline levels.
- Divesiran increased hepcidin and ferritin, resulting in elevation of iron body content and improved iron deficiency.
- Divesiran demonstrated similar results in all patient groups, independent of baseline risk or prior and concurrent therapy.
- White blood cells were not altered over the time-course of the trial.
- Platelets increased, reaching a plateau with no reported dose dependent effect.
- Divesiran was well tolerated with no dose-limiting toxicities.

The ongoing SANRECO Phase 2 trial is a global, randomized, double-blind, placebo-controlled trial evaluating divesiran (6 mg dose level) administered subcutaneously at Q6W and Q12W dosing intervals in 48 PV patients. The trial includes a 36-week, placebo-controlled, double-blind period followed by a three-year double-blind and open-label extension period. The primary endpoint of the trial is the proportion of patients who achieve a response receiving divesiran compared to placebo between 18 and 36 weeks. A responder is defined as a patient with HCT remaining less than 45% in the absence of phlebotomies during this time period. Secondary endpoints include safety

and tolerability, pharmacokinetics and quality of life outcomes. The trial is fully enrolled and initial topline results are anticipated in the third quarter of 2026.

SLN548

Overview

SLN548 is our Phase 1 ready siRNA product candidate that works by "silencing" the CFB gene, potentially playing a therapeutic role in conditions associated with over activation of this pathway, including complement-mediated renal diseases, among others. SLN548 has demonstrated promising preclinical results and we are seeking a third-party partner to initiate clinical development.

Zerlasiran (SLN360)

Overview

Zerlasiran is our Phase 3 ready siRNA product candidate for the treatment of cardiovascular disease associated with elevated Lp(a), a lipoprotein in the blood. Lp(a) is 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.

Elevated levels of Lp(a) ≥ 125 nmol/L or approximately 50mg/dL are considered to affect at least 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 (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.

Zerlasiran is administered subcutaneously and 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). Zerlasiran'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. In Phase 1 and 2 clinical trials, zerlasiran showed the potential to substantially reduce Lp(a) levels in ASCVD patients with maximum reductions exceeding 90% during the treatment period. Lp(a) reductions persisted 60 weeks following the first dose, indicating the potential for infrequent dosing. We have received positive regulatory feedback from the FDA and EMA on the Phase 3 cardiovascular outcomes study design for zerlasiran and have completed core Phase 3 readiness activities. Zerlasiran is Phase 3 ready and we are seeking a third-party partner for potential Phase 3 development.

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.

APOLLO Phase 1 Clinical Program

The APOLLO Phase 1 clinical program was a global randomized, double-blind, placebo controlled, single-ascending dose and multiple-ascending dose study investigating the safety, tolerability, pharmacodynamic and pharmacokinetic response of zerlasiran administered subcutaneously in healthy adults and ASCVD patients with high Lp(a) levels of approximately greater than 60mg/dL or less than 150 nmol/L.

In the APOLLO single dose trial of zerlasiran in healthy adults, participants in the top two zerlasiran 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. Other efficacy measures included the effects of zerlasiran on LDL cholesterol and ApoB, both of which are associated with an increased risk of cardiovascular events. The highest doses of zerlasiran reduced LDL cholesterol and ApoB by about 25%. Zerlasiran was observed to be well tolerated with no serious safety concerns reported.

In the APOLLO multiple dose trial of zerlasiran in 36 adults with stable ASCVD and high Lp(a) greater than 150 nmol/L, zerlasiran dose groups (200 mg, 300 mg and 450 mg) demonstrated a significant reduction from baseline in Lp(a) of up to 99% at 90 days following injection of repeated doses. Lp(a) levels remained approximately 90% lower than baseline at 201 days (end of treatment period) at the two highest doses. A dose dependent reduction in LDL cholesterol and ApoB was also observed. Zerlasiran continued to be observed to be well tolerated with no serious safety issues identified.

ALPACAR-360 Phase 2 Clinical Program

The ALPACAR-360 Phase 2 clinical trial was a randomized, double-blind, placebo-controlled trial in 178 patients with high Lp(a) greater than 125nmol/L at high risk of ASCVD events. Baseline Lp(a) concentration was 213 nmol/L. Patients were randomly assigned to one of three active subcutaneous doses of zerlasiran (300 mg Q16 weeks, 300 mg Q24 weeks, 450 mg Q24 weeks) or placebo. The primary endpoint was time-averaged change in Lp(a) from baseline to 36 weeks. Secondary endpoints included time-averaged changes in LDL-C as well as time-averaged Lp(a) to 48 weeks (end of treatment period) and 60 weeks (end of study).

In the ALPACAR-360 Phase 2 clinical trial, zerlasiran produced greater than 80% mean time-averaged placebo-adjusted reductions from baseline in Lp(a) concentrations over 36 weeks. Maximum Lp(a) reductions exceeded 90%. At the final visit, 60 weeks following initial drug administration, reductions in Lp(a) persisted with infrequent dosing. Zerlasiran was also observed to reduce time-averaged LDL-C by ~25-30% and Apo B by ~10-15%. Zerlasiran was observed to be well tolerated with no major safety issues identified.

SLN312

Overview

SLN312 is our siRNA product candidate under our collaboration with AstraZeneca that works by "silencing" ANGPTL3, an important modulator of lipid metabolism. Inhibition of ANGPTL3 has emerged as a promising new therapeutic approach to reduce LDL-C levels independent of the LDL receptor function. Since ANGPTL3 suppresses lipoprotein lipase, or LPL, and endothelial lipase, or EL, activities, its inhibition facilitates the clearance of very low-density lipoprotein cholesterol, decreasing both LDL-C and triglyceride, or TG, levels. AstraZeneca shared interim results from its Phase 1 randomized, single-blind, placebo-controlled trial assessing SLN312 in 98

patients with dyslipidemia. Interim results showed SLN312 produced durable dose-dependent reductions in ANGPTL3, triglycerides and atherogenic lipoproteins after single and multiple doses. The strong duration of effect observed supports potential for infrequent dosing. SLN312 was well tolerated with no safety concerns identified. Phase 1 data presentations are planned for medical and research congresses in 2026. On March 4, 2026, AstraZeneca notified Silence that they will not pursue further development beyond Phase 1. We will re-gain full development, manufacturing and commercialization rights globally to this clinical asset following Phase 1 and are evaluating plans for further clinical development.

SLN365

Overview

SLN365 is our potential first-in-class siRNA product candidate that works by "silencing" GPR146, a novel mechanism of action for the management of cholesterol levels in patients, independent of LDLR function. Hypercholesterolemia is a highly prevalent indication with an estimated 1 in 300 individuals worldwide living with the familial form HeFH (heterozygous) and around 1 in 300,000 individuals suffering from the form HoFH (homozygous) globally. SLN365 has demonstrated promising preclinical results in non-human primates and we anticipate additional preclinical data in the second quarter of 2026.

SLN098

Overview

SLN098 is our siRNA product candidate that works by "silencing" INHBE, a novel target for obesity supported by human genetics, strong preclinical data and emerging third-party clinical data demonstrating early efficacy and safety. Despite recent advances in obesity treatment, limitations of current standards of care leave millions at risk of further complications. Around one billion patients worldwide are affected by obesity and associated comorbidities. Current obesity treatments offer weight loss around 15-20% which plateaus after 12-24 months and are associated with up to 40% lean muscle mass loss. More than two thirds of weight loss is regained within the first year after discontinuation of treatment. There is also poor tolerability and compliance with up to 30% of patients discontinuing GLP/GIP agonists treatment.

SLN098 has the opportunity to address unmet needs including increasing fat loss, preventing muscle mass loss and slowing weight regain. SLN098 has demonstrated deep and durable knockdown in nonhuman primates and we anticipate additional disease model data in the second quarter of 2026 to further validate the mechanism of action. We believe there is an opportunity to develop SLN098 either as a monotherapy or add-on to GLP/GIP agonists or as a weight maintenance treatment.

Collaborations

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 2020. 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 covered five targets initially with AstraZeneca opting to extend the collaboration to a further five targets. AstraZeneca agreed to pay us \$10.0 million upon the exercise of each option to collaborate on an additional target. For each target selected, we are 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 are

also 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.

In May 2023, AstraZeneca nominated the first product candidate under our collaboration, SLN312 (ANGPTL3), triggering a \$10 million option fee to us. In February 2024, AstraZeneca initiated a Phase 1 clinical trial for SLN312 which triggered another \$10 million milestone payment to us. On March 4, 2026, AstraZeneca notified Silence that they will not pursue further development of SLN312 beyond Phase 1. We will re-gain full development, manufacturing and commercialization rights globally to this clinical asset following Phase 1 and are evaluating plans for further clinical development.

Hansoh

In October 2021, we announced a collaboration agreement with Hansoh, one of the leading biopharmaceutical companies in China, to develop siRNAs for three undisclosed targets leveraging our proprietary mRNAi GOLD™ platform. Under the terms of the agreement, Hansoh had 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 trials. We retained exclusive rights for those two targets in all other territories. We were responsible for all activities up to option exercise and retained responsibility for development outside the China region post phase 1 trials. Hansoh also had the exclusive option to license global rights to a third target at the point of IND filing. Hansoh was 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. In 2023, we achieved two additional preclinical milestones and received \$4 million from the Hansoh collaboration. In 2024, we achieved an additional preclinical milestone of \$2.0 million from the Hansoh collaboration. In December 2024, Hansoh notified us that it will not pursue further development under the Hansoh collaboration. This action represented the conclusion of all required development activities and commitments under the terms of the Hansoh collaboration and we retain the exclusive rights globally for all three targets evaluated under the Hansoh collaboration.

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, European Commission 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, 2025, we have more than 200 granted patents and over 100 more pending patent applications in the U.S., Europe, China, and other jurisdictions. These patents and patent applications cover both our innovative platform technologies as well as our products and pipeline candidates. We regularly file priority patent applications to secure early filing dates for novel inventions, with our R&D and Intellectual Property personnel working in coordination to identify and evaluate potential innovations, and to draft and file corresponding applications with the patent office. We file patent applications and maintain patents in multiple commercially or strategically important jurisdictions, such as the U.S., European Union and U.K., China, Japan, Canada, South Korea, Australia, Israel, India, and New Zealand, and other strategically important markets in South America, Asia, and Africa.

Our granted patents and pending patent applications include compositions of matter claims directed to siRNA molecules and compositions for both pre-clinical candidates and clinical products. For example, the patent families for our SLN124 and SLN360 clinical products cover the corresponding siRNA molecules themselves (e.g., specific nucleic acid sequences) and their specific modifications, linkers, formulations, doses, and therapeutic uses. Our patents and patent applications also include claims directed to different aspects of siRNA conjugation, delivery, and chemical modifications providing improvements to the specificity, stability and efficacy of siRNA molecules.

Our earliest filed patent applications directed to 19-mer blunt-ended siRNAs with particular siRNA modification patterns expired in August 2023. Our current patent application families directed to siRNA chemistry 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 and SLN124 product candidates, if and when granted, would not be expected to expire until at least 2038. Our patent portfolio is continuously expanding, providing multiple layers of exclusivity protection for our products and pipeline candidates. In many jurisdictions including the US, Europe, Japan and China, the lifetime of a product-related patent can be further extended beyond their expected natural expiration date, for example to add back a portion of the time that the corresponding product is under clinical or regulatory evaluation, providing additional product exclusivity (typically not more than 5 years from the expected natural expiration date).

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 the current good manufacturing practice, or 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.

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.

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

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 and their covered subcontractors. 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 (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other healthcare professionals (such as physician assistants and nurse practitioners), 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.

We may be subject to foreign equivalents of all of the above federal or state legislation. For example, outside the United States, interactions between pharmaceutical companies and health care professionals are also governed by strict laws, such as national anti-bribery laws of European countries, national sunshine rules, regulations, industry self-regulation codes of conduct and physicians' codes of professional conduct. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

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, the U.S. Department of Health and Human Services, or HHS, imposes rebates on many Medicare Part B and Medicare Part D products to penalize price increases that outpace inflation on an annual basis. In addition, HHS has been empowered to negotiate the price of certain single-source drugs that have been on the market for at least 7 years covered under Medicare as part of the Medicare Drug Price Negotiation Program. Each year up to twenty (20) products will be selected by HHS for the Medicare Drug Price Negotiation Program. Products subject to the Medicare Drug Price Negotiation Program are expected to experience a significant reduction in reimbursement from the Medicare program on a per unit basis. In addition, 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. Further, coverage policies and third-party payer reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for products for which we receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

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. The PPACA substantially changed the way healthcare is financed by both governmental and private insurers. Since its enactment, there have been amendments and judicial, Congressional and executive branch challenges to certain aspects of the PPACA. For example, on July 4, 2025, the One Big Beautiful Bill Act, or OBBBA, was signed into law, which narrowed access to PPACA marketplace exchange enrollment and declined to extend the PPACA enhanced advanced premium tax

credits that expired at the end of 2025, which, among other provisions in the law, are anticipated to reduce the number of Americans with health insurance. The OBBBA also is expected to reduce Medicaid spending and enrollment by implementing work requirements for some beneficiaries, capping state-directed payments, reducing federal funding, and limiting provider taxes used to fund the program. Congress is considering proposed legislation intended to further reduce healthcare costs with alternatives to replace the expired PPACA subsidies.

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.

The current administration is pursuing policies to reduce regulations and expenditures across government agencies including at HHS, the FDA, CMS and related agencies. These actions, presently directed by executive orders or memoranda from the Office of Management and Budget, may propose policy changes that create additional uncertainty for our business. For example, the current administration has announced agreements with pharmaceutical companies that require the drug manufacturers to offer, through a direct-to-consumer platform, U.S. patients and Medicaid programs prescription drug Most-Favored Nation pricing equal to or lower than those paid in other developed nations, with additional mandates for direct-to-patient discounts and repatriation of foreign revenues. Other recent actions, for example, include (1) directing agencies to reduce agency workforce and cut programs; (2) directing HHS and other agencies to lower prescription drug costs through a variety of initiatives, including by improving upon the Medicare Drug Price Negotiation Program and establishing Most-Favored-Nation pricing for pharmaceutical products; (3) imposing tariffs on imported pharmaceutical products; and (4) as part of the Make America Healthy Again Commission's Strategy Report released in September 2025, working across government agencies to increase enforcement on direct-to-consumer pharmaceutical advertising. Additionally, the current administration recently called on Congress to enact "The Great Healthcare Plan," to codify and expand Most-Favored Nation pricing, lower government subsidies to private insurance companies, increase healthcare price transparency, expand pharmaceutical drugs available for over-the-counter purchase, and enact restrictions on pharmacy benefit manager payment methodologies, among other things. These actions and policies may significantly reduce U.S. drug prices, potentially impacting manufacturers' global pricing strategies and profitability, while increasing their operational costs and compliance risks. In June 2024, in *Loper Bright Enterprises v. Raimondo*, the U.S. Supreme Court greatly reduced judicial deference to regulatory agencies, which could increase successful legal challenges to federal regulations affecting our operations. Congress may introduce and ultimately pass health care related legislation that could impact the drug approval process and make changes to the Medicare Drug Price Negotiation Program. These and other healthcare reform initiatives may result in additional reductions in Medicare and other healthcare funding.

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. Any such approved importation plans, when implemented, may result in lower drug prices for products covered by those programs. It is possible that other healthcare reform measures may be adopted in the future.

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 are subject to extensive pre- and post-market regulation by regulatory authorities at both the European Union and national levels. An evolving global regulatory view on the classification of RNA therapies could impact the requirements applied to our siRNA compounds. 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 and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. Medicines used in clinical trials must be manufactured in accordance with the guidelines on cGMP and in a GMP licensed facility, which can be subject to GMP inspections. The sponsor of clinical trials 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.

In the EU, clinical trials are governed by the Clinical Trials Regulation (EU) No 536/2014, or CTR, which entered into application on January 31, 2022, repealing and replacing the Clinical Trials Directive 2001/20/EC, or CTD. The CTR is intended to harmonize and streamline clinical trial authorizations, simplify adverse-event reporting procedures, improve the supervision of clinical trials and increase transparency. Specifically, the Regulation, which is directly applicable in all EU Member States, introduces a streamlined application procedure through a single-entry point, the "EU portal", the Clinical Trials Information System, or CTIS; a single set of documents to be prepared and submitted for the application; as well as simplified reporting procedures for clinical trial sponsors. A harmonized procedure for the assessment of applications for clinical trials has been introduced and is divided into two parts. Part I assessment is led by the competent authorities of a reference Member State selected by the trial sponsor and relates to clinical trial aspects that are considered to be scientifically harmonized across EU Member States. This assessment is then submitted to the competent authorities of all concerned Member States in which the trial is to be conducted for their review. Part II is assessed separately by the competent authorities and Ethics Committees in each concerned EU Member State. Individual EU Member States retain the power to authorize the conduct of clinical trials on their territory.

The CTR foresaw a three-year transition period that ended on January 31, 2025. Since this date, all new or ongoing trials are subject to the provisions of the CTR. During the development of a medicinal product, the EU and national medicines regulators within the European Union provide the opportunity for dialogue and guidance on the development program. At the EU level, developers of medicinal products can ask the EMA for scientific advice and protocol assistance at any stage of development and regardless of whether the medicinal product is eligible for the centralized authorization procedure or not. Assistance is given by the EMA's Committee for Medicinal Products for Human Use, or CHMP, on the recommendation of the Scientific Advice Working Party. A fee is incurred with each

scientific advice procedure, but this can be waived for orphan medicinal products. Advice from the EMA is provided based on questions concerning, quality aspects (manufacturing, chemical, pharmaceutical and biological testing of the medicine), nonclinical testing (toxicological and pharmacological tests designed to show the activity of the medicine in the laboratory) and clinical aspects (appropriateness of studies in patients or healthy volunteers, selection of endpoints), methodological issues (statistical tests to use, data analysis, modelling and simulation), overall development strategy (conditional marketing authorization, bridging strategy for generics, safety database), significant benefit for maintaining orphan designation, and pediatric developments. To the extent that we do obtain such scientific advice in the future, while the company is expected to respect the outcome of the scientific advice procedure, such advice is not legally binding.

Marketing Authorizations

In the EU, medicinal products can only be commercialized after a related marketing authorization, or MA, has been granted. To obtain an MA for a product in the EU, an applicant must submit a Marketing Authorization Application, or MAA, either under a centralized procedure administered by the European Medicines Agency, or EMA, or one of the procedures administered by the competent authorities of EU Member States (decentralized procedure, national procedure or mutual recognition procedure). An MA may be granted only to an applicant established in the EU.

The centralized procedure provides for the grant of a single MA by the European Commission that is valid throughout the EEA (which is comprised of the 27 EU Member States plus Norway, Iceland and Liechtenstein). Pursuant to Regulation (EC) No 726/2004, the centralized procedure is compulsory for specific products, including for (i) medicinal products derived from biotechnological processes, (ii) products designated as orphan medicinal products, (iii) advanced therapy medicinal products, or ATMPs, and (iv) products with a new active substance indicated for the treatment of HIV/AIDS, cancer, neurodegenerative diseases, diabetes, auto-immune and other immune dysfunctions and viral diseases. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, authorization through the centralized procedure is optional on related approval.

Under the centralized procedure, the EMA's Committee for Medicinal Products for Human Use, or CHMP, conducts the initial assessment of a product. The CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing MA. The maximum timeframe for the evaluation of an MAA under the centralized procedure is 210 days, excluding clock stops when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Accelerated assessment may be granted by the CHMP in exceptional cases, when a medicinal product targeting an unmet medical need is expected to be of major interest from the point of view of public health and, in particular, from the viewpoint of therapeutic innovation. If the CHMP accepts a request for accelerated assessment, the time limit of 210 days will be reduced to 150 days (excluding clock stops). The CHMP can, however, revert to the standard time limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment.

Unlike the centralized authorization procedure, the decentralized MA procedure requires a separate application to, and leads to separate approval by, the competent authorities of each EU Member State in which the product is to be marketed. This application is identical to the application that would be submitted to the EMA for authorization through the centralized procedure. The reference EU Member State prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. The resulting assessment report is submitted to the concerned EU Member States who, within 90 days of receipt, must decide whether to approve the assessment report and related materials. If a concerned EU Member State cannot approve the assessment report and related materials due to concerns relating to a potential serious risk to public health, disputed elements may be referred to the Heads of Medicines Agencies' Coordination Group for Mutual Recognition and Decentralised Procedures – Human, or CMDh, for review. The subsequent decision of the European Commission is binding on all EU Member States.

The mutual recognition procedure allows companies that have a medicinal product already authorized in one EU Member State to apply for this authorization to be recognized by the competent authorities in other EU Member States. Like the decentralized procedure, the mutual recognition procedure is based on the acceptance by the competent authorities of the EU Member States of the MA of a medicinal product by the competent authorities of other EU Member States. The holder of a national MA may submit an application to the competent authority of an EU Member State requesting that this authority recognize the MA delivered by the competent authority of another EU Member State.

An MA has, in principle, an initial validity of five years. The MA may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA or by the competent authority of the EU Member State in which the original MA was granted. To support the application, the MA holder must provide the EMA or the competent authority with a consolidated version of the Common Technical Document providing up-to-date data concerning the quality, safety and efficacy of the product, including all variations introduced since the MA was granted, at least nine months before the MA ceases to be valid. The European Commission or the competent authorities of the EU Member States may decide on justified grounds relating to pharmacovigilance, to proceed with one further five year renewal period for the MA. Once subsequently definitively renewed, the MA shall be valid for an unlimited period. Any authorization which is not followed by the actual placing of the medicinal product on the EU market (for a centralized MA) or on the market of the authorizing EU Member State within three years after authorization ceases to be valid (the so-called sunset clause).

Innovative products that target an unmet medical need and are expected to be of major public health interest may be eligible for a number of expedited development and review programs, such as the Priority Medicines, or PRIME, scheme, which provides incentives similar to the breakthrough therapy designation in the U.S. PRIME is a voluntary scheme aimed at enhancing the EMA's support for the development of medicinal products that target unmet medical needs. Eligible products must target conditions for which there is an unmet medical need (there is no satisfactory method of diagnosis, prevention or treatment in the EU or, if there is, the new medicinal product will bring a major therapeutic advantage) and they must demonstrate the potential to address the unmet medical need by introducing new methods of therapy or improving existing ones. Benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and potentially accelerated MAA assessment once a dossier has been submitted.

In the EU, a "conditional" MA may be granted in cases where all the required safety and efficacy data are not yet available. The European Commission may grant a conditional MA for a medicinal product if it is demonstrated that all of the following criteria are met: (i) the benefit-risk balance of the medicinal product is positive; (ii) it is likely that the applicant will be able to provide comprehensive data post-authorization; (iii) the medicinal product fulfils an unmet medical need; and (iv) the benefit of the immediate availability to patients of the medicinal product is greater than the risk inherent in the fact that additional data are still required. The conditional MA is subject to conditions to be fulfilled for generating the missing data or ensuring increased safety measures. It is valid for one year and must be renewed annually until all related conditions have been fulfilled. Once any pending studies are provided, the conditional MA can be converted into a traditional MA. However, if the conditions are not fulfilled within the timeframe set by the EMA and approved by the European Commission, the MA will cease to be renewed.

An MA may also be granted "under exceptional circumstances" where the applicant can show that it is unable to provide comprehensive data on efficacy and safety under normal conditions of use even after the product has been authorized and subject to specific procedures being introduced. These circumstances may arise in particular when the intended indications are very rare and, in the state of scientific knowledge at that time, it is not possible to provide comprehensive information, or when generating data may be contrary to generally accepted ethical principles. Like a conditional MA, an MA granted in exceptional circumstances is reserved to medicinal products intended to be authorized for treatment of rare diseases or unmet medical needs for which the applicant does not hold a complete data set that is required for the grant of a standard MA. However, unlike the conditional MA, an applicant for authorization in exceptional circumstances is not subsequently required to provide the missing data. Although the MA "under exceptional circumstances" is granted definitively, the risk-benefit balance of the medicinal product is reviewed annually, and the MA will be withdrawn if the risk-benefit ratio is no longer favorable.

Data Exclusivity

The EU provides opportunities for data and market exclusivity related to MAs. Upon receiving an MA, innovative medicinal products are generally entitled to receive eight years of data exclusivity and 10 years of market exclusivity. Data exclusivity, if granted, prevents regulatory authorities in the EU from referencing the innovator's data to assess a generic application or biosimilar application for eight years from the date of authorization of the innovative product, after which a generic or biosimilar MAA can be submitted, and the innovator's data may be referenced. The market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the EU until 10 years have elapsed from the initial MA of the reference product in the EU. The overall ten-year period may, occasionally, be extended for a further year to a maximum of 11 years if, during the first eight years of those ten years, the MA holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. However, there is no guarantee that a product will be considered by the EU's regulatory authorities to be a new chemical/biological entity, and products may not qualify for data exclusivity.

There is a special regime for biosimilars, or biological medicinal products that are similar to a reference medicinal product but that do not meet the definition of a generic medicinal product, for example, because of differences in raw materials or manufacturing processes. For such products, the results of appropriate preclinical or clinical trials must be provided in support of the MAA, 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 EU, Regulation (EC) No 1901/2006 provides that all MAAs for new medicinal products have to include the results of trials conducted in the pediatric population, in compliance with a pediatric investigation plan, or PIP, agreed with the EMA's Pediatric Committee or PDCO. The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the medicinal product for which MA is being sought. The PDCO can grant a deferral of the obligation to implement some or all of the measures provided in the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults. Further, the obligation to provide pediatric clinical trial data can be waived by the PDCO when these data are not needed or appropriate because the product is likely to be ineffective or unsafe in children, the disease or condition for which the product is intended occurs only in adult populations, or when the product does not represent a significant therapeutic benefit over existing treatments for pediatric patients. Once the MA is obtained in all EU Member States and study results are included in the product information, even when negative, the product is eligible for a six-month extension to the Supplementary Protection Certificate, or SPC, if any is in effect at the time of authorization or, in the case of orphan medicinal products, a two-year extension of orphan market exclusivity.

Orphan Designation

In the EU, Regulation (EC) No. 141/2000, as implemented by Regulation (EC) No. 847/2000 provides that a medicinal product can be designated as an orphan medicinal product by the European Commission if its sponsor can establish that: (i) the product is intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions; (ii) either (a) such conditions affect not more than 5 in 10,000 persons in the EU when the application is made, or (b) the product without the benefits derived from orphan status, would not generate sufficient return in the EU to justify the necessary investment in developing the medicinal product; and (iii) there exists no satisfactory authorized method of diagnosis, prevention, or treatment of the condition that has been authorized in the EU, or even if such method exists, the product will be of significant benefit to those affected by that condition.

Regulation (EC) No 847/2000 sets out further provisions for implementation of the criteria for designation of a medicinal product as an orphan medicinal product. An application for the designation of a medicinal product as an orphan medicinal product must be submitted at any stage of development of the medicinal product but before filing of an MAA. An MA for an orphan medicinal product may only include indications designated as orphan. For non-orphan indications treated with the same active pharmaceutical ingredient, a separate marketing authorization has to be sought.

Orphan medicinal product designation entitles an applicant to incentives such as fee reductions or fee waivers, protocol assistance, and access to the centralized marketing authorization procedure. Upon grant of a marketing authorization, orphan medicinal products are entitled to a ten-year period of market exclusivity for the approved therapeutic indication, which means that the EMA cannot accept another marketing authorization application or accept an application to extend for a similar product and the European Commission cannot grant a marketing authorization for the same indication for a period of ten years. The period of market exclusivity is extended by two years for orphan medicinal products that have also complied with an agreed PIP. No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications. Orphan medicinal product designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The period of market exclusivity may, however, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria on the basis of which it received orphan medicinal product designation, including where it can be demonstrated on the basis of available evidence that the original orphan medicinal product is sufficiently profitable not to justify maintenance of market exclusivity or where the prevalence of the condition has increased above the threshold. Additionally, an MA may be granted to a similar medicinal product with the same orphan indication during the 10 year period if: (i) if the applicant consents to a second original orphan medicinal product application, (ii) if the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities; or (iii) if the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior to the original orphan medicinal product. A company may voluntarily remove a product from the register of orphan products.

Post-Approval Controls

Where an MA is granted in relation to a medicinal product in the EU, the holder of the MA is required to comply with a range of regulatory requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. Similar to the United States, both MA holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA, the European Commission and/or the competent regulatory authorities of the individual EU Member States. The holder of an MA must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance 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 MAAs 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 MA. Such risk-minimization measures or post-authorization obligations may include additional safety monitoring, more frequent submission of PSURs, or the conduct of additional clinical trials or post-authorization safety studies.

Other EU Compliance Requirements

In the EU, the advertising and promotion of medicinal products are subject to both EU and EU Member States' laws governing promotion of medicinal products, interactions with physicians and other healthcare professionals, misleading and comparative advertising and unfair commercial practices. General requirements for advertising and promotion of medicinal products, such as direct-to-consumer advertising of prescription medicinal products are established in EU law. However, the details are governed by regulations in individual EU Member States and can differ from one country to another. For example, applicable laws require that promotional materials and advertising in relation to medicinal products comply with the product's Summary of Product Characteristics, or SmPC, which may require approval by the competent national authorities in connection with an MA. The SmPC is the document

that provides information to physicians concerning the safe and effective use of the product. Promotional activity that does not comply with the SmPC is considered off-label and is prohibited in the EU.

Much like the Anti-Kickback Statute prohibition in the United States, described above, the provision of benefits or advantages to physicians and other health care professionals to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the EU. Interactions between pharmaceutical companies and health care professionals are governed by strict laws, such as national anti-bribery laws of European countries, national sunshine rules, regulations, industry self-regulation codes of conduct and physicians' codes of professional conduct. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

Payments made to physicians and other health care professionals in certain EU Member States must be publicly disclosed. Moreover, agreements with health care professionals may require prior notification or approval by the health care professional's employer, his or her competent professional organization and/or the regulatory authorities of the individual EU Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

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. This Health Technology Assessment, or HTA, process is the procedure according to which the assessment of the public health impact, therapeutic impact and the economic and societal impact of use of a given medicinal product in the national healthcare systems of the individual country is conducted. The outcome of HTA regarding specific medicinal products will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU Member States. In December 2021, Regulation No 2021/2282 on Health Technology Assessment, or HTA Regulation, was adopted. The HTA Regulation is intended to boost cooperation among EU Member States in assessing health technologies, including new medicinal products, and establishes the framework for EU level joint clinical assessments, joint scientific consultations, and the early identification of emerging health technologies. The HTA Regulation entered into application on January 12, 2025, through a phased implementation based on the type of product (i.e. oncology and advanced therapy medicinal products as of 2025, orphan medicinal products as of 2028, and all other medicinal products by 2030) and is intended to harmonize the clinical benefit assessment of HTA across the European Union. The Regulation permits EU Member States to use common tools, methodologies, and procedures and requires them to rely on EU-level joint clinical assessment reports for the clinical components of their national HTA evaluations. Individual EU Member States will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technologies, and making decisions on pricing and reimbursement. 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.

Regulatory Framework in the United Kingdom

The Medicines and Healthcare products Regulatory Agency ("MHRA") is the United Kingdom's standalone regulator for medicinal products and medical devices.

While the United Kingdom's regulatory framework for clinical trials was historically based on the Medicines for Human Use (Clinical Trials) Regulations 2004, which implemented the former EU Clinical Trials Directive, this has been significantly reformed by the Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2024. The new legislation, which was adopted in April 2025, modernizes the United Kingdom's approach to make it a more attractive location for research, and includes key features such as: (i) a risk-proportionate approach, including a notification scheme for lower-risk trials; (ii) a combined review process integrating ethics committee and

regulatory approvals into a single, streamlined pathway; (iii) enhanced transparency requirements mandating registration of clinical trials in a public registry and publication of trial results within 12 months of trial completion (with scope for deferrals in certain circumstances); (iv) greater flexibility to support innovation in clinical trial design; and (v) measures to promote patient and public involvement. The amendments will become applicable on April 28, 2026, following a one-year transition period.

Marketing authorizations in the United Kingdom are governed by the Human Medicines Regulations (SI 2012/1916), as amended. In order to obtain a United Kingdom MA to commercialize products in the United Kingdom, an applicant must be established in the United Kingdom and must follow one of the United Kingdom national authorization procedures or one of the remaining post-Brexit international cooperation procedures. Applications are governed by the Human Medicines Regulations (SI 2012/1916) and are made electronically through the MHRA Submissions Portal. The MHRA has introduced changes to national licensing procedures, including procedures to prioritize access to new medicines that will benefit patients, a 150-day assessment (subject to clock-stops) and a rolling review procedure. The rolling-review procedure permits the separate or joint submission of quality, non-clinical, and clinical data to the MHRA which can be reviewed on a rolling basis. After an application under the rolling-review procedure has been validated, the decision should be received within 100 days (subject to clock-stops).

In addition, since January 1, 2024, the MHRA may rely on the International Recognition Procedure (“IRP”), when reviewing certain types of MAAs. Pursuant to the IRP, the MHRA will take into account the expertise and decision-making of trusted regulatory partners (e.g., the regulatory in Australia, Canada, Switzerland, Singapore, Japan, the U.S.A. and the EU). The MHRA will conduct a targeted assessment of IRP applications but retain the authority to reject applications if the evidence provided is considered insufficiently robust. The IRP allows medicinal products approved by such trusted regulatory partners that meet certain criteria to undergo a fast-tracked MHRA review to obtain and/or update a MA in the United Kingdom. Applications should be decided within a maximum of 60 days if there are no major objections identified that cannot be resolved within such 60-day period and the approval from the trusted regulatory partner selected has been granted within the previous 2 years or if there are such major objections identified or such approval hasn’t been granted within the previous 2 years within 110 days. Applicants can submit initial MAAs to the IRP but the procedure can also be used throughout the lifecycle of a product for post-authorization procedures including line extensions, variations and renewals.

All existing marketing authorizations of the EU for centrally authorized products were automatically converted or grandfathered into the United Kingdom’s marketing authorization, effective in Great Britain only, free of charge on January 1, 2021, unless the marketing authorization holder opted-out of this possibility. On January 1, 2025, the “Windsor Framework” came into effect, reintegrated Northern Ireland under the regulatory authority of the MHRA with respect to medicinal products and introducing a United Kingdom-wide licensing process for medicines.

There is no pre-marketing authorization orphan designation for medicinal products in the UK. Instead, the MHRA reviews applications for orphan designation in parallel to the corresponding marketing authorization application. The criteria are essentially the same as those in the EU but have been tailored for the market. This includes the criterion that prevalence of the condition in the United Kingdom, rather than the EU, must not be more than five in 10,000. Upon the grant of a marketing authorization with orphan status, the medicinal product will benefit from up to 10 years of market exclusivity from similar products in the approved orphan indication. The start of this market exclusivity period will be set from the date of first approval of the product in the United Kingdom.

Sales and Marketing

Given our stage of development, we have not yet established a commercial organization or distribution capabilities. Should any of our product candidates be approved for commercialization, we intend to develop a plan to commercialize them in the United States and other key markets, through internal infrastructure and/or external partnerships in a manner that will enable us to realize the full commercial value of our programs.

Manufacturing and Source of Supply

We do not currently own or operate manufacturing facilities for the production of clinical or commercial quantities of our product candidates. Furthermore, there is limited capacity at contract manufacturers that operate under the

cGMP requirements of the FDA to meet our timelines and production needs. We currently rely and intend to continue to rely on contract development and manufacturing organizations, or CDMOs, for both drug substance and drug product. Currently, we contract with eleven third-party manufacturers for the manufacture of our development pipeline. We may engage additional third-party manufacturers to support any clinical trials for our product candidates as well as commercialization thereof, if approved, in the U.S. or other jurisdictions. In addition, as our production needs increase, we intend to recruit additional experienced personnel to manage the CDMOs producing our product candidate and other product candidates or products that we may develop in the future.

We rely on CDMOs to perform all chemistry, manufacturing, and controls activities. Our agreements with CDMOs may obligate them to develop or transfer upstream and downstream processes, develop or transfer drug product manufacturing processes, develop or transfer suitable analytical methods for release and stability testing and qualify these methods for use with our products, produce drug substance for preclinical testing, and produce drug substance or drug product under cGMP for use in clinical studies among other activities. In addition, we rely on CDMOs to operate facilities that meet regulatory requirements for production and testing of clinical and commercial products and to work closely with us to validate manufacturing processes prior to commercial launch. We qualify CDMOs prior to initiation of cGMP regulated activities and periodically thereafter as part of the supplier qualification program. We oversee CDMOs by performing technical and quality assurance review and/or approval of cGMP documentation, establishing quality agreements to define responsibilities and expectations for goods and services, and observing production and testing activities as a person-in-plant, among other activities.

Employees and Human Capital Resources

As of December 31, 2025, we had 88 full-time employees who work primarily in the United Kingdom, Germany and the United States. Of these employees, 62 are engaged in research and development activities and 26 are engaged in business development, finance, information systems, facilities, human resources or administrative support. Further, we have 26 employees who hold M.D. or Ph.D. degrees. None of our employees are subject to collective bargaining agreements. We consider our relationships with our employees to be good.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and additional employees. The principal purposes of our equity incentive plans are to attract, retain and motivate employees and directors through the granting of equity-based compensation awards.

Corporate Information

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 12 Hammersmith Grove, London W6 7AP, United Kingdom and our telephone number is +44 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. In November 2021, the admission of our ordinary shares to trading on AIM of the London Stock Exchange was cancelled. Our website address is www.silence-therapeutics.com. Our agent for service of process in the United States is Silence Therapeutics Inc., c/o Harvard Business Services, Inc., 16192 Coastal Hwy, Lewes, Delaware 19958, USA.

Available Information

Our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and amendments to reports filed pursuant to Sections 13(a) and 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, are filed with the Securities and Exchange Commission, or the SEC. Such reports and other information filed by us with the SEC are available free of charge on our website at www.silence-therapeutics.com when such reports are available on the SEC's website. The SEC maintains a website that contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC at www.sec.gov. The information contained on the websites referenced in this Annual Report is not

incorporated by reference into this filing. Further, our references to website links are intended to be inactive textual references only.

Item 1A. 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 on Form 10-K, including our consolidated financial statements and the related notes and Management's Discussion and Analysis of Financial Condition and Results of Operations, 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.

The risks described below are not intended to be exhaustive and are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations. This Annual Report on Form 10-K also contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in the forward-looking statements as a result of a number of factors, including the risks described below. See also the section titled "Special Note Regarding Forward-Looking Statements" above.

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 of this Annual Report, 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 \$88.6 million for the year ended December 31, 2025 and \$45.3 million for the year ended December 31, 2024. As of December 31, 2025, we had an accumulated deficit of \$562.6 million. Our losses have resulted primarily from costs related to our research and development programs, including our preclinical and clinical development activities.

We expect to continue incurring significant 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 authorities 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 the 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 RNA interference, or 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, and the activities associated with, the 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.

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is expensive. We expect our research and development expenses and net losses 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, including clinical trials for product candidates other than those which are funded by our collaboration partners, and such funding may not be available to us on acceptable terms, or at all. 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 strategic collaboration arrangements, as well as equity 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 current or 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.

We have historically funded our 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. As of December 31, 2025, we had cash and cash equivalents and U.S. treasury bills of \$85.1 million. We expect that our existing cash and cash equivalents will provide sufficient funds to continue to meet our liabilities as they fall due and for at least the next twelve months from the issuance of the December 31, 2025 financial statements. However, it is possible that our costs will be higher than expected, that our operating plan may change as a result of many factors currently unknown to us, and that we may need to seek additional funds sooner than planned, through public or private equity or debt financings or other sources, such as strategic collaborations or license and development agreements.

In accordance with Accounting Standards Codification ("ASC") 205, "Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern, the Company has the responsibility to evaluate whether conditions and/or events raise substantial doubt 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 and U.S. treasury bills as of December, 31, 2025 are sufficient to fund its forecasted operating expenses and capital requirements into 2028.

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 our financial condition and ability to pursue our business strategies, including being required to delay, reduce or eliminate some of our research and development programs, or being unable to continue operations or unable to continue as a going concern.

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 strategic collaboration arrangements, equity or debt financings, and research grants and tax credits.

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.

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 the Sales 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 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. 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. 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.

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 securities. 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 clinical and pre-clinical 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, or in other nucleic acid-based approaches, 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:

- successfully designing preclinical studies which may be predictive of clinical outcomes;
- successfully conducting and completing clinical trials, including timely patient enrollment and acceptable safety and efficacy data;
- obtaining and maintaining marketing approvals from applicable regulatory authorities on a timely basis, if ever;
- obtaining and maintaining patent or trade secret protection for future product candidates;
- establishing and maintaining supply and manufacturing relationships with third parties or establishing our own manufacturing capability; and
- 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.

From time to time, we may publicly disclose preliminary or “topline” data from our clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or clinical trial. As a result, the “topline” or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. “Topline” data should be viewed with caution until the final data are available.

We may also disclose interim data from our clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available or as patients from our clinical trials continue other treatments for their disease. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects. Further, disclosure of interim data by us or by our competitors could result in volatility in the price of our Ordinary Shares.

If the interim, “topline,” or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could significantly harm our business, financial condition, results of operations and prospects.

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 two proprietary 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;
- disruptions at the FDA and other regulatory agencies caused by funding shortages or future global health crises;
- delays in reaching agreement on acceptable terms with prospective contract research organizations, or 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 and clinical investigators to participate in a trial;
- delays in the testing, validation, manufacturing and delivery of the product candidates and patient samples to and from the clinical sites;
- delays in having patients complete participation in a trial or return for post-treatment follow-up or ensuring patient compliance with trial protocols;

- 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, 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; the impact of global health crises. 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.

Delays in subject enrollment may result in increased costs or may affect the timing or outcome of the planned clinical trials, which could prevent completion of these trials and adversely affect our ability to advance the development of our product candidates.

If we are unable to maintain any of our existing collaborations, or if these arrangements are not successful, or we are unable to enter into future licenses, our business could be adversely affected.

In the past, we have entered into collaborations with other parties, including pharmaceutical and biotechnology companies like Hansoh Pharmaceutical Group Company Limited, or Hansoh, and AstraZeneca PLC, or AstraZeneca, to develop products based on our RNAi technology, and such collaborations and licensing arrangements currently represent a significant portion of our product candidate pipeline. Certain of our collaborations have provided us with important funding for some of our development programs and we expect to receive additional funding under collaborations in the future if certain milestones are achieved although not all of our collaborations may result in funding to us, and certain collaborations, licenses and agreements may result in increased expenditures by us.

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, we recently concluded our collaboration with Hansoh in December 2024. As a result, we may have to attract a new collaborator or develop expanded research and development, sales, distribution and marketing capabilities internally, which would require us to invest significant amounts of financial and management resources.

We are actively exploring licenses and other strategic collaborations with additional pharmaceutical and biotechnology companies for development and potential commercialization of therapeutic products. However, we face significant competition in seeking appropriate collaborators. If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail the development of a product candidate, reduce or delay our development programs, delay potential commercialization, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund and undertake development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all.

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 relying, 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 pre-clinical and clinical 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 or comparable foreign submissions and will not be able to, or may be delayed in our efforts to, advance our clinical trials which would prevent us from successfully developing and commercializing our 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 away 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 authorities require us to comply with GCP, other applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki 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 investigational review boards, or IRBs, and ethics committees of progress reports and any significant changes; and obtaining documented IRB approvals or positive ethics committee opinions. 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.

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 and regulatory requirements;
- 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. We, or our contract manufacturers, any future collaborators and their contract manufacturers could be subject to periodic unannounced inspections by the FDA, competent authorities of EU Member States or other comparable foreign regulatory authorities, to monitor and ensure compliance with cGMP. Despite our efforts to audit and verify regulatory compliance, one or more of our third-party manufacturing vendors may be found on regulatory inspection by the FDA, competent authorities of EU Member States or other comparable foreign regulatory authorities to be noncompliant with cGMP regulations. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including shutdown of the third-party vendor or invalidation of drug product lots or processes, fines, injunctions, civil penalties, delays, suspension, variation or withdrawal of approvals, license revocation, seizures or recalls of product candidates or drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products, if approved, and significantly harm our business, financial condition, results of operations and prospects. 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 the then existing 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, European Commission or MHRA, have reviewed and approved the product candidate. The regulatory authorities 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 or authority policy during the period of product development, clinical trials and the review process.

We cannot be sure that the FDA, the EMA or the European Commission or MHRA will accept the outcome of our preclinical testing and studies as sufficient to support the submission of an IND or a comparable foreign application or that the results of our clinical trials will be sufficient to support marketing approval. Furthermore, later clinical trials often produce unsatisfactory results even though prior clinical trials were successful. Moreover, the results of clinical trials may be unsatisfactory to the FDA, the EMA or European Commission, the MHRA or other comparable regulatory authorities even if we believe those clinical trials to be successful. The FDA, the competent authorities of EU Member States, the MHRA or other comparable regulatory authorities may suspend one or all of our clinical trials or the FDA, EMA or MHRA may require that we conduct additional clinical, preclinical, manufacturing, validation or drug product quality studies and submit that data before considering or reconsidering any new drug application, or NDA, or comparable foreign regulatory application that we may submit. Depending on the extent of these additional studies, approval of any applications that we submit may be significantly delayed or may cause the termination of such programs, or may require us to expend more resources than we have available. Regulatory authorities can delay, limit or deny approval of our product candidate for many reasons, including unsatisfactory efficacy and safety data from our trials disagreements over the design of our trial and/or manufacturing issues and a number of other factors which we and the regulators may disagree.

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 European Commission 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 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, state and foreign 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. 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 authority 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 authority 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 shutdown of the third-party vendor or invalidation of drug product lots or processes, warning letters, fines and civil penalties, suspension of production, suspension, variation or delay in product approval, license revocation, product seizure or recall of product candidates or approved products, plant shutdown, operating restrictions and criminal prosecutions or the delay, withholding, variation 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 that apply to the conduct of clinical trials, manufacturing approval, marketing authorization of medicinal products and marketing of such products, both before and after grant of the marketing authorization, or with other applicable 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, varying 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. Failure to comply with EU and EU

Member State laws that apply to the conduct of clinical trials, manufacturing approval, marketing authorization of medicinal products and marketing of such products, both before and after grant of the marketing authorization, or with other applicable regulatory requirements may result in administrative, civil or criminal penalties. These penalties could include delays or refusal to authorize the conduct of clinical trials, or to grant marketing authorization, product withdrawals and recalls, product seizures, suspension, withdrawal or variation of the marketing authorization, total or partial suspension of production, distribution, manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties.

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, if approved.

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, the EU and other European countries, 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 (ii) either (a) such conditions affect not more than 5 in 10,000 persons in the EU when the application is made, or (b) the product without the benefits derived from orphan status, would not generate sufficient return in the EU to justify the necessary investment in developing the medicinal product; and (iii) there exists no satisfactory authorized method of diagnosis, prevention, or treatment of the condition that has been authorized in the EU, or even if such method exists, the product will be of significant benefit to those affected by that condition. In EU, orphan designation entitles a party to a number of incentives, such as fee reductions or fee waivers, protocol assistance, and access to the centralized marketing authorization procedure. Upon grant of a marketing authorization, orphan medicinal products are entitled to a ten-year period of market exclusivity for the approved therapeutic indication, which means that the EMA cannot accept another marketing authorization application or accept an application to extend for a similar product and the European Commission cannot grant a marketing authorization for the same indication for a period of ten years. The period of market exclusivity is extended by two years for orphan medicinal products that have also complied with an agreed PIP. This marketing exclusivity period can however, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria on the basis of which it received orphan medicinal product destination, including where it can be demonstrated on the basis of available evidence that the original orphan medicinal product is sufficiently profitable not to justify maintenance of market exclusivity or where the prevalence of the condition has increased above the threshold.

Our product candidate, divesiran (SLN124), has received orphan drug designation from the European Commission 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, has received orphan drug designation from the FDA for complement 3 glomerulopathy, or C3G. The EMA and the European

Commission will reassess eligibility for 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 European Commission 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.

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 our current product candidates and clinical trials, 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.

Adverse effects, or 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 or comparable foreign 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 educate the medical community and third-party payers on the benefits of 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, 2025, we had 86 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 believe 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 the 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 share 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, data and internet applications and related tools and functions, or those of third parties with whom we work, 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 sensitive data, and, as a result, we and the third parties with whom we work face a variety of evolving threats that could cause security incidents. 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, or the hardware or software of the third parties with whom we work, malfunctions or access to our data by internal research personnel is interrupted, our business could suffer. Cyber-attacks, malicious internet-based activity, online and offline fraud, and other similar activities threaten the confidentiality, integrity, and availability of our sensitive data and information technology systems, and those of the third parties with whom we work. 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 has in the past and may in the future increase our operating costs. While we have implemented security measures designed to protect against security incidents, there can be no assurance that these measures will be effective.

We and the third parties with whom we work are subject to a variety of evolving threats, including but not limited to social-engineering attacks (including through deep fakes, which are increasingly more difficult to identify as fake, and phishing attacks), malicious code (such as viruses and worms), malware (including as a result of advanced persistent threat intrusions), denial-of-service attacks, credential stuffing attacks, credential harvesting, personnel misconduct or error, ransomware attacks, supply-chain attacks, software bugs, server malfunctions, software or hardware failures, loss of data or other information technology assets, adware, attacks enhanced or facilitated by AI, fire, storm, flood, power loss, earthquakes, telecommunications failures, and other similar threats. These events could lead to the unauthorized access, disclosure and use of our sensitive data and information technology systems. The techniques used by criminal elements to attack computer systems can be 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. During times of war and other major conflicts, we, the third parties with whom we work, may be vulnerable to a heightened risk of these attacks, including retaliatory cyber-attacks, that could materially disrupt our systems and operations, supply chain, and ability to produce, sell and distribute our goods and services. In particular, severe ransomware attacks are becoming increasingly prevalent and can lead to significant interruptions in our operations, ability to provide our products or services, loss of sensitive data and income, reputational harm, and diversion of funds. Extortion payments may alleviate the negative impact of a ransomware attack, but we may be unwilling or unable to make such payments due to, for example, applicable laws or regulations prohibiting such payments. It may be difficult and/or costly to detect, investigate, mitigate, contain, and remediate a security incident. Actions taken by us or the third parties with whom we work to detect, investigate, mitigate, contain, and remediate a security incident could result in outages, data losses, and disruptions of our business. Threat actors may also gain access to other networks and systems after a compromise of our networks and systems. For example, threat actors may use an initial compromise of one part of our environment to gain access to other parts of our environment, or leverage a compromise of our networks or systems to gain access to the networks or systems of third parties with whom we work, such as through phishing or supply chain attacks. As a result, we cannot provide assurance that our efforts to address these threats proactively or implement adequate preventative measures will always be successful.

Remote work has increased risks to our information technology systems and data, as our employees utilize network connections, computers, and devices outside our premises or network, including working at home, while in transit and in public locations. Additionally, future or past business transactions (such as acquisitions or integrations) could expose us to additional cybersecurity risks and vulnerabilities, as our systems could be negatively affected by vulnerabilities present in acquired or integrated entities' systems and technologies. We may discover security issues that were not found during due diligence of such acquired or integrated entities, and it may be difficult to integrate companies into our information technology environment and security program. In addition, supply-chain attacks have increased in frequency and severity, and we cannot guarantee that third parties' infrastructure in our supply chain or that of the third parties with whom we work have not been compromised.

We rely on third-parties to operate critical business systems that process sensitive data. Our ability to monitor these third parties' information security practices is limited, and these third parties may not have adequate information security measures in place. If the third parties with whom we work experience a security incident or other interruption, we could experience, and in certain cases have experienced, adverse consequences. While we may be entitled to damages if the third parties with whom we work fail to satisfy their privacy or security-related obligations to us, any award may be insufficient to cover our damages, or we may be unable to recover such award.

We take steps designed to detect, mitigate, and remediate vulnerabilities in our information systems (such as our hardware and/or software, including that of third parties with whom we work). We have not and may not, however, detect and remediate all such vulnerabilities including on a timely basis. Further, we may experience delays in deploying remedial measures and patches designed to address identified vulnerabilities. Vulnerabilities could be exploited and result in a security incident.

Any of the previously identified or similar threats could cause a security incident or other interruption that could result in unauthorized, unlawful, or accidental acquisition, modification, destruction, loss, alteration, encryption, disclosure of, or access to our sensitive data or our information technology systems, or those of the third parties with whom we work. A security incident or other interruption could disrupt our ability (and that of third parties with whom we work) to operate our business. We may expend significant resources or modify our business activities (including our clinical trial activities) to try to protect against security incidents. Certain data privacy and security obligations have required us to implement and maintain specific security measures or industry-standard or reasonable security measures designed to protect our information technology systems and sensitive information.

If we (or a third party with whom we work) experience a security incident or are perceived to have experienced a security incident, we could experience material adverse consequences, such as government enforcement actions (for example, investigations, fines, penalties, audits, and inspections), litigation (including class claims) and enforcement actions, additional reporting requirements and/or oversight, restrictions on processing sensitive information (including personal data), indemnification obligations; negative publicity, reputational harm, monetary fund diversions, diversion of management attention, and interruptions in our operations (including availability of clinical trial data), financial loss, and other similar harms. Security incidents and attendant material consequences may negatively impact our ability to grow and operate our business. In addition, any sustained disruption in internet systems or network access provided by other companies could harm our business. Similarly, if a security incident were to occur, we may be required, or we may voluntarily choose, to notify relevant stakeholders, including affected individuals, customers, regulators, and investors, of security incidents, or to take other actions, such as providing credit monitoring and identity theft protection services. Such disclosures and related actions can be costly, and the disclosure or the failure to comply with such applicable requirements could lead to adverse consequences, including reputational damage, investigations and fines from regulators, as well as litigation. Furthermore, if we are required to disclose the occurrence of a cybersecurity incident, the price of our ADSs may be negatively impacted.

Our contracts may not contain limitations of liability, and even where they do, there can be no assurance that limitations of liability in our contracts are sufficient to protect us from liabilities, damages, or claims related to our data privacy and security obligations. Relatedly, our contracts with third parties with whom we work may limit the types and/or amounts of damages that we can recover from those third parties, even where the third party is responsible for a privacy or cybersecurity incident or violation. We cannot be sure that our insurance coverage will be adequate or sufficient to protect us from or to mitigate liabilities arising out of our privacy and security practices, that such coverage will continue to be available on commercially reasonable terms or at all, or that such coverage will pay future claims.

In addition to experiencing a security incident, third parties may gather, collect, or infer sensitive information about us from public sources, data brokers, or other means that reveals competitively sensitive details about our organization and could be used to undermine our competitive advantage or market position. Additionally, sensitive data of the Company could be leaked, disclosed, or revealed as a result of or in connection with our employees', personnel's, or vendors' use of generative artificial intelligence ("AI"), technologies.

We and the third parties with whom we work are subject to stringent and evolving U.S. and foreign data privacy and security laws, regulations contractual obligations, industry standards, policies, and other obligations, and our (or the third parties with whom we work) actual or perceived failure to comply with such obligations could lead to regulatory investigations or actions; litigation (including class actions); fines and penalties; disruptions of our business operations; reputational harm; loss of revenue or profits; and other adverse business consequences.

In the ordinary course of business, we collect, receive, store, process, generate, use, transfer, disclose, make accessible, protect, secure, dispose of, transmit, and share (collectively, process) personal data and other sensitive information, including proprietary and confidential business data, trade secrets, intellectual property, data we collect about trial participants in connection with clinical trials, sensitive third-party data, business plans, transactions, and financial information (collectively, sensitive data).

Our data processing activities subject us to privacy and data protection obligations, such as various laws, regulations, guidance, industry standards, external and internal privacy and security policies, contractual requirements, and other obligations relating to data privacy and security.

Outside the United States, an increasing number of laws, regulations, guidance and industry standards govern data privacy and security. For example, the European Union's General Data Protection Regulation (EU GDPR) and the United Kingdom's GDPR (U.K. GDPR) (collectively, the GDPR) impose strict requirements for processing personal data (including health data). Under the GDPR, companies may face temporary or definitive bans on data processing and other corrective actions; fines of up to 20 million Euros under the EU GDPR, 17.5 million pounds sterling under the UK GDPR or, in each case, 4% of annual global revenue, whichever is greater; or private litigation related to processing of personal data brought by classes of data subjects or consumer protection organizations authorized at law to represent their interests.

In the ordinary course of business, we may transfer personal data from Europe and other jurisdictions to the United States or other countries. Europe and other jurisdictions have enacted laws requiring data to be localized or limiting the transfer of personal data to other countries. In particular, the European Economic Area (EEA) and the United Kingdom have significantly restricted the transfer of personal data to third countries, including the United States, whose privacy laws it generally believes are inadequate. Other jurisdictions may adopt or have already adopted similarly stringent interpretations of their data localization and cross-border data transfer laws. Although there are currently various mechanisms that may be used to transfer personal data from the EEA and UK to the United States in compliance with law (e.g., the EEA Standard Contractual Clauses, the United Kingdom's International Data Transfer Agreement / Addendum, and the EU-U.S. Data Privacy Framework and the United Kingdom's extension thereto (which allows for transfers to relevant U.S.-based organizations who self-certify compliance and participate in the Framework)), these mechanisms are subject to legal challenges, and there is no assurance that we can satisfy or rely on these measures to lawfully transfer personal data to the United States. If there is no lawful manner for us to transfer personal data from the EEA, the UK or other jurisdictions to the United States, or if the requirements for a legally-compliant transfer are too onerous, we could face significant adverse consequences, including the interruption or degradation of our operations, the need to relocate part of or all of our business or data processing activities to other jurisdictions (such as Europe) at significant expense, increased exposure to regulatory actions, substantial fines and penalties, the inability to transfer data and work with partners, vendors and other third parties, and injunctions against our processing or transferring of personal data necessary to operate our business. Additionally, companies that transfer personal data out of the EEA and UK to other jurisdictions, particularly to the United States, are subject to increased scrutiny from regulators, individual litigants, and activist groups. Some European regulators have ordered certain companies to suspend or permanently cease certain transfers out of Europe for allegedly violating the GDPR's cross-border data transfer limitations. Additionally, the U.S. Department of Justice issued a rule entitled the Preventing Access to U.S. Sensitive Personal Data and Government-Related Data by Countries of Concern or Covered Persons, which places additional restriction on certain data transactions involving countries of concern (e.g., China, Russia, Iran) and covered persons (i.e., individuals and entities who are designated as such by the U.S. Attorney General or considered "foreign persons" and are majority owned by, organized under the laws of, a primary resident in, or a contractor of, a covered person or country of concern, as applicable) that may impact certain business activities such as vendor engagements, sale or sharing of data, employment of certain individuals, and investor agreements. Violations of the rule could lead to significant civil and criminal fines and penalties. The rule applies regardless of whether data is anonymized, key-

coded, pseudonymized, de-identified or encrypted, which presents particular challenges for companies like ours and may impact our ability engage in transactions or agreements with certain third parties in the future.

In the United States, federal, state, and local governments have enacted numerous data privacy and security laws, including data breach notification laws, personal data privacy laws, consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act), and other similar laws (e.g., wiretapping laws). Numerous U.S. states have enacted comprehensive privacy laws that impose certain obligations on covered businesses, including providing specific disclosures in privacy notices and affording residents with certain rights concerning their personal data. As applicable, such rights may include the right to access, correct, or delete certain personal data, and to opt-out of certain data processing activities, such as targeted advertising, profiling, and automated decision-making. The exercise of these rights may impact our business and ability to provide our products and services. Certain states also impose stricter requirements for processing certain personal data, including sensitive information, such as conducting data privacy impact assessments. These state laws allow for statutory fines for noncompliance. For example, the California Consumer Privacy Act of 2018 (CCPA) applies to the personal data of consumers, business representatives, and employees who are California residents and requires businesses to provide specific disclosures in privacy notices and honor requests of such individuals to exercise certain privacy rights. The CCPA provides for fines and allows private litigants affected by certain data breaches to recover significant statutory damages. The CCPA and other comprehensive U.S. state privacy laws exempt some data processed in the context of clinical trials, these developments further complicate compliance efforts, and increase legal risk and compliance costs for us and the third parties with whom we work, should we become subject to such laws in the future. Similar laws are being considered in several other states, as well as at the federal and local levels, and we expect more states to pass similar laws in the future. Failure to comply with federal and state laws in the United States regarding privacy and security of personal data 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.

In addition, our employees and personnel use generative AI or automated decision-making technologies (collectively, AI technologies) to perform their work, and the disclosure and use of personal data in AI technologies is subject to various privacy laws and other privacy obligations. Governments have passed and are likely to pass additional laws regulating AI technologies. Our use of this technology could result in additional compliance costs, regulatory investigations and actions, and lawsuits. If we are unable to use AI technologies, it could make our business less efficient and result in competitive disadvantages.

We are bound by contractual obligations related to data privacy and security, and our efforts to comply with such obligations may not be successful. We also publish policies, marketing materials, and other statements concerning data privacy and security. Regulators are increasingly scrutinizing these statements, and if these policies, materials or statements are found to be deficient, lacking in transparency, deceptive, unfair, misleading, or misrepresentative of our practices, we may be subject to investigation, enforcement actions by regulators, or other adverse consequences.

Obligations related to data privacy and security (and individuals' data privacy expectations) are quickly changing, becoming increasingly stringent, and creating uncertainty. Additionally, these obligations may be subject to differing applications and interpretations, which may be inconsistent or conflict among jurisdictions. Preparing for and complying with these obligations requires us to devote significant resources, which may necessitate changes to our services, information technologies, systems, and practices and to those of any third parties that process personal data on our behalf. In addition, these obligations may require us to change our business model.

We may at times fail (or be perceived to have failed) in our efforts to comply with our data privacy and security obligations. Moreover, despite our efforts, our personnel or third parties with whom we work may fail to comply with such obligations, which could negatively impact our business operations and compliance posture. For example, any failure by a third party with whom we work to comply with applicable law, regulations, or contractual obligations could result in adverse effects, including inability to or interruption in our ability to operate our business and proceedings against us by governmental entities or others. If we or the third parties with whom we work fail, or are perceived to have failed, to address or comply with applicable data privacy and security obligations, we could face significant consequences, including but not limited to: government enforcement actions (e.g., investigations, fines, penalties, audits, inspections, and similar); litigation (including class-action claims) and mass arbitration

demands; additional reporting requirements and/or oversight; bans or restrictions on processing personal data (including clinical trial data); orders to destroy or not use personal data; and imprisonment of company officials. In particular, plaintiffs have become increasingly more active in bringing privacy-related claims against companies, including class claims and mass arbitration demands. Some of these claims allow for the recovery of statutory damages on a per violation basis, and, if viable, carry the potential for monumental statutory damages, depending on the volume of data and the number of violations.

Any of these events could have a material adverse effect on our reputation, business, or financial condition, including but not limited to: loss of customers; interruptions or stoppages in our business operations (including, as relevant, clinical trials); inability to process personal data or to operate in certain jurisdictions; limited ability to develop or commercialize our products; expenditure of time and resources to defend any claim or inquiry; adverse publicity; or revision or restructuring of our operations.

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 EU Member 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.

Our relationships with U.S. healthcare providers, including physicians, and third-party payers will be subject to applicable U.S. anti-kickback, fraud and abuse, anti-bribery and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers and third-party payers play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our current and future arrangements with healthcare providers, third-party payers and customers may expose us to broadly applicable U.S. federal and state fraud and abuse, transparency, health data privacy, and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we research as well as market, sell and distribute our products for which we obtain marketing approval. If we are found to be in violation of any of any healthcare laws or any other federal or state regulations, we may be subject to significant administrative, civil and/or criminal penalties, damages, fines, disgorgement, imprisonment, exclusion from federal health care programs, additional reporting requirements and/or oversight, and the curtailment or restructuring of our operations. For more information regarding the healthcare laws to which we may be subject, see “*Business—Federal and State Fraud and Abuse, Data Privacy and Security, and Transparency Laws and Regulations and Foreign Equivalents*”.

Healthcare legislative and other regulatory 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, require direct price negotiations for certain high-expenditure, single-source prescription drugs and biologics covered by the Medicare program, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. For example, on July 4, 2025, the annual reconciliation bill, the “One Big Beautiful Bill Act,” or OBBBA, was signed into law which is expected to reduce Medicaid spending and enrollment by implementing work requirements for some beneficiaries, capping state-directed payments, reducing federal funding, and limiting provider taxes used to fund the program. OBBBA also narrows access to Affordable Care Act, or ACA, marketplace exchange enrollment and declines to extend the ACA enhanced advanced premium tax credits, set to expire at the end of 2025, which, among other provisions in the law, are anticipated to reduce the number of Americans with health insurance. In addition, there have been actions and proposals from the Trump administration that include: reducing agency workforce and cutting programs; directing HHS and other agencies to lower prescription drug costs through a variety of initiatives, including by improving upon the Medicare Drug Price Negotiation Program and establishing Most-Favored-Nation pricing for pharmaceutical products; imposing tariffs on imported pharmaceutical products; directing certain federal agencies to enforce existing law regarding hospital and plan price transparency and by standardizing prices across hospitals and health plans; and as part of the Make America Healthy Again (MAHA) Commission’s recent Strategy Report, working across government agencies to increase enforcement on direct-to-consumer pharmaceutical advertising. In addition, on September 30, 2025, the current administration announced the first agreement with a major pharmaceutical company that requires the drug manufacturer to offer, through a direct-to-consumer platform, U.S. patients and Medicaid programs prescription drug Most-Favored Nation pricing equal to or lower than those paid in other developed nations, with additional mandates for direct-to-patient discounts and repatriation of foreign revenues. While many of these 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.

In addition, the policies of the FDA, the competent authorities of the EU Member States, the EMA, the European Commission and other comparable regulatory authorities responsible for clinical trials may change and additional government regulations may be enacted. For instance, the regulatory landscape related to clinical trials in the EU recently evolved. The EU Clinical Trials Regulation, or CTR, which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. The CTR introduces, among other changes, a centralized application system, coordinated review procedures, expanded reporting and increased transparency obligations. The CTR foresaw a three-year transition period that ended on January 31, 2025. Since this date, all new or ongoing trials are subject to the provisions of the CTR. Compliance with the CTR requirements by us and our third-party service providers, such as CROs, may impact our developments plans.

Following a public consultation that began in 2022, the United Kingdom government has enacted new legislation to overhaul the clinical trials regulatory framework. In April 2025, the UK adopted an amendment to the Medicines for Human Use (Clinical Trials) Regulations 2004 intended to support a more streamlined and flexible regulation of clinical trials, remove unnecessary administrative burdens on trial sponsors, and protect the interests of trial participants. It also intends to bring the UK regulatory framework for clinical trials into closer alignment with the CTR. The amendment will become applicable on April 28, 2026, following a one-year transition period. While these changes introduce efficiencies and align with some principles of the EU's CTR, divergence between the United Kingdom and EU regulatory systems remains. Any significant divergence could affect the cost and complexity of conducting clinical trials in the United Kingdom and may impact the acceptability of United Kingdom-based trial data for seeking marketing authorizations in the EU, and vice versa.

Moreover, in order to obtain reimbursement for our products in some European countries, including some EU Member States, we may be required to compile additional data comparing the cost-effectiveness of our products to other available therapies. This Health Technology Assessment, or HTA, of medicinal products is becoming an increasingly common part of the pricing and reimbursement procedures in some EU Member States, including those representing the larger markets. The HTA process is the procedure to assess therapeutic, economic and societal impact of a given medicinal product in the national healthcare systems of the individual country. The outcome of an HTA will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU Member States. The extent to which pricing and reimbursement decisions are influenced by the HTA of the specific medicinal product currently varies between EU Member States. The HTA Regulation has applied from January 12, 2025, although it will enter into force iteratively and initially apply to new active substances to treat cancer and to all advanced therapy medicinal products (ATMPs), it will then be expanded to orphan medicinal products in January 2028, and to all centrally authorized medicinal products as of 2030. Selected high-risk medical devices will also be assessed under the HTA Regulation as of 2026. The HTA Regulation is intended to harmonize the clinical benefit assessment of HTA across the EU and permits EU Member States to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the most potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. However, there is concern that there are insufficient slots available for joint scientific advice during development. If advice is unavailable during development, there is a higher risk of data gaps and therefore delays in access for patients. Individual EU Member States will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technologies, and making decisions on pricing and reimbursement. If we are unable to maintain favorable pricing and reimbursement status in EU Member States for product candidates that we may successfully develop and for which we may obtain regulatory approval, any anticipated revenue from and growth prospects for those products in the EU could be negatively affected. In light of the fact that the United Kingdom has left the EU, Regulation No 2021/2282 on HTA does not apply in the United Kingdom. However, MHRA is working with UK HTA bodies and other national organizations, such as the Scottish Medicines Consortium, the National Institute for Health and Care Excellence, or NICE, and the All-Wales Medicines Strategy Group, to introduce new pathways supporting innovative approaches to the safe, timely and efficient development of medicinal products, including, effective as of 31 March, 2025, relaunching the Innovative Licensing and Access Pathway with more predictable timelines and closer involvement of the National Health Service.

In addition, on December 11, 2025, the European Commission, the Parliament and the European Council reached a political agreement on a comprehensive overhaul of EU pharmaceutical legislation (the Pharma Package). The reform has been under negotiation since the European Commission submitted its proposal in April 2023. This package - comprised of a new directive and regulation to replace existing legislation - aims to modernize the EU framework. The political agreement is still subject to formal approval by the European Parliament and Council. If approved in the form proposed, the Pharma Package will, among other changes, reduce the baseline market protection period by one year, with limited opportunities for extensions; reshape the incentives regime for orphan medicinal products; and expand the Bolar exemption. A decrease in market exclusivity opportunities for our product candidates in the EU, combined with the expanded Bolar exemption, could open them to generic or biosimilar competition earlier than under the current regime, potentially impacting reimbursement status and the commercial prospects of our product candidates.

If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, our development plans may be impacted. For more information regarding the healthcare reforms that may affect our business, see “*Business—Coverage and Reimbursement in the United States*”.

We may face uncertainty related to pricing, coverage and reimbursement for our product candidates.

Sales of our product candidates in the United States, if approved, will depend, in part, on the extent to which such products will be covered by third-party payers, such as government health care programs, commercial insurance and managed healthcare organizations. These third-party payers are increasingly limiting coverage and/or reducing reimbursements for medical products and services. A third-party 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 ensure that other payers will also provide coverage for the drug product. Coverage policies and third-party payer reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for products for which we receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future. In addition, the U.S. government, state legislatures and foreign governments have continued implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. Decreases in third-party payer reimbursement or a decision by a third-party payer to not cover any of our product candidates, if approved, could reduce physician usage of our product candidates, and have a material adverse effect on our sales, results of operations and financial condition. If we are unable to obtain adequate levels of reimbursement, our ability to successfully market and sell any product candidates will be harmed.

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

Our consolidated financial statements are presented in U.S. dollars. The individual financial statements of each subsidiary is prepared in the currency of the primary economic environment in which the entity operates (its functional currency). Our transactions are commonly denominated in U.K pounds sterling; however, we incur a portion of our expenses in other currencies, primarily U.S. dollars and in the past, we received payments under collaboration agreements in U.S. dollars. 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 proceedings did not or will 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, which may or may not cover our current or future products and product candidates, 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 and affect us adversely 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 Europe and in other jurisdictions outside the United States. 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, if approved, 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 or methods of use, including combination therapies, 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 seek to obtain injunctive or other equitable relief, which if successful 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, could 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 licensed specified patents to Alnylam, and Alnylam paid us a tiered royalty of up to one percent of its net sales of ONPATTRO in the European Union through December 2023.

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 any future licensor 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 which could negatively impact our ability to develop and potentially commercialize our product candidates, if approved.

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 partners or future 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 even 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

We are a "smaller reporting company" and, as a result of the reduced disclosure requirements applicable to smaller reporting companies, our ADSs may be less attractive to investors.

We are a "smaller reporting company," as defined in the Exchange Act, and we intend to take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not "smaller reporting companies," including reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. We are also a non-accelerated filer and are not required to comply with the auditor attestation requirements of Section 404(b) of the Sarbanes-Oxley Act of 2002. Our internal controls over

financial reporting will not receive the level of review provided by the process relating to the auditor attestation included in annual reports of issuers that are subject to these requirements.

We cannot predict if investors will find our ADSs less attractive because we may rely on 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 may take advantage of these reporting exemptions until we are no longer a “smaller reporting company.” We will remain a “smaller reporting company” until (a) the aggregate market value of our outstanding ADSs held by non-affiliates as of the last business day of our most recently completed second fiscal quarter is \$250 million or more and we reported annual net revenues as of our most recently completed fiscal year of \$100 million or more, or (b) the aggregate market value of our outstanding ADSs held by non-affiliates as of the last business day of our most recently completed second fiscal quarter is \$700 million or more, regardless of annual revenue.

We have incurred and will continue to incur increased costs as a result of operating as a public company, and our management has devoted and will continue to be required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, we will incur significant legal, accounting and other expenses that we did not previously incur as a private company or as an emerging growth company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the Nasdaq Global Select Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Once we are no longer able to take advantage of the exemptions from various reporting requirements that are applicable to emerging growth companies, we will be required to comply with auditor attestation requirements, increased disclosure obligations and other reporting requirements which will likely increase our costs in the upcoming fiscal year. Our management and other personnel devote and will need to continue to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs, particularly as we hire additional financial and accounting employees to meet public company internal control and financial reporting requirements and will make some activities more time-consuming and costly compared to when we were a private company. For example, as a public company it is more difficult and more expensive for us to obtain director and officer liability insurance, and we may be forced to accept reduced policy limits and coverage or incur substantial costs. The impact of these events could also make it more difficult for us to attract and retain qualified members of our board of directors.

Pursuant to Section 404 of the Sarbanes-Oxley Act, or Section 404, we are required to furnish a report by our management on our internal control over financial reporting. However, while we remain a smaller reporting company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we are 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, including through hiring additional financial and accounting personnel, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses in our internal control over financial reporting, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

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 has been and will likely continue to be highly volatile and 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 Annual 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, or perceived 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 authorities with respect to our clinical trials or manufacturers;
- commencement of, or involvement in, litigation involving us;
- 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 ADSs by third parties, including market manipulation;
- publication of information, including in the media, online blogs and social media, about our company by third parties, including equity research analysts;
- sales of our ADSs 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 wars in Ukraine and Israel and global and regional economic and political disruptions;
- 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 and any failure to meet expectations of investors or equity research analysts.

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 securities 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 could adversely affect the price of such securities.

Future sales of a substantial number of ADSs, or the perception that such sales will occur, could cause a decline in the market price of our ADSs. If our shareholders 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 may 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. 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 46% of our issued and outstanding ordinary shares, based on the number of ordinary shares issued and outstanding as of December 31, 2025. 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 may identify material weaknesses in our internal control over financial reporting in the future. If we experience material weaknesses or significant 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.

There can be no assurance that we will not identify additional control deficiencies or material weaknesses in the future.

In addition, if we identify 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 when required, 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.

If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, shareholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our ADSs.

Effective internal control over financial reporting is necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, is designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal control over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could harm our business and have a negative effect on the trading price of our ADSs.

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 of 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.

Based on the nature of our activities and the composition of our income and assets, we believe we were classified as a PFIC for our taxable year ended December 31, 2025. 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 each year we are treated as a PFIC with respect to U.S. Holders (as defined below), U.S. Holders will be subject to adverse U.S. federal income tax consequences, such as ineligibility for any preferential tax rates for individuals on capital gains or on actual or deemed dividends, interest charges on certain taxes treated as deferred, and additional reporting requirements under U.S. federal income tax laws and regulations, unless 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 our ordinary shares constitute “marketable stock” and such U.S. Holder makes a mark-to-market election.

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 our ordinary shares or ADSs in a PFIC if such company agrees to furnish such U.S. Holder with certain tax information annually. For the taxable year ending December 31, 2025, we intend to make available, upon request, certain information to enable U.S. Holders to make a QEF Election with respect to our ordinary shares or ADSs. However, we cannot guarantee that we will make such information available for all years in which we are a PFIC or that the information will be available at the time required for any particular U.S. Holder to make a QEF Election.

If we are a PFIC and our ordinary shares or ADSs are "marketable stock," U.S. Holders can avoid the interest charge on excess distributions or gain relating to the common shares by making a mark-to-market election on our ordinary shares or ADSs. Our ordinary shares or ADSs will be marketable stock if they are "regularly traded" on certain stock exchanges (including Nasdaq). 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 the ordinary shares or ADSs at the close of the taxable year over the U.S. Holder's adjusted tax basis in the common shares. 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.

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 makes 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.

Each U.S. Holder should consult its own tax advisors with respect to the potential adverse U.S. tax consequences to it if we are or were to become a PFIC and any elections (including a QEF Election, mark-to-market election, or deemed sale election) that may be available to such U.S. Holder that relate to our status as a PFIC.

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

- a citizen or individual resident of the United States;
- a corporation, or other entity taxable as a corporation, created or organized in or under the laws of the United States, any state therein or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust that (a) is subject to the primary supervision of a U.S. court and the control of one or more "United States persons" (within the meaning of Section 7701(a)(30) of the Code) or (b) has a valid election in effect to be treated as a United States person for U.S. federal income tax purposes.

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, 2025, we had cumulative U.K. carryforward tax losses of \$231.6 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, or R&D, activities, we seek to benefit from the U.K. R&D tax credit regime. In respect of accounting periods in which we qualify as a Small and Medium-sized Enterprise, or SME, and in which qualifying R&D expenditure represents 30% (for periods from April 1, 2024) or more of the total (meaning we are considered as "R&D-intensive" during such accounting period), we may, under this regime, surrender the trading losses that arise from our R&D activities for a cash rebate of up to 26.97% of qualifying R&D expenditure. Accordingly, if we cease to qualify as an R&D-intensive SME, in future, we will either cease to be able to claim cash rebates in respect of our R&D activities, or only be able to receive cash payments or other tax relief (under other provisions of the U.K. R&D tax credit regime) at a significantly lower rate than at present. Further, the regime's rules are complex, and if a tax authority were to challenge or seek to disallow our claims (in whole or in part), for example by asserting that we do not (or the relevant expenditure does not) meet the technical conditions to be granted tax credits (or cash rebates), then such challenge or disallowance, if successful, could have a material impact on our cash-flow and financial performance. In addition, future changes to the U.K. R&D tax credit regime may mean that we no longer qualify for it or have a material impact on the extent to which we can make claims (or benefit from them).

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%. Our patent families, whether solely owned or jointly owned, create rights in current or future 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 R&D 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. R&D tax credit regime or the "patent box" regime, or for any reason we are unable to qualify for such advantageous tax legislation, or we are unable to use net operating loss and tax credit carryforwards and certain built-in losses to reduce future tax payments, then 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 or being implemented (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, or the stamp duty or stamp duty reserve tax treatment of our ADSs or ordinary shares.

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, will not apply if our place of management and control remains outside the United Kingdom.

Following the cancellation of admission of our ordinary shares to trading on AIM in November 2021 and under transitional provisions that apply until February 2027, the Takeover Code will only apply to us if we are considered by the Panel on Takeovers and Mergers, or the Takeover Panel, to have our place of central management and control in the United Kingdom (or the Channel Islands or the Isle of Man). This is known as the “residency test”. 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 it is applied by the United Kingdom tax authorities. Under the Takeover Code, the Takeover Panel looks to where the majority of the directors of the company are resident, amongst other factors, for the purposes of determining where the company has its place of central management and control.

The Takeover Panel has confirmed that based on the composition of our board of directors following Alistair Gray’s retirement from the board, effective May 1, 2024, we are no longer subject to the Takeover Code. As a result, our shareholders are not currently entitled to the benefit of certain takeover offer protections provided under the Takeover Code. We believe that this position is unlikely to change until the end of the transitional period, but, in accordance with good practice, we will review the situation on a regular basis and consult with the Takeover Panel if there is any change in our circumstances which may have a bearing on whether the Takeover Panel would determine our place of central management and control to be in the United Kingdom.

Following the end of the transitional period, with effect from February 3, 2027, the “residency test” will be abolished in its entirety and we expect we will no longer be subject to the jurisdiction of the Takeover Code at all from that time, unless our securities are listed in the United Kingdom.

We have incorporated certain takeover protections in our articles of association, which apply in circumstances where the Takeover Code does not apply to us. A resolution was passed at our annual general meeting held on June 26, 2025, to approve the continued application of these provisions until our 2026 annual general meeting.

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 stockholders 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). At our annual general meeting of shareholders held on April 27, 2023, we obtained authority from our shareholders to allot new shares or to grant rights to subscribe for or to convert any security into shares in the company up to a maximum aggregate nominal amount of £5,402,633.25 for a period of five years from the date of such annual general meeting of shareholders, which authorization will need to be renewed upon expiration (i.e., at least every five years) but may be sought more frequently for additional five-year terms (or any shorter period).

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). At our annual general meeting of shareholders held on April 27, 2023, we obtained authority from our shareholders to disapply preemptive rights in connection with the allotment of equity securities up to a maximum aggregate nominal amount of £5,402,633.25 for a period of five years from the date of such annual general meeting of shareholders which disapplication will need to be renewed upon expiration (i.e., at least every five years), but may be sought more frequently for additional five year terms (or any shorter period).

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. 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 for 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 depository 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 depository 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 depository 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 depository. If a lawsuit is brought against us or the depository 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 1B. Unresolved Staff Comments

Not applicable to us since we are not an accelerated filer, a large accelerated filer or a well-known seasoned issuer under SEC rules.

Item 1C. Cybersecurity

Risk management and strategy

We have implemented and maintain various information security processes designed to identify, assess, and manage material risks from cybersecurity threats to our critical computer networks, third party hosted services, communications systems, hardware and software, and our critical data, including intellectual property, confidential information that is proprietary, strategic or competitive in nature, and our clinical trial and related data, or Information Systems and Data.

Our information security function, which is led by our Vice President and Head of Information Technology, known as our Head of IT, and supported by our security management, risk management, and legal teams, helps identify, assess, and manage our cybersecurity threats and risks, including through the use of our risk register. The information security function identifies and assesses cybersecurity threats and risks by monitoring and evaluating our threat environment and risk profile using various methods including, for example: automated tools, subscribing to reports and services that identify cybersecurity threats, analyzing reports of threats, evaluating threats reported to us, coordinating with law enforcement concerning threats, internal and external audits, leveraging internal and third party threat assessments, conducting vulnerability identification assessments, and leveraging external threat intelligence.

Depending on the environment or system, we implement and maintain various technical, physical, and organizational measures, processes, standards and policies designed to manage and mitigate material risks from cybersecurity threats to our Information Systems and Data, including, for example: incident detection and response, vulnerability management, disaster recovery and business continuity plans, risk assessments, achievement of certain security certifications, encryption of certain data, network security controls, data segregation for certain data, access controls, physical controls, systems monitoring, employee training, penetration testing, and asset management and disposal.

Our assessment and management of identified material risks from cybersecurity threats are integrated into our overall risk management processes. For example, certain information about our assessment and management of material risks from cybersecurity threats is included in risk management reports as applicable to senior leadership and the audit committee.

We use third-party service providers to assist us from time to time to identify, assess, and manage material risks from cybersecurity threats, including for example: threat intelligence providers, cybersecurity consultants and software providers, managed cybersecurity service providers, and penetration testing service providers.

We use third-party service providers to perform a variety of functions throughout our business, such as software-as-a-service providers, hosting companies, contract research organizations, and contract manufacturing organizations. Depending on the nature of the services provided, the sensitivity of the critical systems, information and assets at issue, and the identity of the provider, we may conduct a review of security assessments provided by the vendor, review the vendor's written security program and/or requested security assessment and security questionnaire responses, and impose contractual obligations on vendors regarding their cybersecurity practices.

For a description of the risks from cybersecurity threats that may materially affect us, please, see our risk factors under Part 1. Item 1A. Risk Factors in this Annual Report, including "Cybersecurity risks and the failure to maintain the confidentiality, integrity, and availability of our computer hardware, software, data and internet applications and related tools and functions, or those of third parties with whom we work, could result in damage to our reputation and/or subject us to costs, fines or lawsuits."

Governance

Our board of directors addresses the review of our IT and cybersecurity risk management as part of its general oversight function. The board of directors' audit and risk committee is responsible for overseeing our cybersecurity risk management processes.

Our cybersecurity risk assessment and management processes are implemented and maintained by our Head of IT, who has achieved ACC Internetworking Engineer and Global Secure Systems Internetworking Engineer qualifications and has over 25 years of experience leading international IT departments and owning responsibility for organizations' cybersecurity efforts.

Our Head of IT is responsible for hiring appropriate personnel, helping to integrate cybersecurity risk considerations into the Company's overall risk management strategy, and communicating key priorities to relevant personnel. Our Head of IT is also responsible for approving budgets, helping prepare for cybersecurity incidents, approving cybersecurity processes, and reviewing security assessments and other security-related reports.

Our cybersecurity incident response processes are designed to escalate certain cybersecurity incidents to members of management depending on the circumstances, including the Executive Leadership Team, or ELT. The ELT works with our incident response team to help us mitigate and remediate cybersecurity incidents of which they are notified. In addition, our incident response process includes notifying the audit and risk committee of the board of directors, as appropriate.

The board of directors' audit and risk committee receives annual reports from our Head of IT, concerning our significant cybersecurity threats and risk and the processes we have implemented to address them. The audit and risk committee also has access to various reports, summaries or presentations related to cybersecurity threats, risk, and mitigation.

Item 2. Properties

We lease office space in London, England for our corporate headquarters and general and administrative functions, which consists of approximately 4,000 square feet, under a lease with a term through September 2027. 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 (six leases: current lease end dates of April 2026, August 2026, October 2026, 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.

Item 3. 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 do not currently have any pending litigation that, separately or in the aggregate, would, in the opinion of management, have a material adverse effect on our results of operations, financial condition or cash flows. The results of any current or future litigation cannot be predicted with certainty, and regardless of the outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Market Information

Our ordinary shares, nominal value £0.05 per share, are not publicly traded. Our ADSs each represent three ordinary shares of Silence Therapeutics plc and began trading on Nasdaq in September 2020 under the symbol "SLN". Prior to that date, there was no public trading market for ADSs. Our ordinary shares were admitted to trading on AIM from 1995 to November 2021.

Holdings

As of February 21, 2026, there were approximately 1,259 holders of record of our ordinary shares and 95 holders of record of our ADSs. The actual number of holders is greater than these numbers of record holders and includes beneficial owners whose ordinary shares or ADSs are held in street name by brokers and other nominees. This number of holders of record also does not include holders whose shares may be held in trust by other entities.

Dividends

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 or ADSs. 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.

Recent Sales of Unregistered Securities

None.

Issuer Purchases of Equity Securities

None.

Item 6. [Reserved]

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and the related notes thereto appearing elsewhere in this Annual Report. The following discussion is based on our financial information prepared in accordance with U.S. GAAP and regulations of the SEC. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks and uncertainties. You should review the section titled "Risk Factors" for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis, as well as the section titled "Special Note Regarding Forward-Looking Statements."

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 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™ (GalNAc Oligonucleotide Discovery) platform consists of siRNA product candidates designed to precisely target and 'silence' specific disease-associated genes in the liver. Using our mRNAi GOLD platform, we have generated siRNA product candidates targeting areas of high unmet need across rare and common diseases where treatments are limited or inadequate.

Rare Diseases

Divesiran (SLN124) is our potential first-in-class siRNA in Phase 2 development for polycythemia vera, or PV. PV is a rare myeloproliferative neoplasm characterized by the overproduction of red blood cells, or RBCs. Elevated hematocrit, or HCT, - an index of RBC mass - is a hallmark of the disease and HCT levels above 45% increases the risk of thrombotic and cardiovascular events. The current standard of care in all PV patients to control HCT is phlebotomy, daily low-dose aspirin therapy, sometimes in combination with cytoreductive therapies. PV patients have low levels of hepcidin the body's master regulator of iron. Divesiran works by "silencing" the TMPRSS6 gene, lifting the natural brake on hepcidin - the body's master iron regulator. When TMPRSS6 is turned down in people living with PV, hepcidin levels rise, reducing iron availability to the bone marrow. With less iron available, the overproduction of RBCs seen in PV is reduced. This helps keep HCT levels in a safer range and can reduce or eliminate the need for phlebotomies. Additionally, siRNA therapies have a highly potent and durable effect - enabling less frequent and more convenient dosing. In the Phase 1 part of the SANRECO clinical trial evaluating divesiran treatment in 21 PV patients, divesiran produced durable HCT control and substantially reduced phlebotomy use following infrequent dosing (Q6W). Based on the strong durability observed in Phase 1, the ongoing Phase 2 part of the SANRECO trial is evaluating both a Q6W and Q12W dosing interval. The SANRECO Phase 2 trial is fully enrolled and topline results are anticipated in the third quarter of 2026. The U.S. Food and Drug Administration, or FDA, has granted divesiran Fast Track and orphan drug designations for PV. Divesiran has also been granted orphan drug designation by the European Commission for PV in Europe. While our initial focus is on PV, divesiran has shown the potential in preclinical studies to address multiple hematological conditions through the unifying mechanism of elevating hepcidin in conditions with dysregulation of iron homeostasis.

SLN548 is our Phase 1 ready siRNA product candidate that works by "silencing" the complement factor B, or CFB, gene, potentially playing a therapeutic role in conditions associated with over activation of this pathway, including complement-mediated renal diseases, among others. SLN548 has demonstrated positive preclinical results and we are seeking a third-party partner to initiate clinical development.

Cardiometabolic Diseases

Zerlasiran (SLN360) is our Phase 3 ready siRNA product candidate for cardiovascular disease that works by "silencing" the LPA gene, lowering production of apolipoprotein(a), a key component of lipoprotein(a), or Lp(a), that has been associated with an increased risk of cardiovascular events. High Lp(a), defined as 125nmol/L or higher, is a genetically determined cardiovascular risk factor affecting at least 20% of the world's population and is associated with a high risk of heart attack, stroke and aortic stenosis. Unlike low-density lipoprotein, or LDL, Lp(a) levels are predominantly genetically determined, typically by age five, and unaffected by diet or lifestyle. There are currently no approved medicines that selectively lower Lp(a). Guidelines from the European Atherosclerosis Society, or EAS, Canadian Cardiovascular Society, or CCS, and the National Lipid Association, or NLA, suggest at least one test in an adult lifetime. The American College of Cardiology, or ACC, and American Heart Association, or AHA, recommend testing for those with a family history of premature atherosclerotic cardiovascular disease, or ASCVD, or personal history of ASCVD. In Phase 1 and Phase 2 clinical trials, zerlasiran showed the potential to substantially lower Lp(a) levels in ASCVD patients with persisting effects following infrequent dosing and was well tolerated with no major safety concerns. We have received positive regulatory feedback from the FDA and European Medicines Agency, or EMA, on the Phase 3 cardiovascular outcomes study design for zerlasiran in patients with high Lp(a). In 2025, we completed core Phase 3 readiness activities, including manufacturing and supply scale up. Zerlasiran is Phase 3 ready and we are seeking a third-party partner for potential Phase 3 development as well as potential future commercialization.

SLN312 is our siRNA product candidate under our collaboration with AstraZeneca that works by "silencing" ANGPTL3, an important modulator of lipid metabolism. Inhibition of ANGPTL3 has emerged as a promising new therapeutic approach to reduce triglycerides (TG) and LDL-C levels, the latter independent of the LDL-C receptor (LDLR) function. Since ANGPTL3 suppresses lipoprotein lipase, or LPL, and endothelial lipase, or EL, activity, its inhibition facilitates the clearance of very low-density lipoprotein cholesterol, decreasing both LDL-C and TG levels. AstraZeneca shared interim results from its Phase 1 randomized, single-blind, placebo-controlled trial assessing SLN312 in 98 patients with dyslipidemia. Interim results showed SLN312 produced durable dose-dependent reductions in ANGPTL3, triglycerides and atherogenic lipoproteins after single and multiple doses. The strong duration of effect observed supports potential for infrequent dosing. SLN312 was well tolerated with no safety concerns identified. Phase 1 data presentations are planned for medical and research congresses in 2026. On March 4, 2026, AstraZeneca notified Silence that they will not pursue further development of SLN312 beyond Phase 1. We will re-gain full development, manufacturing and commercialization rights globally to this clinical asset following Phase 1 and are evaluating plans for further clinical development.

SLN365 is our potential first-in-class siRNA product candidate that works by "silencing" GPR146, a novel mechanism of action for the management of cholesterol levels in patients, independent of LDLR function. Hypercholesterolemia is a highly prevalent indication with an estimated one in 300 individuals worldwide living with the familial form HeFH (heterozygous) and around one in 300,000 individuals suffering from the form HoFH (homozygous) globally. SLN365 has demonstrated promising preclinical results in non-human primates and we anticipate additional preclinical data in the second quarter of 2026.

SLN098 is our siRNA product candidate that works by "silencing" INHBE, a novel target for obesity supported by human genetics, strong preclinical data and emerging third-party clinical data demonstrating early efficacy and safety. Despite recent advances in obesity treatment, limitations of current standards of care leave millions at risk of further complications. Around one billion patients worldwide are affected by obesity and associated co-morbidities. Current obesity treatments offer weight loss around 15-20% which plateaus after 12-24 months and are associated with up to 40% lean muscle mass loss. More than two thirds of weight loss is regained within the first year after discontinuation of treatment. There is also poor tolerability and compliance with up to 30% of patients discontinuing GLP/GIP agonists treatment. SLN098 has the opportunity to address unmet needs including increasing fat loss, preventing muscle mass loss and slowing weight regain. SLN098 has demonstrated deep and durable knockdown in nonhuman primates and we anticipate additional disease model data in the second quarter of 2026 to further validate the mechanism of action. We believe there is an opportunity to develop SLN098 either as a monotherapy or add-on to GLP/GIP agonists or as a weight maintenance treatment.

Fourth Quarter and Fiscal Year 2025 and Recent Business Highlights

Divesiran: Potential first-in-class siRNA for polycythemia vera (PV)

- Accelerated timing for topline results in the Phase 2 SANRECO trial of divesiran, a potential first-in-class siRNA for PV; now anticipated in the third quarter of 2026, as opposed to our prior guidance of the second half of 2026 due to faster than expected enrollment.

Zerlasiran: Phase 3 ready program for cardiovascular disease due to high Lp(a)

- Completed core Phase 3 readiness activities; program is well positioned for a potential third-party partner to initiate Phase 3 development.

SLN312: Phase 1 siRNA with a competitive profile for dyslipidemia

- AstraZeneca shared results from an interim analysis of a Phase 1 randomized, single-blind, placebo-controlled trial of SLN312, an siRNA silencing ANGPTL3 discovered using Silence's mRNAi GOLD™ platform and developed by AstraZeneca, in 98 patients with dyslipidemia. Data highlights include:
 - SLN312 demonstrated durable dose-dependent reductions in ANGPTL3, triglycerides and atherogenic lipoproteins after single and multiple doses.
 - Strong durability profile observed supporting potential for infrequent dosing.
 - SLN312 was observed to be well tolerated with no safety concerns identified.
 - Phase 1 data presentations are planned for medical and research congresses in 2026.
- On March 4, 2026, AstraZeneca notified Silence that they will not pursue further development of SLN312 beyond Phase 1. Silence will re-gain exclusive rights globally to this clinical asset following Phase 1 and is evaluating plans for further development. AstraZeneca and Silence maintain a broader collaboration leveraging Silence's mRNAi GOLD™ platform for cardiovascular, cardiometabolic, renal and respiratory diseases.

Discovery Pipeline

- Generated promising preclinical data for two new mRNAi GOLD™ platform programs.
 - SLN365, a potential first-in-class siRNA silencing GPR146, a novel mechanism-of-action for cholesterol management independent of LDL-C receptor function.
 - SLN098, an siRNA silencing INHBE, a novel target for obesity supported by human genetics and strong pre-clinical data
- Advanced extra-hepatic cell targeting leveraging our proprietary siRNA platform, generating promising preliminary results in several cell types.

Anticipated 2026 Milestones

- Topline results for the Phase 2 SANRECO trial of divesiran in PV in the third quarter of 2026.
- Additional preclinical data for SLN365 (GPR146) in the second quarter of 2026.
- Additional preclinical data for SLN098 (INHBE) in the second quarter of 2026.
- Phase 1 data presentations for SLN312 at medical and research congresses in 2026.

Corporate Updates

- On December 15, 2025, Iain Ross, Chairman of the Board of Directors, was announced as Interim Principal Executive Officer following the departure of the Company's former CEO; a search is underway for a new CEO.
- In December 2025, James Ede Golightly, a former Silence Non-Executive Director, was reappointed to the Board. Additionally, Rhonda Hellums, CFO of Silence, was appointed to the Board as an Executive Director.

We have incurred significant operating losses and expect to continue to incur significant expenses and operating losses for the near future. These net losses were \$88.6 million and \$45.3 million for the years ended December 31, 2025 and 2024, respectively. As of December 31, 2025, our accumulated deficit was \$562.6 million. We expect to continue to incur significant and increasing expenses and to incur operating losses for the foreseeable future, as we advance our product candidates through preclinical and clinical development and seek regulatory approvals, manufacture drug product and drug supply, maintain and expand our intellectual property portfolio, as well as hire additional personnel, pay for further accounting, audit, legal, regulatory and consulting services, and pay costs associated with maintaining compliance with Nasdaq listing rules and the requirements of the U.S. Securities and Exchange Commission, or SEC, director and officer liability insurance, investor and public relations activities and other expenses associated with operating as a public company.

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 2020. 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 covered five targets initially with AstraZeneca opting to extend the collaboration to a further five targets. AstraZeneca agreed to pay us \$10.0 million upon the exercise of each option to collaborate on an additional target. For each target selected, we are 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 are also 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.

In May 2023, AstraZeneca nominated the first product candidate under our collaboration, SLN312 (ANGPTL3), triggering a \$10.0 million option fee to us. In February 2024, AstraZeneca initiated a Phase 1 clinical trial for SLN312 which triggered another \$10.0 million milestone payment to us. On March 4, 2026, AstraZeneca notified Silence that they will not pursue further development of SLN312 beyond Phase 1. We will re-gain full development, manufacturing and commercialization rights globally to this clinical asset following Phase 1 and are evaluating plans for further clinical development.

Collaboration Agreement with Hansoh

In October 2021, we announced a collaboration agreement with Hansoh, one of the leading biopharmaceutical companies in China, to develop siRNAs for three undisclosed targets leveraging our proprietary mRNAi GOLD™ platform. Under the terms of the agreement, Hansoh had 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 trials. We retained exclusive rights for those two targets in all other territories. We were responsible for all activities up to option exercise and retained responsibility for development outside the China region post phase 1 trials. Hansoh also had the exclusive option to license global rights to a third target at the point of IND filing. Hansoh was 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. In 2023, we achieved two additional preclinical milestones and received \$4 million from the collaboration. In 2024, we achieved an additional preclinical milestone of \$2.0 million from the Hansoh collaboration. In December 2024, Hansoh notified us that it will not pursue further development under the Hansoh collaboration. This represented the conclusion of all required development activities and commitments under the terms of the Hansoh Collaboration and we retain exclusive rights globally for all three targets.

Components of Results of Operations

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 AstraZeneca, we received an upfront cash payment of \$20.0 million in May 2020 and an additional payment of \$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. During the year ended December 31, 2024, we achieved milestone payments totaling \$10.0 million. During the year ended December 31, 2025, we did not achieve any milestone payments. We recognize the upfront payment and milestone payments over time. During the year ended December 31, 2025, we recognized a total of \$0.6 million in revenue under the AstraZeneca agreement.

We entered into a collaboration agreement with Hansoh in October 2021. We received a \$16.0 million 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, 2024, we achieved milestone payments totaling \$2.0 million related to the Hansoh collaboration. We did not achieve any milestone payments for the year ended December 31, 2025. We recognized the upfront payment and milestone payments over time.

In December 2024, Hansoh notified us that it will not pursue further development under the Hansoh collaboration. This represented the conclusion of all required development activities and commitments under the terms of the Hansoh collaboration. During the year ended December 31, 2025, we did not recognize any revenue related to the Hansoh collaboration.

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 costs and general and administrative expenses. Personnel costs, including salaries, benefits, bonuses and share-based payment expenses, 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 Costs

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 costs primarily consist of:

- costs incurred under agreements with CROs and investigative sites that conduct our preclinical studies and clinical trials;
- costs related to manufacturing active pharmaceutical ingredients and drug products for our 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 expenses, 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 costs primarily consists of

- costs of related facilities, equipment and other overhead expenses that are considered directly attributable to research and development; 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 authorities;
- 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 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 costs, 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 remain consistent to support our continued research and development and potential commercialization of our product candidates. We also expect to continue incurring 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.

Restructuring Charges

We have incurred non-recurring restructuring charges associated with a limited reduction in workforce during the year ended December 31, 2025.

Foreign Currency Gain/(Loss), net

Foreign exchange gains and losses relate to cash held in foreign currencies (primarily U.S. Dollars and Euros).

Other Income, net

Other income (expense) primarily relates to interest earned on our cash, cash equivalents, as well as accretion earned on our U.S. treasury bills.

Taxation and Benefit from R&D Tax Credit

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 “Benefit from R&D tax credit.”

As a company that carries out extensive research and development, or R&D, activities, we seek to benefit from the U.K. R&D tax credit regime. In respect of accounting periods in which we qualify as a Small and Medium-sized Enterprise, or SME, and in which our qualifying R&D expenditure represents 30% (for periods from April 1, 2024) or more of the total (meaning we are considered as “R&D-intensive” during such accounting period), we may, under this regime, surrender the trading losses that arise from our R&D activities for a cash rebate of up to 26.97% of qualifying R&D expenditure. Accordingly, if we cease to qualify as an R&D-intensive SME, in future, we will either cease to be able to claim cash rebates in respect of our R&D activities, or only be able to receive cash payments or other tax relief (under other provisions of the U.K. R&D tax credit regime) at a significantly lower rate than at present. Further, the regime’s rules are complex, and if a tax authority were to challenge or seek to disallow our claims (in whole or in part), for example by asserting that we do not (or the relevant expenditure does not) meet the technical conditions to be granted tax credits (or cash rebates), then such challenge or disallowance, if successful, could have a material impact on our cash-flow and financial performance. In addition, future changes to the U.K. R&D tax credit regime may mean that we no longer qualify for it or have a material impact on the extent to which we can make claims (or benefit from them).

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 \$231.6 million as of December 31, 2025 (\$164.8 million as of December 31, 2024). 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 \$52.1 million of accumulated tax losses as of December 31, 2025 (\$47.0 million as of December 31, 2024) related to our operations in Germany for corporate income taxes. We also had \$50.4 million of accumulated losses related to trade taxes in our German entity (\$45.6 million as of December 31, 2024). Foreign tax expenses in Germany were negligible (2024: \$0.6 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, 2025 and 2024

The following tables summarize the results of our operations for the years ended December 31, 2025 and 2024.

	Year ended December 31,		
	2025	Change	2024
	\$000s		\$000s
Revenue	\$ 559	\$ (42,699)	\$ 43,258
Cost of sales	(215)	11,595	(11,810)
Gross profit	344	(31,104)	31,448
Research and development costs	(67,753)	130	(67,883)
General and administrative expenses	(22,344)	4,540	(26,884)
Restructuring charges	(1,324)	(1,324)	-
Operating loss	(91,077)	(27,758)	(63,319)
Foreign currency (loss)/gain, net	(8,467)	(9,113)	646
Other income, net	3,480	(992)	4,472
Benefit from R&D tax credit	7,463	(6,274)	13,737
Loss for the year before taxation	(88,601)	(44,137)	(44,464)
Income tax expense	(11)	834	(845)
Net Loss	\$ (88,612)	\$ (43,303)	(45,309)
Loss per share (basic and diluted)	\$ (0.63)		\$ (0.33)
Weighted average shares outstanding (basic and diluted)	141,694,702		138,752,224

Revenue

Revenue for the year ended December 31, 2025 was \$0.6 million (2024: \$43.3 million). The significant decrease in revenue for 2025 was primarily due to the recognition of revenue associated with the Hansoh collaboration in 2024. In 2024, we recognized \$24.6 million related to the Hansoh collaboration resulting from a cumulative catch up as we have now completed all required obligations under the Hansoh collaboration. Revenue from our AstraZeneca collaboration also decreased by \$17.4 million due to decreased activity under the AstraZeneca collaboration. Further, we did not achieve any milestones under the AstraZeneca collaboration in 2025 as compared to achievement of a milestone payment of \$10.0 million in 2024.

Cost of Sales

Cost of sales consists of research and development expenditure that is directly related to work carried out on revenue generating contracts, which decreased to \$0.2 million for the year ended December 31, 2025 (2024: \$11.8 million). The change was due to activity associated with our collaboration agreements, which fluctuates based on the timing of activities and project progression.

Research and Development Expenses

The following table summarizes our research and development costs for the years ended December 31, 2025 and 2024.

	Year ended December 31,	
	2025	2024
	\$000s	\$000s
Contracted development costs	(44,873)	(42,902)
Personnel costs	(18,086)	(20,503)
Other costs	(4,794)	(4,478)
Total	<u>\$ (67,753)</u>	<u>\$ (67,883)</u>

Research and development costs for the year ended December 31, 2025, were \$67.8 million as compared to \$67.9 million for the year ended December 31, 2024. This slight decrease was mainly due to a reduction in personnel costs of \$2.4 million associated with decreased headcount. Contracted development costs in 2025 increased by \$2.0 million from 2024 as a result of additional clinical trials and an increase in contract manufacturing activities for our proprietary programs.

The following table summarizes our research and development costs by program for our clinical development candidates for the years ended December 31, 2025 and 2024.

	Year ended December 31,	
	2025	2024
	\$000s	\$000s
Contracted development costs		
Zerlasiran	27,701	30,270
Divesiran	12,764	9,036
Other contracted development costs	4,408	3,596
Total	<u>\$ 44,873</u>	<u>\$ 42,902</u>

The increase in contracted development costs was largely due to advancement of our proprietary programs, including specifically our Phase 2 clinical trial for divesiran and an increase in costs related to contract manufacturing activities related to our zerlasiran Phase 3 readiness.

General and Administrative Expenses

General and administrative expenses were \$22.3 million for the year ended December 31, 2025, as compared to \$26.9 million for the year ended December 31, 2024. The slight decrease general and administrative expenses for 2025 is mainly due to reduced personnel costs and reduced legal expenses. The reduced personnel costs are largely due a \$1.9 million credit in share-based compensation expense related to forfeiture of certain awards for executive officer that is no longer with the company, which was partly offset by the accrued expense related to their cash severance payment.

Restructuring Charges

We have incurred non-recurring restructuring charges associated with a limited reduction in workforce, which was implemented in June 2025.

Foreign Currency Gain/(Loss), Net

Net foreign exchange gains and losses result primarily from foreign currency (U.S. dollar and EUR) denominated bank accounts. As the functional currency for our parent entity is U.K. pounds sterling and our cash

and cash equivalents and U.S. treasury bills are primarily held in U.S. dollars, the loss in the year ended December 31, 2025 is mainly related to the fluctuation in the U.S. dollar.

Other Income, Net

Other income (expense) relates to accretion from U.S. treasury bills and interest on cash accounts.

Benefit from R&D Credit

Benefit from R&D tax credit relates to U.K. research and development tax credits. The decrease in benefit in the current year was mainly related to changes in the U.K R&D tax credit regime which apply in respect of accounting periods commencing on or after April 1, 2024. These changes led to a reduction in costs that are eligible for the claim.

Taxation

Taxation expense relates to foreign taxation.

Functional Currency

On January 1, 2026, the functional currency of our U.K. entity has changed from U.K. pound sterling to U.S. dollar as the primary economic environment in which the entity operates had changed. This is a prospective change and will not impact historical reporting periods.

Liquidity and Capital Resources

Sources of Liquidity

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.

As of December 31, 2025, we had cash, cash equivalents and U.S. treasury bills of \$85.1 million. We believe that our current cash, cash equivalents and U.S. treasury bills will be sufficient to fund our forecasted operating expenses and capital expenditure requirements into 2028, based on the Company's evaluation as described in the consolidated financial statements, footnote 2.5 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, or at all.

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.

On October 15, 2021, we entered into an Open Market Sale Agreement, or the Sales Agreement, with Jefferies LLC, or Jefferies, pursuant to which we may offer and sell, from time to time, our ADSs through Jefferies. On October 15, 2021, we filed a registration statement, which became effective on October 22, 2021, for the issuance and sale of up to \$100.0 million of ADSs. In 2024, we raised proceeds of \$27.7 million before deducting \$0.9 million in placement agent fees and other expenses, from sales of ADSs under the Sales Agreement. On October 22, 2024, we filed a new registration statement on Form F-3, which replaced the registration statement originally filed on October 15, 2021, for the issuance and sale, if any, of up to an additional \$100.0 million of its shares represented by ADSs under the Sales Agreement. As of this filing, approximately \$139.6 million of ADSs remained for potential issuance under the ADS facility.

On February 2, 2024, we entered into a Securities Purchase Agreement, or the Purchase Agreement, with the purchasers named therein, or the Investors. Pursuant to the Purchase Agreement, we agreed to sell an aggregate of 5,714,286 of our ADSs to the Investors, at a purchase price equal to \$21.00 per ADS, or the Private Placement. The Purchase Agreement contained customary representations and warranties from us and the investors and customary closing conditions. The closing of the Private Placement occurred on February 7, 2024, and we received aggregate gross proceeds from the Private Placement of approximately \$120.0 million before deducting \$7.7 million in placement agent fees and other expenses.

Pursuant to the Purchase Agreement, we filed a registration statement on Form F-3 (File No. 333-279185), which was declared effective by the SEC on May 14, 2024, covering the resale of the Registrable Securities (as such term is defined in the Purchase Agreement). We have agreed to use our commercially reasonable efforts to keep such registration statement effective until the earlier of (i) the date on which all Registrable Securities covered by such Registration Statement, as amended from time to time, have been sold, and (ii) the date on which there cease to be any Registrable Securities.

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.

Refer to Note 2 of our consolidated financial statements appearing elsewhere in this Annual Report on for additional discussion of liquidity and capital resources.

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, at least for the next twelve months from the issuance of the December 31, 2025 financial statements.

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 growth and the related costs of leasing additional office space.

Cash Flows

The following table summarizes the results of our cash flows for the years ended December 31, 2025 and 2024.

	Year ended December 31,	
	2025	2024
	\$000s	\$000s
Net cash outflow from operating activities	(62,271)	(67,640)
Net cash outflow from investing activities	(47,992)	(21,966)
Net cash inflow from financing activities	15	142,087
(Decrease)/increase in cash and cash equivalents	<u>\$ (110,248)</u>	<u>\$ 52,481</u>

Operating activities

Net cash outflow from operating activities was \$62.3 million for the year ended December 31, 2025, reflecting a decrease from a net cash outflow of \$67.6 million for the year ended December 31, 2024. This decrease in cash outflow is largely due to decreased spend in fiscal 2025 associated with partnered programs and our efforts to reduce general and administrative expenses.

Investing activities

Net cash used in investing activities was \$48.0 million for the year ended December 31, 2025, as compared to an outflow of \$22.0 million for the year ended December 31, 2024. This change was primarily due to the purchase of U.S. treasury bills with maturities over three months of \$166.4 million in 2025 partially offset by redemptions of \$118.5 million. For the year ended December 31, 2024, we had purchases of \$139.2 million partially offset by redemptions of \$117.4 million.

Financing activities

In 2024, we raised aggregate gross proceeds from the Private Placement of \$120.0 million before deducting \$7.7 million in placement agent fees and other expenses. The remainder of the inflow was due to proceeds from sales under our at-the-market facility. There were no related financing activities in 2025.

Contractual Obligations and Commitments

Research and Development and Manufacturing Agreements

We enter into agreements with certain vendors for the provision of goods and services, which includes manufacturing services with CDMOs and development and clinical trial services with CROs. These agreements may include certain provisions for purchase obligations and termination obligations that could require payments for the cancellation of committed purchase obligations or for early termination of the agreements. The amount of the cancellation or termination payments vary and are based on the timing of the cancellation or termination and the specific terms of the agreement. These obligations and commitments are not separately presented.

Collaboration Agreements

See “—Collaboration Agreements” included above for further details on our collaboration agreements. We have not included milestone or royalty payments or other contractual payment obligations under such collaboration agreements as the timing and amount of such obligations are unknown or uncertain and are contingent upon the initiation and successful completion of future activities.

Critical Accounting Policies and Critical Accounting Estimates

Our financial statements are prepared in accordance with U.S. GAAP. The preparation of the financial statements and related disclosures requires management to make estimates and judgments that affect the reported amounts of assets, liabilities, costs and expenses, and the disclosure of contingent assets and liabilities in our financial statements. We base our estimates on historical experience, known trends and events and various other factors that management believes are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Management evaluates estimates and assumptions on a periodic basis. Our actual results may differ from these estimates.

While our significant accounting policies are described in more detail in the notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe the following accounting policies to be most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

Revenue Recognition under Collaboration Agreements

During the years ended December 31, 2025 and 2024, a significant portion of our revenue recognized under collaboration agreements was derived from our collaborations with AstraZeneca and Hansoh.

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 \$60.0 million, of which \$20.0 million was paid in May 2020 and the remaining \$40.0 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 \$140.0 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 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 made a \$16.0 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 us 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 recognized 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 years ended December 31, 2025 and 2024, 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. In 2025 the estimated forecasted cost for partnered programs was not material and the related judgment was not significant.

Recognition of Clinical Trial Expenses

As part of the process of preparing our consolidated financial statements, we may be required to estimate stage of completion of our preclinical studies and clinical trials to calculate the contracted research and development costs. 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 expenses include fees paid to CROs for services performed on preclinical studies and clinical trials and fees paid for professional services, which was approximately 13% of our total research and development expense for the year ended December 31, 2025.

Recently Issued and Adopted Accounting Pronouncements

We discuss the effect of recently issued and adopted pronouncements in Note 2.20 to the consolidated financial statements appearing elsewhere in this Annual Report.

Recent Accounting Pronouncements

See note 2.20 to our consolidated financial statements for the year ended December 31, 2025, appearing elsewhere in this Annual Report for a discussion of new standards and interpretations recently and not yet adopted by us.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

We are a smaller reporting company as defined in Item 10(f)(1) of Regulation S-K. As a result, pursuant to Item 305(e) of Regulation S-K, we are not required to provide the information required by this Item 7A.

Item 8. Financial Statements and Supplementary Data

Our consolidated financial statements, together with the report of the independent registered public accounting firm required to be filed pursuant to this Item 8 are appended at the end of this Annual Report. An index of those financial statements is found in Item 15 of Part IV of this Annual Report.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures

Disclosure Controls and Procedures

We maintain “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC’s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate to allow timely decisions regarding required disclosure.

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, has evaluated the effectiveness of our disclosure controls and procedures (as 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 Chief Executive Officer and Chief Financial Officer have concluded that as of December 31, 2025, our disclosure controls and procedures were effective.

Management’s Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Exchange Act Rules 13a-15(f) and 15d-15(f) define this as a process designed by, or under the supervision of, our Chief Executive Officer and our Chief Financial Officer and effected by the Board of Directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with U.S. GAAP.

Due to its inherent limitations, internal control over financial reporting may not prevent or detect all misstatements. Furthermore, projections of any evaluation of the effectiveness of internal controls to future periods may prove invalid due to changes in our circumstances and the risk that compliance with policies, procedures and controls is not sustained.

Management has assessed the effectiveness of internal control over financial reporting as of December 31, 2025, based on the Internal Control — Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). Based on this assessment, management has concluded that our internal control over financial reporting as of December 31, 2025, was effective.

This Annual Report on Form 10-K does not include an attestation report of our independent registered public accounting firm regarding internal control over financial reporting. Pursuant to rules of the SEC, such attestation is

not required for non-accelerated filers, which permit us to provide only management's report in this Annual Report on Form 10-K.

Changes in Internal Control over Financial Reporting

There was no change in our internal control over financial reporting that occurred during the quarter ended December 31, 2025, that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

During the three months ended December 31, 2025, no director or officer (as defined in Rule 16a-1(f) under the Exchange Act) of the Company adopted or terminated a "Rule 10b5-1 trading arrangement" or "non-Rule 10b5-1 trading arrangement," as each term is defined in Item 408(a) of Regulation S-K.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information required by this item is incorporated by reference to our Proxy Statement for our 2026 Annual General Meeting of Shareholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2025.

We have adopted a Code of Business Conduct and Ethics that is applicable to all our employees, executive officers, including our principal executive, principal financial and principal accounting officers, members of our board of directors, and consultants. If we make any amendment to the Code of Business Conduct and Ethics or grant any waivers, including any implicit waiver, to the principal executive officer, principal financial officer and principal accounting officer or controller or persons performing similar functions from a provision of the Code of Business Conduct and Ethics, we will disclose the nature of such amendment or waiver on our website to the extent required by the rules and regulations of the SEC. The Code of Business Conduct and Ethics is available on our website at <https://silence-therapeutics.com/investors/governance/governance-documents>. Information contained on, or that can be accessed through, our website does not constitute a part of this Annual Report and is not incorporated by reference herein.

We have adopted an Insider Trading Policy governing the purchase, sale and/or other dispositions of our securities by our directors, officers and employees. A copy of the Insider Trading Policy is filed as an exhibit to this Annual Report. In addition, it is our practice to comply with the applicable laws and regulations relating to insider trading.

Item 11. Executive Compensation

The information required by this item is incorporated by reference to our Proxy Statement for our 2026 Annual General Meeting of Shareholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2025.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required by this item is incorporated by reference to our Proxy Statement for our 2026 Annual General Meeting of Shareholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2025.

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information required by this item is incorporated by reference to our Proxy Statement for our 2026 Annual General Meeting of Shareholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2025.

Item 14. Principal Accountant Fees and Services

The information required by this item is incorporated by reference to our Proxy Statement for our 2026 Annual General Meeting of Shareholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2025.

PART IV

Item 15. Exhibits and Financial Statement Schedules

(a) Documents filed as part of Form 10-K.

- (1) Financial Statements
Report of Independent Registered Public Accounting Firm
Consolidated Balance Sheets
Consolidated Statements of Income (Loss)
Consolidated Statements of Comprehensive Income (Loss)
Consolidated Statements of Changes in Equity
Consolidated Statements of Cash Flows
Notes to the Consolidated Financial Statements
- (2) Schedules
Schedules have been omitted as all required information has been disclosed in the financial statements and related footnotes.
- (3) Exhibits

The following exhibits are filed as part of this Annual Report on Form 10-K or are incorporated herein by reference.

Exhibit Number	Exhibit Description	Incorporated by Reference to Filings Indicated				
		Form	File No.	Exhibit No.	Filing Date	Filed/Furnished Herewith
3.1	Amended and Restated Articles of Association	10-Q	001-39487	3.1	8/7/2025	
4.1+	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	3/9/2021	
4.2	Form of American Depositary Receipt (included in Exhibit 4.1)	F-1	333-254021	4.2	3/9/2021	
4.3	Description of Share Capital and Articles of Association	10-K	001-39487	4.3	2/27/2025	
4.4	Description of American Depositary Shares	20-F	001-39487	2.4	3/15/2023	
10.1#	Silence Therapeutics plc 2018 Long-Term Incentive Plan	S-8	333-273576	99.2	8/1/2023	
10.2#	Silence Therapeutics plc 2018 Non-Employee Long-Term Incentive Plan	S-8	333-273576	99.3	8/1/2023	
10.3#	Employee U.S. Sub-Plan under the 2018 Employee Long-Term Incentive Plan	F-1	333-248203	10.3	8/20/2020	
10.4#	Non-Employee U.S. Sub-Plan under the 2018 Non-Employee Long-Term Incentive Plan	F-1	333-248203	10.4	8/20/2020	
10.5†+	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	
10.6†+	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	20-F	001-39487	4.7	3/15/2023	
10.7	Form of Deed of Indemnity between the registrant and its directors	F-1	333-248203	10.7	8/20/2020	

10.8	Form of Deed of Indemnity between the registrant and its executive officers	F-1	333-248203	10.8	8/20/2020	
10.9	2023 Equity Incentive Plan with Non-Employee Sub-Plan and CSOP Plan	20-F	001-39487	4.10	3/13/2024	
10.10	Open Market Sale AgreementSM by and between the Registrant and Jefferies LLC (incorporated by reference to Exhibit 1.1 to the Registration Statement on Form F-3 (File No. 333-260265) filed with the Commission on October 15, 2021)	F-3	333-260265	1.1	10/15/2021	
10.11	Registration Rights Agreement, dated as of February 2, 2024, by and among the Registrant and the investors named in the Securities Purchase Agreement	6-K	001-39487	99.2	02/05/2024	
10.12	Employment Agreement, dated as of March 5, 2022, by and between the Registrant and Craig Tooman	10-K/A	001-39487	10.13	4/30/2025	
10.13	Employment Agreement, dated as of March 8, 2022, by and between the Registrant and Rhonda Hellums	10-K/A	001-39487	10.14	4/30/2025	
10.14	Employment Agreement, dated as of March 9, 2023, by and between the Registrant and Steven Romano	10-K/A	001-39487	10.15	4/30/2025	
10.15	Addendum to Letter of Appointment as Chairman to Iain Ross, dated December 14, 2025					X
19.1	Insider Trading Policy	10-K	001-39487	19.1	2/27/2025	
21.1	Subsidiaries of the Registrant	F-1	333-248203	21.1	8/20/2020	
23.1	Consent of PricewaterhouseCoopers LLP					X
24.1	Power of Attorney (incorporated by reference to the signature pages of this Annual Report on Form 10-K).					X
31.1	Certification by the Principal Executive Officer pursuant to Securities Exchange Act Rules 13a-14(a) and 15d-14(a) as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002					X
31.2	Certification by the Principal Financial Officer pursuant to Securities Exchange Act Rules 13a-14(a) and 15d-14(a) as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002					X
32.1*	Certification by the Principal Executive Officer and the Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002					X
97.1	Silence Therapeutics plc Compensation Clawback Policy	20-F	001-39487	97.1	3/13/2024	
101.INS	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document.					X
101.SCH	Inline XBRL Taxonomy Extension Schema with Embedded Linkbase Documents					X
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).					X

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.

* These certifications are being furnished solely to accompany this annual report pursuant to 18 U.S.C. Section 1350 and are not being filed for purposes of Section 18 of the Securities Exchange Act of 1934 and are not to be incorporated by reference into any filing of the registrant, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15 (d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

SILENCE THERAPEUTICS PLC

By: /s/ Iain Ross

Iain Ross
Interim Principal Executive Officer and Chairman of
the Board of Directors
(Principal Executive Officer)

Date: March 5, 2026

POWER OF ATTORNEY

Each of the undersigned officers and directors of Silence Therapeutics plc hereby constitutes and appoints Iain Ross and Rhonda Hellums, and each of them, their true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for them and in their name, place and stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, with all exhibits thereto, and other related documents, and to cause the same to be filed with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing necessary and proper to be done in connection therewith, as fully to all intents and purposes as the undersigned could do if personally present, and each of the undersigned for himself or herself hereby ratifies and confirms that all said attorneys-in-fact and agents, or any of them, or his or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Iain Ross</u> Iain Ross	Interim Principal Executive Officer and Chairman of the Board of Directors <i>(Principal Executive Officer)</i>	March 5, 2026
<u>/s/ Rhonda Hellums</u> Rhonda Hellums	Chief Financial Officer <i>(Principal Financial Officer and Principal Accounting Officer)</i>	March 5, 2026
<u>/s/ Dave Lemus</u> Dave Lemus	Director	March 5, 2026
<u>/s/ Tim McInerney</u> Tim McInerney	Director	March 5, 2026
<u>/s/ James Ede-Golightly</u> James Ede-Golightly	Director	March 5, 2026

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting firm (PCAOB ID 876)	F-2
Consolidated Balance Sheets	F-3
Consolidated Statements of Income (Loss)	F-4
Consolidated Statements of Comprehensive Income (Loss)	F-5
Consolidated Statements of Changes in Shareholders' Equity	F-6
Consolidated Statements of Cash Flows	F-7
Notes to the Consolidated Financial Statements	F-8

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 “Company”) as of December 31, 2025 and 2024, and the related consolidated statements of income (loss), of comprehensive income (loss), of changes in shareholders’ equity and of cash flows for the years then ended, 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 Company as of December 31, 2025 and 2024, and the results of its operations and its cash flows for the years then ended in conformity with accounting principles generally accepted in the United States of America

Basis for Opinion

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

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

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

Emphasis of Matter

As discussed in Note 2.5 to the consolidated financial statements, the Company has incurred recurring losses since inception and expects to incur operating losses for the foreseeable future as it continues its research and development efforts. Management’s evaluation of the events and conditions and management’s plans to mitigate these matters are also described in Note 2.5.

Critical Audit Matters

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

critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Third party contracted research and development costs

As described in Notes 2.8, 4, 13 and 15 to the consolidated financial statements, third party contracted research and developments costs of \$44.9 million were incurred during the year ended December 31, 2025 and associated prepayments and accruals and other payables were \$6.8 million and \$3.0 million as of December 31, 2025, respectively. Management recognizes expenditure incurred in carrying out its research and development activities in line with their best estimation of the costs incurred to date for each separately contracted study or activity. This requires estimation of the full costs to complete each study or activity and also estimation of the current stage of completion for open contracts and purchase orders. 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.

The principal considerations for our determination that performing procedures relating to third party contracted research and development costs is a critical audit matter are (i) the significant judgment by management when developing the estimate of the third party contracted research and development costs for open contracts and purchase orders; (ii) a high degree of auditor judgment, subjectivity and effort in performing procedures and evaluating management's significant assumption related to the stage of completion.

Addressing the matter involved performing procedures and evaluating audit evidence in connection with forming our overall opinion on the consolidated financial statements. These procedures included, among others (i) reading significant research and development contracts; (ii) testing external research and development costs on a sample basis, which included tracing relevant information to the underlying contracts, purchase orders, invoices received, and information received from certain third party providers, where applicable; (iii) testing management's process for estimating the third party contracted research and development costs for open contracts and purchase orders; (iv) testing the completeness and accuracy of underlying data used by management; and (v) evaluating the reasonableness of the significant assumption used by management related to the stage of completion on a sample of contracts. Evaluating management's assumption related to the stage of completion involved (i) obtaining and examining a sample of third party contracts to evaluate the completeness and consistency of the costs and milestones in the contract with those used in developing the estimate; and (ii) considering whether the assumption is consistent with external confirmations, other information received from suppliers or other areas of the audit.

/s/PricewaterhouseCoopers LLP
Reading, United Kingdom
March 5, 2026

We have served as the Company's auditor since 2014.

SILENCE THERAPEUTICS PLC
CONSOLIDATED BALANCE SHEETS
(in thousands, except share data)

	Note	Year ended December 31,	
		2025	2024
Current assets			
Cash and cash equivalents	12	\$ 11,277	\$ 121,330
Short-term investments	12	73,837	26,004
R&D benefit receivable		22,007	24,396
Other current assets	13	11,537	14,664
Trade receivables	14	-	972
Total current assets		118,658	187,366
Property, plant and equipment, net	9	1,581	1,818
Operating lease right-of-use assets	16	167	157
Goodwill	10	10,621	9,392
Intangible assets	11	288	312
Other long-term assets	13	127	3,590
Total assets		\$ 131,442	\$ 202,635
Current liabilities			
Contract liabilities	17	\$ (168)	\$ (306)
Trade and other payables	15	(13,356)	(16,399)
Operating lease liabilities, current	16	(89)	(117)
Total current liabilities		(13,613)	(16,822)
Contract liabilities	17	(55,454)	(51,790)
Operating lease liabilities, long-term	16	(71)	-
Total liabilities		\$ (69,138)	\$ (68,612)
Commitments and contingencies (Note 21)			
Shareholders' equity			
Ordinary shares - par value £0.05 per share; 141,701,848 shares issued at December 31, 2025 (2024: 141,674,074)	19	(10,290)	(10,288)
Additional paid-in capital		(617,562)	(609,560)
Accumulated deficit		562,572	474,044
Accumulated other comprehensive loss		2,976	11,781
Total shareholders' equity		(62,304)	(134,023)
Total liabilities and shareholders' equity		\$ (131,442)	\$ (202,635)

The accompanying notes form an integral part of these consolidated financial statements.

SILENCE THERAPEUTICS PLC
CONSOLIDATED STATEMENTS OF INCOME (LOSS)
(in thousands, except for loss per share and share data)

	Note	Year ended December 31,	
		2025	2024
Revenue	3	\$ 559	\$ 43,258
Cost of sales		(215)	(11,810)
Gross profit		344	31,448
Research and development costs		(67,753)	(67,883)
General and administrative expenses		(22,344)	(26,884)
Restructuring charges	6	(1,324)	-
Operating loss		(91,077)	(63,319)
Foreign currency (loss)/gain, net		(8,467)	646
Other income, net	7	3,480	4,472
Benefit from R&D credit		7,463	13,737
Loss before income tax expense		(88,601)	(44,464)
Income tax expense	18	(11)	(845)
Net Loss		\$ (88,612)	\$ (45,309)
Loss per share (basic and diluted)	8	\$ (0.63)	\$ (0.33)
Weighted average shares outstanding (basic and diluted)		141,694,702	138,752,224

The accompanying notes form an integral part of these consolidated financial statements.

SILENCE THERAPEUTICS PLC
CONSOLIDATED STATEMENTS OF COMPREHENSIVE INCOME (LOSS)
(in thousands)

	Year ended December 31,	
	2025	2024
Net Loss	\$ (88,612)	\$ (45,309)
Other comprehensive income (loss) net of tax:		
Foreign exchange differences arising on consolidation of foreign operations (net of tax)	8,804	(1,055)
Total other comprehensive income/(loss) for the year	8,804	(1,055)
Total comprehensive loss for the year	\$ (79,808)	\$ (46,364)

The accompanying notes form an integral part of these consolidated financial statements.

SILENCE THERAPEUTICS PLC
CONSOLIDATED STATEMENTS OF CHANGES IN SHAREHOLDERS' EQUITY
(in thousands, except share data)

	Ordinary Shares				Accumulated other comprehensive income	Accumulated deficit	Total shareholders' equity
	Note	Shares	Cost	Additional paid- in capital			
At January 1, 2024		118,846,966	\$ 8,847	\$ 455,765	\$ (10,725)	\$ (431,894)	\$ 21,993
Net loss		-	-	-		(45,309)	(45,309)
Foreign currency translation adjustments (net of tax)		-	-	-	(1,055)	-	(1,055)
Recognition of share-based payments	20	-	-	16,307	-	-	16,307
Options exercised in the year	19/20	1,408,443	-	(3,158)	-	3,158	-
Proceeds from shares issued		21,418,665	1,441	140,646	-	-	142,087
At December 31, 2024		141,674,074	\$ 10,288	\$ 609,560	\$ (11,780)	\$ (474,045)	\$ 134,023
Net loss		-	-	-		(88,612)	(88,612)
Foreign currency translation adjustments (net of tax)		-	-	-	8,804	-	8,804
Recognition of share-based payments	20	-	-	8,074	-	-	8,074
Options exercised in the year	19/20	27,774	-	(85)	-	85	-
Proceeds from shares issued		-	2	13	-	-	15
At December 31, 2025		141,701,848	\$ 10,290	\$ 617,562	\$ (2,976)	\$ (562,572)	\$ 62,304

The accompanying notes form an integral part of these consolidated financial statements.

SILENCE THERAPEUTICS PLC
CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	Year ended December 31,	
	2025	2024
Cash flow from operating activities		
Net loss after tax	\$ (88,612)	\$ (45,309)
Adjustments to reconcile net loss to net cash (used in) provided by operating activities:		
Depreciation expense	312	336
Amortization expense	243	257
Share-based compensation expense	8,074	16,307
Net foreign exchange impacts	11,022	(2,581)
Other income, net	(3,480)	(4,472)
Income tax expense	11	845
Change in operating assets and liabilities:		
Decrease/(increase) in trade receivables	1,024	(904)
Decrease/(increase) in other current assets	6,016	(1,330)
Decrease/(increase) in R&D benefit receivable	4,041	(2,337)
Decrease in other long-term assets	3,658	-
(Decrease)/increase in trade and other payables	(4,078)	499
Decrease in contract liabilities	(334)	(28,786)
Decrease in operating lease liabilities	(168)	(165)
Net cash used in operating activities	<u>(62,271)</u>	<u>(67,640)</u>
Cash flow from investing activities		
Redemption of term deposits	118,476	117,412
Purchase of term deposits	(166,413)	(139,167)
Purchase of property, plant and equipment	(55)	(211)
Net cash used in investing activities	<u>(47,992)</u>	<u>(21,966)</u>
Cash flow from financing activities		
Proceeds from issue of ordinary shares	15	142,087
Net cash provided by financing activities	<u>15</u>	<u>142,087</u>
(Decrease)/increase in cash and cash equivalents	<u>(110,248)</u>	<u>52,481</u>
Cash and cash equivalents at start of period	121,330	68,789
Effect of exchange rate fluctuations on cash and cash equivalents held	195	60
Cash and cash equivalents at end of period	<u>\$ 11,277</u>	<u>\$ 121,330</u>
Supplemental disclosures of cash flow information:		
Income Tax Paid net of refunds	(637)	(433)

The accompanying notes form an integral part of these consolidated financial statements.

SILENCE THERAPEUTICS PLC
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS

1. General information

1.1. Nature of the business

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 12 Hammersmith Grove, London, W6 7AP.

2. Summary of significant accounting policies

2.1. Basis of preparation

The Group's consolidated financial statements are prepared in conformity with accounting principles generally accepted in the United States of America ("U.S. GAAP") and the rules and regulations of the U.S. Securities and Exchange Commission ("SEC"). Any reference in these notes to the applicable guidance is meant to refer to authoritative U.S. GAAP as found in the Accounting Standards Codification ("ASC") and Accounting Standards Update ("ASU") of the Financial Accounting Standards Board ("FASB"). The consolidated financial statements include the accounts of the Group and its wholly owned subsidiaries, after elimination of intercompany accounts and transactions.

2.2. Functional and reporting currency

The reporting currency of the consolidated financial statements is the U.S. Dollars ("USD" or "\$"). The functional currency of the Group's subsidiaries reflects the economic environment of their respective operations. All amounts disclosed have been rounded to the nearest thousand, unless otherwise stated.

2.3. Principles of consolidation

The consolidated financial information comprises the financial statements of Silence Therapeutics plc and its wholly owned subsidiaries. All intercompany balances and transactions have been eliminated on consolidation.

2.4. Use of estimates

The preparation of the consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, the reported amounts of revenues and expenses during the reporting period, and compensation. Significant estimates and assumptions reflected in the Group's consolidated financial statements include, but are not limited to, the recognition of revenue and research and development expenses. The Group bases its estimates on historical experience, known trends and other market-specific or other relevant factors that it believes to be reasonable under the circumstances. On an ongoing basis, management evaluates its estimates when there are changes in circumstances, facts and experience. Changes in estimates are recorded in the period in which they become known. Actual results could differ materially from those estimates.

2.5. Going concern

The Group has incurred recurring losses since inception, including net losses of \$88.6 million for the year ended December 31, 2025. As of December 31, 2025, the Group had accumulated losses of \$562.6 million and cash outflows from operating activities for the year ended 31, December 2025 of \$62.3 million.

SILENCE THERAPEUTICS PLC
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS – (Continued)

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. In 2024, the Group raised additional proceeds of \$27.7 million before deducting \$0.9 million in placement agent fees and other expenses, from sales of ADSs under its Sales Agreement. On February 5, 2024, the Group announced a private placement of 5,714,286 of the Group's American Depositary Shares ("ADSs"), each representing three ordinary shares, at a price of \$21.00 per ADS, with new and existing institutional and accredited investors (the "Private Placement"). The aggregate gross proceeds of the Private Placement were \$120.0 million before deducting approximately \$7.7 million in placement agent fees and other expenses. In 2024, the Group received a \$10.0 million milestone payment from the AstraZeneca Collaboration and achieved another \$2.0 million in milestone payments from the Hansoh collaboration. As of December 31, 2025, the Group had cash and cash equivalents and short-term investments of \$85.1 million.

In accordance with Accounting Standards Codification ("ASC") 205, "Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern, the Group has the responsibility to evaluate whether conditions and/or events raise substantial doubt 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 and U.S. treasury bills as of December 31, 2025 are sufficient to fund its forecasted operating expenses and capital expenditure requirements into 2028.

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 from collaboration agreements which will extend the ability to fund operations. However, these future milestone payments are dependent on achievement of certain development or regulatory objectives that may not occur. 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 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.

2.6. Segment reporting

The Group has determined that its chief executive officer is the chief operating decision maker ("CODM"). The CODM reviews financial information presented on a consolidated basis. Resource allocation decisions are made by the CODM based on consolidated results. There are no segment managers who are held accountable by the CODM for operations, operating results, and planning for levels or components below the consolidated unit level. As such, the Group has concluded that it operates as a single reportable segment (see Note 4).

2.7. Revenue recognition

The Group's revenue for the year ended December 31, 2025, consists of revenue from collaboration agreements (royalty income and revenue from collaboration agreements for the year ended December 31, 2024). To determine revenue recognition for arrangements that the Group determines are within the scope of *ASC 606: Revenue from Contracts with Customers*, ("ASC 606"), it performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when, or as, the

SILENCE THERAPEUTICS PLC
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS – (Continued)

Group satisfies the performance obligations. The Group only applies the five-step model to contracts when it is probable that the entity will collect substantially all the consideration it is entitled to in exchange for the goods or services it transfers to the customer. As part of the accounting for these arrangements, the Group must make significant judgments, including identifying performance obligations in the contract, estimating the amount of variable consideration to include in the transaction price and allocating the transaction price to each performance obligation.

Revenue from collaboration agreements

The Group has considered the 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 the Group has concluded the license of the intellectual property and the R&D services are not distinct, as 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, the Group has 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. The Group recognizes 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, 2025:

- Total contract costs which includes actual FTE and direct costs incurred up to December 31, 2025 and forecast FTE and direct costs for the remainder of the contract
- Actual costs incurred up until December 31, 2025 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. In 2025 the estimated forecasted cost for partnered programs was not material and the related Judgment was not significant.

Further details of the revenue amounts recognized in the year ended December 31, 2025 can be found in note 3.

2.8. Research and development

Research and development costs consist of salary and personnel related costs and third party costs for the Group's research and development activities. Personnel related costs include a share based compensation charge relating to its stock option plan. The largest component of third party costs is for clinical trials, as well as manufacturing for

SILENCE THERAPEUTICS PLC
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS – (Continued)

clinical supplies and associated development, and pre-clinical studies. Research and development costs are expensed as incurred.

The Group recognizes 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 and prepayments 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 for open contracts and purchase orders. 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.

2.9. 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.

As a company that carries out extensive research and development activities, the Group currently benefits from the U.K. research and development tax credit regime for small or medium-sized enterprises ("SMEs"). A benefit 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. Amounts receivable under the scheme are presented within the consolidated statements of income (loss) within Benefit from R&D credit. The U.K. R&D tax credit is fully refundable to the Group and is not dependent on current or future taxable income. As a result, the Company has recorded the entire benefit from the U.K. R&D tax credit as a benefit which is included in net loss before income tax and, accordingly, not reflected in it as part of the income tax provision.

Deferred tax assets and liabilities are recognized for the estimated future tax consequences attributable to differences between the financial reporting basis and the respective tax basis of the Group's assets and liabilities, and expected benefits of utilizing net operating loss, capital loss, and tax-credit carryforwards. The Group assesses the likelihood that its deferred tax assets will be realized and, to the extent management does not believe these assets are more likely than not to be realized, a valuation allowance is established. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates or laws is recognized in consolidated statements of income (loss) in the period that includes the enactment date.

2.10. Foreign currency translation

Monetary assets and liabilities denominated in currencies other than the functional currency are remeasured into the functional currency at exchange rates prevailing at the balance sheet dates. Non-monetary assets and liabilities denominated in foreign currencies are remeasured into the functional currency at the exchange rates prevailing at the date of the transaction. Exchange gains or losses arising from foreign currency transactions are included in the consolidated statements of income (loss) and comprehensive income (loss) for each respective period.

For financial reporting purposes, the consolidated financial statements of the Group have been presented in USD, the reporting currency. The financial statements of the Group's entities are translated from their functional currency into USD as follows: assets and liabilities are translated at the exchange rates at the balance sheet dates, revenues and expenses are translated at the average exchange rates for the periods presented, and shareholders' equity is translated at the prevailing historical exchange rates. Translation adjustments are not included in determining net loss but are included as a foreign exchange adjustment to other comprehensive income, a component of shareholders' equity.

2.11. Cash and cash equivalents

SILENCE THERAPEUTICS PLC
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS – (Continued)

The Group considers cash and cash equivalents to comprise of 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.

2.12. Property, plant and equipment

The Group only holds equipment and furniture. These are stated at cost, net of accumulated depreciation. Depreciation is calculated using the straight-line method over the estimated useful life of the asset. The estimated useful life of furniture and equipment is 3 to 10 years. Estimated useful life and residual values are reviewed each year and amended if necessary.

Property, plant and equipment is assessed for impairment upon triggering events that indicate the carrying value of an asset group may not be recoverable. Recoverability is measured by a comparison of the carrying amount to future net undiscounted cash flows of the asset group expected to be generated from its use and eventual disposition. If the asset group's carrying value is determined to not be recoverable, the impairment to be recognized is measured by which the carrying amount exceeds the fair value of the asset group. No impairment charges related to property and equipment were recorded in any of the periods presented.

2.13. Leases

The Group determines if an arrangement contains a lease at inception. The Group currently only has operating leases. The Group recognizes a right-of-use ("ROU") operating lease asset and associated short- and long-term operating lease liability in its consolidated balance sheets for operating leases greater than one year. Its right-of-use assets represent its right to use an underlying asset for the lease term and its lease liabilities represent its obligation to make lease payments arising from the lease arrangement. The Group recognizes its right-of-use operating lease assets and lease liabilities based on the present value of the future minimum lease payments it will pay over the lease term. The Group determines the lease term at the inception of each lease, and in certain cases its lease term could include renewal options if the Group concludes it is reasonably certain to exercise the renewal option. When the Group exercises a lease option that was not previously included in the initial lease term, it reassesses its right-of-use asset and lease liabilities for the new lease term.

As its operating lease do not provide an interest rate implicit in the lease, the Group uses its incremental borrowing rate, based on the information available as of the lease inception date or at the lease option extension date in determining the present value of future payments. The Group recognizes lease expense for its minimum lease payments on a straight-line basis over the expected term of its lease. Its leases do not include material variable or contingent lease payments.

Leases with an initial term of 12 months or less are not recorded on the balance sheet. Instead, these lease payments are recognized on the consolidated statements of income (loss) on a straight-line basis over the lease term.

Similar to property, plant and equipment, ROU lease asset impairment is assessed upon triggering events that indicate the carrying amount may not be recovered by comparison to the future net undiscounted cash flows.

SILENCE THERAPEUTICS PLC
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS – (Continued)

2.14. Goodwill

Goodwill is the excess of the purchase price over the estimated fair values of the underlying net assets of an acquired business. The Group assesses goodwill for impairment annually, or immediately if conditions indicate that such impairment could exist. Impairment testing for goodwill is performed at the reporting unit level. The Group first evaluates qualitative factors to determine whether it is more likely than not that the fair value of a reporting unit is less than its carrying amount. If the qualitative assessment indicates potential impairment, or if the Group elects to bypass the qualitative assessment, a quantitative test is performed. The quantitative test calculates the excess of the reporting unit's fair value over its carrying amount, including goodwill, utilizing a discounted cash flow method. The test for impairment of goodwill requires the Group to make several assumptions and estimates regarding market conditions and its future profitability to determine the fair value of the goodwill at the reporting unit. Significant assumptions used in the reporting unit fair value measurements include forecasted cash flows, including revenue and expense growth rates, discount rates, and revenue and earnings multiples. An impairment loss is recognized when the carrying amount of the reporting unit net assets exceeds the estimated fair value of the reporting unit. Impairment losses recognized for the reporting unit 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 reporting unit.

All goodwill for the Group is attributed to an acquisition that occurred in 2005 and the Group has determined that no impairment was recorded as of December 31, 2025 and 2024.

2.15. 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 is charged to the consolidated statements of income (loss) 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: 3 - 10 years.

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 software 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 software 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.

SILENCE THERAPEUTICS PLC
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS – (Continued)

2.16. Fair value measurements

The Group's financial instruments include cash and cash equivalents, trade receivables, U.S. treasury bills, trade and other payables and accrued expenses. These are initially recorded at fair value and subsequently measured at cost, which is considered to approximate their fair value due to the short-term nature of such financial instruments.

Fair value is defined as the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. The guidance prioritizes the inputs used in measuring fair value into the following hierarchy:

- Level 1: Unadjusted quoted prices in active markets that are accessible at the measurement date for identical, unrestricted assets or liabilities;
- Level 2: Quoted prices for similar assets and liabilities in active markets, quoted prices in markets that are not active, or inputs which are observable, either directly or indirectly, for substantially the full term of the asset or liability; or
- Level 3: Prices or valuation techniques that require inputs that are both significant to the fair value measurement and unobservable (i.e., supported by little or no market activity).

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

2.17. Share-based compensation expense

Historically the Group has issued equity settled share-based compensation to certain employees (see note 20). 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 number of stock 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 therefore any amount unrecognized that would otherwise have been recorded in future accounting periods is recognized immediately. The Group has elected to recognize the effect of forfeitures on share-based compensation when they occur. Any differences in compensation recognized at the time of forfeiture are recorded as a cumulative adjustment in the period in which the forfeiture occurs.

Fair value is measured using a Black Scholes 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.

SILENCE THERAPEUTICS PLC
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS – (Continued)

2.18. Equity

Ordinary shares is determined using the nominal value of shares issued.

The additional paid-in capital account includes any premiums received on the initial issuing of the ordinary shares. Any transaction costs associated with the issuing of shares are deducted from the additional paid-in capital account, net of any related income tax benefits.

Equity settled share-based payments are credited to a share-based payment reserve as a component of additional paid-in capital, until related options or warrants are exercised.

Foreign currency translation differences are included in the accumulated other comprehensive income.

Accumulated deficit includes all current and prior period results as disclosed in the consolidated statements of income (loss).

2.19. Loss per share

Basic income/(loss) per share is computed by dividing the net income/(loss) attributable to ordinary shareholders by the weighted-average number of ordinary shares outstanding for the reporting period without consideration for potentially dilutive securities. Net income/(loss) attributable to ordinary shareholders is computed as if all net income/(loss) for the period had been distributed.

The Group computes diluted income/(loss) per ordinary share after giving consideration to all potentially dilutive ordinary equivalents, except where the effect of such non-participating securities would be antidilutive. The Group been loss making for each fiscal year and therefore all potentially dilutive ordinary equivalents are considered to be antidilutive.

2.20. Recently Issued Accounting Pronouncements

Recently adopted accounting standards

In December 2023, the FASB issued ASU 2023-09, *Income Taxes (Topic 740): Improvements to Income Tax Disclosures*, which provides for improvements to income tax disclosures primarily related to the rate reconciliation and income taxes paid information. The company adopted this guidance for the year ended December 31, 2025 and applied the guidance prospectively. See Note 18 below for further detail.

Accounting standards issued but not yet adopted

In November 2024, the FASB issued ASU 2024-03, *Income Statement—Reporting Comprehensive Income—Expense Disaggregation Disclosures (Subtopic 220-40)*. The amendments in this update require disclosure, in the notes to financial statements, of specified information about certain costs and expenses at each interim and annual reporting period. The amendments are effective for annual periods beginning after December 15, 2026, and reporting periods beginning after December 15, 2027, with early adoption permitted. The Group is currently evaluating the impact to its consolidated financial statements.

In December 2025, the FASB issued ASU 2025-10, *Accounting for Government Grants Received by Business Entities* which adds guidance to ASC 832 on the recognition, measurement, and presentation of government grants. The amendments are effective for annual periods beginning after December 15, 2028. The Group is currently evaluating the impact to its consolidated financial statements.

3. Revenue

SILENCE THERAPEUTICS PLC
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS – (Continued)

Revenue from collaboration agreements for the years ended December 31, 2025 and 2024 predominately relates to the research collaboration agreements the Group entered into with AstraZeneca in March 2020 and Hansoh in October 2021.

Disaggregation of revenue from contracts with customers is as follows:

	Year ended December 31,	
	2025	2024
	\$000s	\$000s
Revenue from Contracts with Customers		
Research collaboration - AstraZeneca	559	17,957
Research collaboration - Hansoh	-	24,573
Research collaboration - other	-	584
Research collaboration - total	<u>559</u>	<u>43,114</u>
Royalties	-	144
Total revenue from contracts with customers	<u><u>559</u></u>	<u><u>43,258</u></u>

Under its collaboration agreement with AstraZeneca, the Group received an upfront cash payment of \$20.0 million in 2020 with a further amount of \$40.0 million received in May 2021. The Group is also eligible to receive specified development and commercial milestone payments as well as tiered royalties on net sales, if any. The Group recognizes the upfront payment and milestone payments over time, in accordance with ASC 606. During the year ended December 31, 2025, the Group did not achieve any milestone payments (2024: \$10.0 million). During the year ended December 31, 2025, the Group recognized a total of \$0.6 million in revenue under this agreement (2024: \$18.0 million).

The Group entered into a collaboration agreement with Hansoh on October 15, 2021. The Group received a \$16.0 million (\$14.4 million, net of taxes) upfront payment to us in December 2021. The Group is eligible to receive development, regulatory and commercial milestones as well as royalties on Hansoh net product sales. During the year ended December 31, 2025, the Group did not achieve any milestone payments (2024: \$2.0 million). The Group recognizes the upfront payment and milestone payments over time, in accordance with ASC 606.

In December 2024, Hansoh notified the Group that it will not pursue further development under the Hansoh Collaboration. This represented the conclusion of all required development activities and commitments under the terms of the Hansoh Collaboration. During the year ended December 31, 2025, the Group did not recognize revenue under this agreement (2024: \$24.6 million).

4. Segment reporting

The CODM reviews Consolidated net loss for the year when assessing the Group's performance, allocating resources and establishing management's compensation. In addition to Consolidated net loss, the CODM receives discrete information for revenue by major customer and geographic location. Consolidated net loss is used to monitor budget versus actual results and is reviewed against the Group's peers and competitors as benchmarking. The Group operates as one reportable segment in the specific technology field of RNA therapeutics.

The accounting policies of its operating segment are the same as those described in the Group's summary of significant accounting policies.

The Group derives revenues from customers through royalty income and research collaboration agreements, each representing a major customer, specifically related to the development of RNAi-based medicines. Refer to Note 3 – Revenue for a further description of the types of products from which the Group derives its revenues.

The measure of segment assets is reported on the balance sheet as total consolidated assets.

The table below provides segment information about the Group:

SILENCE THERAPEUTICS PLC
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS – (Continued)

	Year Ended December 31,	
	2025	2024
	\$000s	\$000s
Revenue	559	43,258
Less:		
Cost of sales	(215)	(11,810)
Contracted research and development costs (a)	(44,873)	(42,902)
Personnel research and development costs (b)	(18,086)	(20,503)
Other R&D costs (c)	(4,794)	(4,478)
General & administrative expenses	(22,344)	(26,884)
Restructuring	(1,324)	-
Tax expense	(11)	(845)
Other segment items (d)	2,476	18,855
Consolidated net loss	(88,612)	(45,309)

- (a) Contracted research and development costs primarily consist of costs incurred under agreements with CROs and investigative sites that conduct its preclinical studies and clinical trials; costs related to manufacturing active pharmaceutical ingredients and drug products for its preclinical studies and clinical trials; and costs for materials used for in-house research and development activities.
- (b) Personnel R&D costs primarily consist of salaries and personnel-related costs for personnel performing R&D 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.
- (c) Other R&D costs include associated facility costs, equipment and other overheads that are directly attributable to R&D and depreciation of capital assets used for research and development activities.
- (d) The other segment items include foreign currency gain/(loss), net, benefit from R&D credit, and other income/(expense), net inclusive of bank interest receivable and accretion on U.S. Treasury Bills.

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, 2024	-	4,103	11,166	15,269
As at December 31, 2025	-	600	12,184	12,784
Revenue analysis for the year ended December 31, 2023				
Research collaboration	-	30,934	-	30,934
Royalties	-	-	709	709
	<u>-</u>	<u>30,934</u>	<u>709</u>	<u>31,643</u>
Revenue analysis for the year ended December 31, 2024				
Research collaboration	-	43,114	-	43,114
Royalties	-	-	144	144
	<u>-</u>	<u>43,114</u>	<u>144</u>	<u>43,258</u>
Revenue analysis for the year ended December 31, 2025				
Research collaboration	-	559	-	559
Royalties	-	-	-	-
	<u>-</u>	<u>559</u>	<u>-</u>	<u>559</u>

SILENCE THERAPEUTICS PLC
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS – (Continued)

5. Directors and staff costs

Staff costs, including Directors' remuneration, during the year for the Group were as follows:

	Year ended December 31,	
	2025	2024
	\$000s	\$000s
Wages and salaries	19,254	19,434
Social security costs	1,673	1,744
Other pension costs	748	666
Share-based payments charge	8,074	16,307
Total aggregate remuneration	29,749	38,151

The decrease in costs for share-based payments is largely due to credit of previously accrued expense for those grants forfeited or cancelled due to reduction in number of employees, as well as lower fair value of 2025 issued grants.

6. Restructuring charges

During the twelve months ended December 30, 2025, the Group initiated a non-recurring reduction in workforce which resulted in total restructuring charges of \$1.3 million. The charges consist of severance costs for terminated employees. The remaining accrual at December 31, 2025 was \$0.1 million.

7. Other income, net

	Year ended December 31,	
	2025	2024
	\$000s	\$000s
Bank interest receivable	15	704
Accretion on U.S. Treasury Bills	3,465	3,768
Total other income	3,480	4,472

8. Loss per share (basic and diluted)

Basic net loss per share is computed by dividing net loss (the numerator) by the weighted average shares outstanding for the period (the denominator). Diluted net loss per share is computed by dividing net income by the weighted average shares outstanding during the period adjusted for the dilutive effects of the exercise of the stock options. In periods when losses from continuing operations are reported, the weighted-average shares outstanding excludes common stock equivalents because their inclusion would be anti-dilutive. The computation of net loss per share for the years ended December 31, 2025 and 2024, respectively was as follows:

	Year ended December 31,	
	2025	2024
	\$000s	\$000s
Net loss	(88,612)	(45,309)
Weighted-average shares outstanding (basic and diluted)	141,694,702	138,752,224
Net loss per share (basic and diluted)	\$ (0.63)	\$ (0.33)

The following outstanding potentially dilutive securities were excluded from the calculation of diluted net loss per share because their impact would have been anti-dilutive for the period presented.

SILENCE THERAPEUTICS PLC
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS – (Continued)

	Year ended December 31,	
	<u>2025</u>	<u>2024</u>
Potentially Dilutive Securities		
Stock options	20,884,098	17,455,390

SILENCE THERAPEUTICS PLC
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS – (Continued)

9. Property, plant and equipment

Property, plant, and equipment balances were as follows:

	Year ended December 31,	
	2025	2024
	\$000s	\$000s
Equipment & Furniture	5,542	6,343
Accumulated Depreciation	(3,961)	(4,525)
Property, plant, and equipment, net	1,581	1,818

Depreciation expense of \$0.3 million and \$0.3 million, was recognized in fiscal years 2025 and 2024 respectively.

10. Goodwill

Goodwill is assessed annually at a reporting unit level, or whenever events and circumstances indicate impairment may have occurred. The Group has one reporting unit and performs a qualitative impairment test (also known as “Step 0”), and when necessary, a quantitative test. After assessing the totality of events and circumstances as part of the Step 0 test, it was determined that it is not more likely than not (a likelihood that is more than 50%) that the fair value of the reporting unit is less than its carrying amount and therefore a quantitative test is unnecessary. No triggering events were identified during the year.

The following table presents the changes in the carrying amount of goodwill:

	Year ended December 31,	
	2025	2024
	\$000s	\$000s
Balance at start of year	9,392	9,981
Translation adjustment	1,229	(589)
Balance at end of year	10,621	9,392

11. Other intangible assets

Intangible assets as of December 31, 2025 are as follows:

	Year ended December 31,	
	2025	2024
	\$000s	\$000s
License and software	481	481
Accumulated Depreciation	(193)	(169)
License and software, net	288	312

The intangible assets are amortized beginning from the date of acquisition, over their useful life or written down if they are considered to be impaired.

Amortization expense is included in General and administrative expenses, which included on the consolidated statements of income (loss), and was nominal for the years ended December 31, 2025 and 2024, respectively.

SILENCE THERAPEUTICS PLC
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS – (Continued)

Expected future amortization expense is as follows:

Year	Expected Amortization
2026	46
2027	41
2028	41
2029	41
2030	41
Thereafter	78

No impairment charges related to intangible assets were recorded for the years ended December 31, 2025 and 2024.

12. Cash and cash equivalents and short-term investments

	Year ended December 31,	
	2025	2024
	\$000s	\$000s
Cash at bank and in hand	11,277	56,590
U.S. treasury bills	-	64,740
Total cash and cash equivalents	11,277	121,330
U.S. treasury bills	73,837	26,004
Total short-term investments	73,837	26,004

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.

13. Other assets

	Year ended December 31,	
	2025	2024
	\$000s	\$000s
Prepayments	8,930	13,124
VAT receivable	2,607	1,540
Total other current assets	11,537	14,664
Deposits for properties	-	356
Prepayments	127	3,234
Other long-term assets	127	3,590

SILENCE THERAPEUTICS PLC
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS – (Continued)

At December 31, 2025 and 2024, the largest component of prepayments are prepaid third party costs for clinical trials, as well as manufacturing for clinical supplies and associated development, and pre-clinical studies which fluctuate based on timing of payments and related expense.

Included within prepayments at December 31, 2025 and 2024 is \$6.8 million and \$11.0 million respectively, are expenditures relating to contracted research and development costs.

14. Trade receivables

	Year ended December 31,	
	2025	2024
	\$000s	\$000s
Trade receivables	-	972

The Group considers that the carrying amount of trade receivables approximates 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 no allowance is required for the periods ended December 31, 2025 and 2024.

15. Trade and other payables

	Year ended December 31,	
	2025	2024
	\$000s	\$000s
Trade payables	4,409	3,697
Social security and other taxes	195	244
Accruals and other payables	5,749	8,361
Bonus accrual	2,964	3,445
Corporate income tax payable	39	652
Total trade and other payables	13,356	16,399

The Group considers that the carrying amount of trade and other payables approximates their fair value. Bonus accrual and accruals and other payables include accrued severance and other compensation costs that are currently subject to ongoing negotiation.

Included within accruals and other payables at December 31, 2025 and 2024 is \$3.0 million and \$5.9 million respectively, are expenditures relating to contracted research and development costs.

16. Leases

The Group has one operating lease for office space in London, which was moved to a new location upon completion of the original lease term, with the new lease beginning in September 2025. The Group determines whether a contract is a lease or contains a lease at inception date. Upon commencement, the Group recognizes a right-of-use asset and lease liability. Right-of-use assets represent the Group's right to use the underlying asset for the lease term. Lease liabilities are the Group's obligation to make the lease payments arising from a lease. As the Group's lease does not provide an implicit rate, the Group's lease liabilities are measured on a discounted basis using the Group's incremental borrowing rate. Lease terms used in the recognition of right-of-use assets and lease liabilities include only options to extend the lease that are reasonably certain to be exercised. Additionally, lease terms underlying the right-of-use assets and lease liabilities consider terminations that are reasonably certain to be executed.

There are two short-term leases in Berlin, Germany and six leases in Hoboken, U.S., that have not been recognized as right-of-use assets. Both leases in Berlin are on a rolling contract basis with either party being able to end the

SILENCE THERAPEUTICS PLC
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS – (Continued)

lease with a cancellation notice period of 11.5 months, while the leases in the United States are on a rolling contract basis with a notice period of 3 months. Expense related to these short-term leases are recorded to the consolidated statements of income (loss) over the lease term.

The following table presents supplemental balance sheet information related to the Group’s operating lease:

	Classification	Year ended December 31,	
		2025	2024
		\$000s	\$000s
Operating lease right-of-use asset	Other non-current assets	167	157
Lease liability - current	Current liabilities	89	117
Lease liability - non-current	Non-current liabilities	71	-

The following table summarizes the weighted-average remaining lease term and weighted-average discount rate for the Group’s operating leases at December 31, 2025 and 2024:

	2025	2024
Weighted-average remaining lease term	1.75 years	0.75 years
Weighted-average discount rate	10.5%	7.0%

The following table summarizes the components of total operating lease cost for fiscal year 2025 and 2024:

	Year ended December 31,	
	2025	2024
	\$000s	\$000s
Operating lease cost	197	248
Short-term lease cost	721	736
Total operating lease cost	918	984

The following table summarizes the maturities of the Group’s operating leases at December 31, 2025:

Fiscal year	Operating Leases
2026	89
2027	71
2028	-
2029	-
2030	-
Thereafter	-
Total expected lease payments	160
Less: Imputed interest	-
Total lease liability	160

17. Contract liabilities

Contract liabilities represent the Group’s obligation to transfer services to a customer for which the Group has received advanced consideration, before the performance obligation has been satisfied. These liabilities are recognized when a customer prepays for services or when the Group has an unconditional right to consideration before the performance obligation is fulfilled.

Contract liabilities comprise entirely of advance consideration received from customers (deferred revenue) in respect of the AstraZeneca research collaboration. The current contract liabilities represent the amount of estimated revenue to be reported in the next 12 months related to amounts invoiced to its partners, while the non-current portion

SILENCE THERAPEUTICS PLC
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS – (Continued)

represents everything beyond 12 months. Current and non-current contract liabilities include future revenue from collaboration recharged expenses, upfront payments, and milestones achieved to December 31, 2025.

	Year ended December 31,	
	2025	2024
	\$000s	\$000s
Contract liabilities:		
Current	168	306
Non-current	55,454	51,790
Total contract liabilities	55,622	52,096
Contract liabilities:		
At January 1, 2025	52,096	81,572
Foreign exchange impact	3,860	(691)
Additions during period	225	14,328
Revenue unwound during period	(559)	(43,113)
At December 31, 2025	55,622	52,096

During the years ended December 31, 2025 and 2024 contract liabilities decreased primarily due to the recognition of revenue in the amount of \$0.6 million and \$43.1 million, respectively, that was included in the contract liabilities balance at the beginning of the year.

18. Income taxes

The Group operates in the U.K. and is subject to income taxes in that jurisdiction. The U.K. tax rate applied for 2025 was 25% (25% for 2024). U.K. deferred tax assets and liabilities have been measured at a rate of 25%. The entire tax expense relates to current tax as shown below. No deferred tax was recognized in the year.

Income (loss) from continuing operations before income taxes:

	Year ended December 31,
	2025
	\$000s
(Loss)/Income from continuing operations:	
UK	(89,679)
Foreign	1,078
Total	(88,601)

The significant components of income tax expense attributable to income from continuing operations for the years ended December 31, 2025 and December 31, 2024 are as follows:

	Year ended December 31,	
	2025	2024
	\$000s	\$000s
Current Tax Expense		
Current Year	11	845
Changes in estimate related to prior years	-	-
Total current tax	11	845
Deferred Tax Expense		
Origination and reversal of temporary differences	-	-
Recognition of previously unrecognized tax losses	-	-
Recognition of previously unrecognized tax losses (derecognition of previously recognized) deductible temporary differences	-	-
Taxation	11	845

SILENCE THERAPEUTICS PLC
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS – (Continued)

Income tax expense (benefit) attributable to income (loss) from continuing operations for the year ended December 31, 2025 differed from the amounts computed by applying the statutory UK federal income tax rate of 25 percent to pretax income (loss) from continuing operations as a result of the following:

	Year Ended December 31,	
	2025	%
	\$000s	
UK Statutory Income Tax (Benefit) at 25%	(22,150)	25.00%
Domestic Federal		
Tax credits	(1,948)	2.20%
Changes in valuation allowance	14,857	-16.77%
Non-taxable and non-deductible items		
Stock Compensation	1,726	-1.95%
Research and Development costs	7,881	-8.89%
Other reconciling items	(108)	0.12%
Foreign tax effects		
Other foreign jurisdictions	(269)	0.30%
Total	(11)	0.01%

Reconciliation of the income tax credit at standard rate of U.K. corporation tax to the current tax credit for the year ended December 31, 2024 is as follows:

	Year Ended
	December 31,
	2024
	\$000s
Loss before tax	(44,464)
UK Statutory Income Tax (Benefit) at 25%	11,116
Income not taxable	3,356
Foreign Tax Rate Differential	308
Change in valuation allowance	(15,423)
Effect of overseas taxes	(202)
Total	(845)

A schedule of income taxes paid by jurisdiction is as follows:

	2025
	\$000s
UK Federal	—
Foreign	
Germany	637
Other	—
Total	637

SILENCE THERAPEUTICS PLC
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS – (Continued)

The Group did not have any deferred tax liabilities as at December 31, 2025 and 2024. Components of the Group's deferred tax assets as at December 31, 2025 and 2024 are as follows:

	Year ended December 31,	
	Gross 2025 \$000s	Gross 2024 \$000s
Deferred tax assets:		
Trading Losses ¹	73,529	55,316
Share-based payments	4,233	3,663
Capital losses	2,651	2,467
Gross deferred tax asset	80,413	61,446
Valuation allowance	(80,413)	(61,446)
Total deferred tax, net	-	-

(1) Included in trading losses is \$8.2 million of accumulated tax losses as of December 31, 2025 (\$7.4 million as of December 31, 2024) related to its operations in Germany for corporate income taxes and \$7.1 million of accumulated losses related to trade taxes in its German entity (\$6.5 million as of December 31, 2024).

Movements in deferred tax valuation allowance:

	Year ended December 31,	
	2025	2024
Valuation allowance at January 1	61,446	63,739
Increase/(decrease) in valuation allowance	18,967	(2,293)
Valuation allowance at December 31	80,413	61,446

Management has reviewed cumulative tax losses and projections of future taxable losses and determined that it is not more likely than not that they will be realized. Accordingly, valuation allowances have been provided over deferred tax assets.

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. In 2024 the Group received a milestone payment of \$2.0 million, which required withholding tax of \$0.2 million. We did not receive a milestone in 2025.

During the year, the Group had not yet received the research and development tax credit related to the prior year. The Group has recognized \$7.5 million in respect of the current year for unfunded projects that are permissible to claim under the SME scheme (2024: \$13.2). In addition, in 2024 we have also recognized \$0.3 million related to the RDEC scheme which is not applicable for 2025.

19. Shareholders' equity

	Year ended December 31,	
	2025	2024
Authorized, allotted, called up and fully paid ordinary shares, par value £0.05	10,290	10,288
	Number	Number
Number of shares in issue	141,701,848	141,674,074
Number of ADS in issue	47,233,949	47,224,691

SILENCE THERAPEUTICS PLC
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS – (Continued)

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 August 11, 2022, the Group announced a registered direct offering (the “Offering”) of 5,950,000 of the Group’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 were \$56.5 million before deducting \$4.1 million in underwriting discounts, commissions and estimated offering expenses.

On October 15, 2021, the Group entered into an Open Market Sale Agreement (the "Sales Agreement"), with Jefferies LLC ("Jefferies"), pursuant to which the Group may offer and sell, from time to time, its ADSs through Jefferies. On October 15, 2021, the Group filed a registration statement, which became effective on October 22, 2021, for the issuance and sale of up to \$100.0 million of ADSs. During the year ended December 31, 2024 the Group raised proceeds of \$27.7 million before deducting \$0.9 million in placement agent fees and other expenses, from sales of ADSs under the Sales Agreement. On October 22, 2024, the Group filed a new registration statement on Form F-3 which replaced the registration statement originally filed on October 15, 2021, for the issuance and sale, if any, of up to an additional \$100 million of its shares represented by ADSs under the Sales Agreement. As of this filing, approximately \$139.6 million of ADSs remained.

On February 5, 2024, the Group announced a private placement of 5,714,286 of the Group’s ADSs, each representing three ordinary shares, at a price of \$21.00 per ADS, with new and existing institutional and accredited investors. The aggregate gross proceeds of the Private Placement were \$120.0 million before deducting \$7.7 million in placement agent fees and other expenses.

Details of the shares issued during the current year is as follows:

Number of shares in issue at December 31, 2024	141,674,074
Number of ADS in issue at December 31, 2024	47,224,691
Shares issued during the year	
Options exercised at \$0.20/ADS or \$0.07/ordinary share	17,775
Options exercised at \$4.23/ADS or \$1.41/ordinary share	9,999
Number of shares in issue at December 31, 2025	141,701,848
Number of equivalent ADS in issue at December 31, 2025	47,233,949

At December 31, 2025, there were options outstanding of 20,884,098 (2024: 17,455,390) unissued ordinary shares.

Details of the options outstanding are as follows:

Year of issue	Weighted average Exercise price (\$)	At January 1, 2025	Options granted	Options forfeited	Options expired	Options exercised	At December 31, 2025	Weighted average years to expiry date
2014	4.23	-	-	-	-	-	-	-
2015	4.23	3,333	-	-	-	(3,333)	-	0.00
2016	5.14	6,524	-	-	-	-	6,524	0.18
2017	8.05	23,333	-	-	-	-	23,333	1.91
2018	0.20	30,593	-	-	(568)	(2,259)	27,766	2.27
2019	5.36	229,997	-	-	-	-	229,997	3.76
2020	8.23	234,178	-	(2,400)	(3,833)	(3,666)	224,279	4.41
2021	22.37	576,136	-	(1,615)	(5,999)	-	568,522	5.81
2022	18.49	1,310,498	-	(123,132)	(12,668)	-	1,174,698	6.29
2023	13.88	2,148,357	-	(290,974)	(9,287)	-	1,848,096	7.21
2024	18.05	1,255,514	-	(138,543)	(4,438)	-	1,112,533	8.05
2025	6.96	-	1,966,485	(220,867)	-	-	1,745,618	8.87
Total (ADSs)		5,818,463	1,966,485	(777,531)	(36,793)	(9,258)	6,961,366	
Total (Ordinary Shares)		17,455,390	5,899,455	(2,332,593)	(110,379)	(27,774)	20,884,098	

ADSs represent three ordinary shares.

SILENCE THERAPEUTICS PLC
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS – (Continued)

20. Equity-settled share-based compensation

The Group has issued share options under the 2018 Long Term Incentive Plan (“LTIP”), 2018 Non-Employee Long Term Incentive 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, 2024). Under the 2023 Plan, LTIP, Non-Employee LTIP, individual contracts and schemes available, the options typically vest after three 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.

	2025		2024		
	Number of ADSs	Weighted Average Exercise price \$	Aggregate Intrinsic Value \$	Number of ADSs	Weighted Average Exercise price \$
Options					
Outstanding at the beginning of the year	5,818,463	15.95	-	5,284,486	14.80
Granted during the year	1,966,485	6.96	-	1,267,514	18.05
Lapsed or forfeited during the year	(814,324)	13.11	-	(264,056)	19.82
Exercised during the year	(9,258)	1.65	-	(469,481)	6.55
Outstanding at the year-end (ADS/\$)	6,961,366	13.76	-	5,818,463	15.95
Exercisable at the year-end	4,211,644	16.12	-	2,870,106	15.94

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.

The options outstanding at the year-end have a weighted average remaining contractual life of 7.28 years (2024: 7.7 years).

As of December 31, 2025, there was \$6.0 million of total unrecognized compensation cost related to stock options granted but not vested under the Company’s plans. That cost will be recognized over an expected remaining weighted-average period of 1.3 years.

In the years ended December 31, 2025 and 2024 the total intrinsic value of stock options exercised was negligible and \$6.8 million, respectively. The weighted average share price at the date of exercise of the options during the year was \$1.65 per ADS (2024: \$20.99).

The Group granted 5,899,455 share options during the year (2024: 3,802,542). The fair value of options granted were calculated using Black Scholes model. Inputs into the model were as follows:

	2025	2024
Inputs and assumptions for options granted in the year:		
Weighted average ADS price (\$)	7.0	18.1
Option life (years)	6.2	6.2
Expected volatility	77.5%-79.8%	74.4%-78.6%
Risk free rate	3.75%-4.7%	3.39%-3.97%
Expected dividend yield	nil	nil
Weighted average grant date fair value (\$)	6.93	12.6

The Group recognized total charges of \$8.1 million (2024: \$16.3 million) related to equity settled share-based payment transactions during the year. The decrease in costs for share-based payments is largely due to credit of previously accrued expense for those grants forfeited or cancelled due to reduction in number of employees, as well as lower fair value of 2025 issued grants.

SILENCE THERAPEUTICS PLC
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS – (Continued)

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 negligible for 2025 and 2024.

21. Capital commitments and contingent liabilities

There were no capital commitments at December 31, 2025 (2024: nil).

22. Commitments under short leases

At December 31, 2025, the Group had a gross commitment on its office rental and service charge in Berlin, Germany and the Hoboken, U.S. lease equal to \$0.6 million (2024: \$0.5 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.

23. 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.

Concentration of credit risk

Financial instruments that potentially subject the Company to concentration of credit risk consist of principally cash and cash equivalents and U.S. Treasury Bills. 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 remote.

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

SILENCE THERAPEUTICS PLC
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS – (Continued)

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.

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's transactions are commonly denominated in U.K pounds sterling; however, the Group receives payments under its collaboration agreements in U.S. dollars and it incurs a portion of its expenses in other currencies, primarily U.S. dollars, and are exposed to the effects of these exchange rates. The Group seeks 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, the Group considers the use of forward exchange contracts to manage its exchange rate exposure.

24. Related party transactions

The Group did not have any related party transactions in 2024 or 2025.

25. Subsequent events

None.