UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 6-K

REPORT OF FOREIGN PRIVATE ISSUER
PURSUANT TO RULE 13a-16 OR 15d-16
UNDER THE SECURITIES EXCHANGE ACT OF 1934

For the Month of November 2021

Commission File Number: 001-39487

Silence Therapeutics plc

(Exact Name of Registrant as Specified in Its Charter)

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

Indicate by check mark whether the registrant files or will file annual reports under cover of Form 20-F or Form 40-F.

Form 20-F ☒ Form 40-F ☐

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(1): ☐

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(7): ☐

On November 16, 2021, Silence Therapeutics plc published its unaudited financial statements as of and for the three and nine months ended September 30, 2021. The interim condensed consolidated financial statements, as well as the Management's Discussion and Analysis and Risk Factors sections, are attached hereto as Exhibit 99.1 to this Report on Form 6-K.

This Report on Form 6-K (including Exhibit 99.1) shall be deemed to be incorporated by reference into the registration statements on Form S-8 (File No. 333-248682), Form F-1 (File No. 333-248203) and Form F-3 (File No. 333-260265) of Silence Therapeutics plc and to be a part thereof from the date on which this report is filed, to the extent not superseded by documents or reports subsequently filed or furnished.

EXHIBIT INDEX

Exhibit No.	Description
99.1	Report for the Three and Nine Months Ended September 30, 2021

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Silence Therapeutics plc

By: /s/ Mark Rothera

Name: Mark Rothera
Title: President and Chief Executive Officer

Date: November 16, 2021

Exhibit 99.1

Condensed consolidated income statement (unaudited)

£000s (except per share information)	Three months ended September 30, 2021	Three months ended September 30, 2020	Nine months ended September 30, 2021	Nine months ended September 30, 2020
Revenue	**3,156**	1,988	**9,001**	3,134
Cost of sales	**(2,052)**	(2,331)	**(5,414)**	(2,331)
Gross profit	**1,104**	(343)	**3,587**	803
Research and development costs	**(7,916)**	(3,468)	**(23,541)**	(13,647)
Administrative expenses	**(5,472)**	(2,666)	**(14,597)**	(7,826)
Other losses - net	**-**	(3,091)	**-**	(3,091)
Operating loss	**(12,284)**	(9,568)	**(34,551)**	(23,761)
Finance and other expenses	**(64)**	(119)	**(86)**	(119)
Finance and other income	**296**	147	**8**	1,011
Loss for the period before taxation	**(12,052)**	(9,540)	**(34,629)**	(22,869)
Taxation	**2,123**	462	**4,653**	2,762
Loss for the period after taxation	**(9,929)**	(9,078)	**(29,976)**	(20,107)
Loss per ordinary equity share (basic and diluted)	**(11.1) pence**	(11.0) pence	**(33.8) pence**	(24.7) pence

Condensed consolidated statement of comprehensive income (unaudited)

	Three months ended September 30, 2021 £000s	Three months ended September 30, 2020 £000s	Nine months ended September 30, 2021 £000s	Nine months ended September 30, 2020 £000s
Loss for the period after taxation	**(9,929)**	(9,078)	**(29,976)**	(20,107)
Other comprehensive expense, net of tax:				
Items that may subsequently be reclassified to profit and loss:				
Foreign exchange differences arising on consolidation of foreign operations	**18**	(12)	**(434)**	573
Total other comprehensive income/(expense) for the period	**18**	(12)	**(434)**	573
Total comprehensive expense for the period	**(9,911)**	(9,090)	**(30,410)**	(19,534)

Condensed consolidated balance sheet (unaudited)

	September 30, 2021 £000s	December 31, 2020 £000s
Non-current assets		
Property, plant and equipment	**1,535**	1,127
Goodwill	**7,786**	8,125
Other intangible assets	**3**	17
Financial assets at amortized cost	**302**	303
	9,626	9,572
Current assets		
Cash and cash equivalents	**71,469**	27,449
Derivative financial instrument	**-**	1,492
Financial assets at amortized cost – term deposit	**5,000**	10,000
Financial assets at amortized cost – other	**-**	-
R&D tax credit receivable	**3,778**	3,536
Other current assets	**2,882**	4,616
Trade receivables	**-**	29,306
	83,129	76,399
Non-current liabilities		
Contract liabilities	**(57,998)**	(51,337)
	(57,998)	(51,337)
Current liabilities		
Contract liabilities	**(9,030)**	(17,042)
Trade and other payables	**(9,236)**	(8,192)
Lease liability	**(131)**	(341)
	(18,397)	(25,575)
Net assets	**16,360**	9,059
Capital and reserves attributable to the owners of the parent		
Share capital	**4,489**	4,165
Capital reserves	**223,637**	186,891
Translation reserve	**1,784**	2,218
Accumulated losses	**(213,550)**	(184,215)
Total shareholders equity	**16,360**	9,059

Condensed consolidated statement of changes in equity (unaudited)

	Share Capital	Capital Reserves	Translation Reserve	Accumulated Losses	Total
	£000s	£000s	£000s	£000s	£000s
At January 1, 2020	3,919	167,243	1,746	(151,999)	20,909
Recognition of share-based payments	-	4,395	-	-	4,395
Options exercised in the period	-	(331)	-	331	-
Proceeds from shares issued	246	15,584	-	-	15,830
Transactions with owners recognized directly in equity	246	19,648	-	331	20,225
Loss for the period	-	-	-	(32,547)	(32,547)
Other comprehensive income					
Foreign exchange differences arising on consolidation of foreign operations	-	-	472	-	472
Total comprehensive expense for the period	-	-	472	(32,547)	(32,075)
At December 31, 2020	4,165	186,891	2,218	(184,215)	9,059
At January 1, 2021	4,165	186,891	2,218	(184,215)	9,059
Recognition of share-based payments	-	6,790	-	-	6,790
Options exercised in the period	-	(641)	-	641	-
Proceeds from shares issued	324	30,597	-	-	30,921
Transactions with owners recognized directly in equity	324	36,746	-	641	37,711
Loss for the period	-	-	-	(29,976)	(29,976)
Other comprehensive expense					
Foreign exchange differences arising on consolidation of foreign operations	-	-	(434)	-	(434)
Total comprehensive expense for the period	-	-	(434)	(29,976)	(30,410)
At September 30, 2021	**4,489**	**223,637**	**1,784**	**(213,550)**	**16,360**

Condensed consolidated statement of cash flows (unaudited)

	Nine months ended	
	September 30, 2021	September 30, 2020
	£000s	£000s
Cash flow from operating activities		
Loss before tax	**(34,629)**	(22,869)
Depreciation charges	**347**	295
Amortization charges	**14**	15
Charge for the period in respect of share-based payments	**6,790**	1,353
Net foreign exchange (gain)/loss	**(226)**	3,410
Finance and other expenses	**86**	(801)
Finance and other income	**(8)**	(91)
Decrease/(increase) in trade and other receivables	**29,306**	(31,905)
Decrease/(increase) in other current assets	**1,735**	(2,325)
Decrease in current financial assets at amortized cost – other	**-**	7
Increase/(decrease) in trade and other payables	**1,044**	(912)
Decrease in derivative financial instrument	**1,492**	-
(Decrease)/increase in contract liabilities	**(1,351)**	48,454
Cash provided/(spent) on operations	**4,600**	(5,369)
R&D tax credits received	**4,411**	-
Net cash inflow/(outflow) from operating activities	**9,011**	(5,369)
Cash flow from investing activities		
Redemption of financial assets at amortized cost – term deposits	**5,000**	10,000
Purchase of financial assets at amortized cost – term deposits	**-**	(20,021)
Interest received	**8**	86
Purchase of property, plant and equipment	**(784)**	(417)
Net cash (outflow)/inflow from investing activities	**4,224**	(10,352)
Cash flow from financing activities		
Repayment of lease liabilities	**(210)**	(272)
Proceeds from issue of share capital	**30,921**	15,806
Net cash inflow from financing activities	**30,711**	15,534
Increase/(decrease) in cash and cash equivalents	**43,946**	(187)
Cash and cash equivalents at start of the period	**27,449**	13,515
Effect of exchange rate fluctuations on cash and cash equivalents held	**74**	587
Cash and cash equivalents at end of the period	**71,469**	13,915

1. General information

Silence Therapeutics plc and its subsidiaries (together the 'Group') are primarily involved in the discovery, delivery and development of RNA therapeutics. Silence Therapeutics plc (the 'Company'), a public company limited by shares registered in England and Wales, with company number 02992058, is the Group's ultimate parent company. The Company's registered office is 27 Eastcastle Street, London, W1W 8DH and the principal place of business is 72 Hammersmith Road, London, W14 8TH.

These condensed interim financial statements were approved for issue on November 15, 2021.

These condensed interim financial statements do not comprise statutory accounts within the meaning of section 434 of the Companies Act 2006. Statutory accounts for the year ended December 31, 2020 were approved by the board of directors on March 31, 2021 and delivered to the Registrar of Companies. The report of the auditors on those accounts was unqualified, did not contain an emphasis of matter paragraph and did not contain any statement under section 498 of the Companies Act 2006.

The financial statements have not been reviewed or audited.

Basis of Preparation and Accounting Policies

Silence Therapeutics plc transitioned to UK-adopted international accounting standards in its consolidated financial statements on January 1, 2021. This change constitutes a change in accounting framework. However, there is no impact on recognition, measurement or disclosure in the period reported as a result of the change in framework.

This condensed consolidated interim financial report for the nine-month reporting period ended September 30, 2021 has been prepared in accordance with International Accounting Standard 34, Interim Financial Reporting (IAS 34) as issued by the International Accounting Standards Board (IASB).

The interim report does not include all of the notes of the type normally included in an annual financial report. Accordingly, this report is to be read in conjunction with the annual report for the year ended December 31, 2020, which was prepared in accordance with international accounting standards in conformity with the requirements of IFRS as issued by the IASB.

The accounting policies adopted are consistent with those of the previous financial year and corresponding interim reporting period.

The preparation of interim financial statements requires management to make judgements, estimates and assumptions that affect the application of accounting policies and the reported amounts of assets and liabilities, income and expense. Actual results might differ from these estimates.

In preparing these condensed interim financial statements, the significant judgements made by management in applying the Group's accounting policies and the key sources of estimation uncertainty are disclosed in the 'Critical Accounting Policies, Judgments and Estimates' section on Page 21.

2. Going concern

The financial statements have been prepared on a going concern basis that assumes that the Group will continue in operational existence for the foreseeable future.

Since 2020, the coronavirus (COVID-19) pandemic has been prevalent in Europe, the UK and the US where the Group's principal operations are conducted. Significant restrictions have been imposed by the governments of those countries where the Group has operations, as well as the countries of external parties with which we conduct our

business. In compliance with these restrictions, the Group and its employees have adapted to new working arrangements to ensure business continuity as far as is reasonably practicable in the short to medium term. This has so far proven to be effective, with Management maintaining a strong line of communication with all employees during this period.

The main risk posed to the Group by the pandemic is the potential slowing of Research & Development activities including possible knock-on delays in clinical trial data and sustained fixed costs during periods of relative inactivity. Whilst this would result in a lengthening of the Group's cash runway in the medium term, in the longer term these factors could limit the Group's ability to meet its corporate objectives. This risk is mitigated by the receipt of $60 million (£47.9 million) of the upfront payments in respect of the AstraZeneca collaboration, the $45 million private placement (or approximately $42.0 million / £30.8 million, net of expenses) and the expected mid-December 2021 receipt of $14.4 million of the upfront payment, net of taxes withheld, related to Hansoh collaboration executed on October 14, 2021, all of which significantly increase the Group's forecasted baseline cash runway.

Based on the current operating forecasts and plans and, considering the cash, cash equivalents and term deposit at September 30, 2021, the Directors are confident that the Group has sufficient funding through early 2023. For this reason, they continue to adopt the going concern basis in preparing the financial statements.

3. Revenue

Revenue from collaboration agreements for the nine months ended September 30, 2021 relates to the research collaboration agreements the Group entered into with Mallinckrodt plc in July 2019, Takeda Pharmaceutical Company Limited in January 2020 and AstraZeneca plc in March 2020.

Revenue for the nine months ended September 30, 2021 comprised £8,728k of research collaboration income (nine months to September 30, 2020: £2,983k) and £273k of royalty income (nine months to September 30, 2020: £151k).

	Three months ended		Nine months ended	
	September 30, 2021	September 30, 2020	September 30, 2021	September 30, 2020
	£000s	£000s	£000s	£000s
Revenue from Contracts with Customers				
Research collaboration - Mallinckrodt plc	**2,574**	1,826	**6,362**	2,300
Research collaboration - AstraZeneca	**506**	11	**1,777**	11
Research collaboration - Other	**(29)**	151	**589**	672
Research collaboration - total	**3,051**	1,988	**8,728**	2,983
Royalties	**105**	-	**273**	151
Total revenue from contracts with customers	**3,156**	1,988	**9,001**	3,134

Under our collaboration agreement with Mallinckrodt, we received an upfront cash payment of £16.4 million ($20 million) in 2019 and are eligible to receive specified development, regulatory and commercial milestone payments. We received milestone payments of £2.9 million (or $4 million) during the nine months ended September 30, 2021, and £1.4 million (or $2 million) in respect of the nine months ended September 30, 2020. In addition to these payments, Mallinckrodt has agreed to fund some of our research personnel and preclinical development costs. We recognize the upfront payment, milestone payments, payments for personnel costs and other research funding payments over time, in accordance with IFRS 15. During the nine months ended September 30, 2021, we recognized a total of £6.4 million in revenue under this agreement.

Under our collaboration agreement with AstraZeneca, we received an upfront cash payment of £17.1 million ($20 million) in 2020 with a further amount of £30.8 million ($40 million) received in May 2021. We recognize the upfront payment and milestone payments over time, in accordance with IFRS 15. During the nine months ended September 30, 2021, we recognized a total of £1.8 million in revenue under this agreement.

We entered into a Technology Evaluation Agreement with Takeda on January 7, 2020 to explore the potential of our platform to generate siRNA molecules against a novel, undisclosed target controlled by Takeda. Under our collaboration agreement, we received a milestone payment of £1.6 million ($2 million) during the year ended December 31, 2020. We recognize the milestone payments over time, in accordance with IFRS 15. Our activities under the Technology Evaluation Agreement were effectively complete as of September 30, 2021. We may negotiate to enter into an exclusive follow-on license and collaboration agreement covering the Takeda target at some point in the future.

4. Segment reporting

Operating segments are reported in a manner consistent with the internal reporting provided to the Board. The chief operating decision maker (CODM), who has been identified as the Chief Executive Officer responsible for allocating resources and assessing performance of the operating segments.

For the nine months ended September 30, 2021 and nine months ended September 30, 2020, the CODM determined that the Group had one business segment, the development of RNAi-based medicines. This is in line with reporting to senior management. The information used internally by the CODM is the same as that disclosed in the financial statements.

	U.S. £000s	U.K. £000s	Germany £000s	Total £000s
Non-current assets				
As at December 31, 2020	54	689	8,829	9,572
As at September 30, 2021	**17**	**521**	**9,088**	**9,626**
Revenue analysis for the year ended December 31, 2020				
Research collaboration	**-**	5,253	-	5,253
Royalties	**-**	-	226	226
	-	5,253	226	5,479
Revenue analysis for the nine months ended September 30, 2021				
Research collaboration	-	**8,728**	-	**8,728**
Royalties	-	-	**273**	**273**
	-	**8,728**	**273**	**9,001**

5. Loss per ordinary equity share (basic and diluted)

The calculation of the loss per share is based on the loss for the nine months to September 30, 2021 after taxation of £29,976k (nine months ended September 30, 2020: loss of £20,107k) and on the weighted average ordinary shares in issue during the nine months ended September 30, 2021 of 88,670,141 (nine months ended September 30, 2020: 81,360,203). For the three months ended September 30, 2021, the calculation of the loss per share is based on the loss after taxation of £9,929k (three months ended September 30, 2020: loss of £9,078k) and on the weighted average ordinary shares in issue during the three months ended September 30, 2021 of 89,740,014 (three months ended September 30, 2020: 82,826,351).

The options outstanding at September 30, 2021 and September 30, 2020 are considered to be anti-dilutive as the Group is loss-making.

6. Goodwill

	September 30, 2021 £000s	December 31, 2020 £000s
Balance at start of the period	**8,125**	7,692
Translation adjustment	**(339)**	433
Balance at end of the period	**7,786**	8,125

7. Derivative financial instruments

Derivative financial instruments related to an open forward currency contract measured at fair value through the income statement. The fair value was calculated from data sourced from an independent financial market data provider using mid-market-end-of-day data as of December 31, 2020. The derivative contract in place at December 31, 2020 was closed out on May 28, 2021.

The fair value of the derivative is calculated based on level 2 inputs under IFRS 13.

	September 30, 2021 £000s	December 31, 2020 £000s
Derivatives carried at fair value	**-**	1,492

The fair value of financial instruments that are not traded in active market, in the case of an over-the-counter derivative, is determined using valuation techniques which maximize the use of observable market data and rely as little as possible on entity specific estimates. As all significant inputs required to fair value an instrument are observable, this derivative financial instrument is included in level 2.

The specific valuation technique used to value this derivative is the present value of future cash flow based on the forward exchange rate relative to its value based on the year-end exchange rate.

The derivative fair value movement is disclosed in the Income Statement under “Other (losses)/gains – net”. For the nine-month period to September 30, 2021 the gain on the derivative financial instrument (£1.02 million), which was closed out in May 2021, matched the related loss (£1.02 million) on the receivable, resulting in a net nil impact on the Income Statement.

8. Contract liabilities

Contract liabilities comprise entirely deferred revenue in respect of the Mallinckrodt, Takeda and AstraZeneca plc Research collaborations. The current contract liabilities represent the amount of estimated revenue to be reported in

the next 12 months related to amounts invoiced to our partners. The current and non-current contract liabilities include only recharge expenses and milestones achieved through September 30, 2021.

	September 30, 2021	December 31, 2020
	£000s	£000s
Contract liabilities:		
Current	**9,030**	17,042
Non-current	**57,998**	51,337
Total contract liabilities	**67,028**	68,379

	Current	Non-current	Total
	£000s	£000s	£000s
Contract liabilities:			
At January 1, 2020	2,478	15,515	17,993
Additions during period	19,779	35,822	55,601
Revenue unwound during period	(5,215)	-	(5,215)
At December 31, 2020	17,042	51,337	68,379
At January 1, 2021	17,042	51,337	68,379
Additions during period	3,419	3,958	7,377
Revenue unwound during period	(8,728)	-	(8,728)
Program rephasing	(2,703)	2,703	-
At September 30, 2021	**9,030**	**57,998**	**67,028**

9. Taxation

A £3.8 million current tax asset was recognized in respect of research and development tax credits in the nine months ended September 30, 2021 (nine months ended September 30, 2020: £5.8 million). The asset at September 30, 2020 comprised £2.8 million in respect of research and development activity for the nine months ended September 30, 2020 and £3.0 million in respect of the year ended December 31, 2019. Additionally, during the third quarter of 2021, we received research and development tax credits for the year ended December 31, 2020 of £4.4 million, which resulted in an adjustment to the credit recorded in the year ended December 31, 2020 of a further £0.9 million.

10. Capital reserves

	Share premium account	Merger reserve	Share based payment reserve	Capital redemption reserve	Total
	£000s	£000s	£000s	£000s	£000s
At January 1, 2019	133,242	22,248	2,437	5,194	163,121
Shares issued	3,767	-	-	-	3,767
On options in issue during the year	1,141	-	584	-	1,725
On vested options lapsed during the year	-	-	-	-	-
On options exercised during the year	-	-	(1,370)	-	(1,370)
Movement in the year	4,908	-	(786)	-	4,122
At December 31, 2019	138,150	22,248	1,651	5,194	167,243
Shares issued	15,396	-	-	-	15,396
On options in issue during the year	188	-	4,395	-	4,583
On vested options lapsed during the year	-	-	-	-	-
On options exercised during the year	-	-	(331)	-	(331)
Movement in the year	15,584	-	4,064	-	19,648
At December 31, 2020	153,734	22,248	5,715	5,194	186,891
Shares issued	32,585	-	-	-	32,585
On options in issue during the period	-	-	7,090	-	7,090
On vested options lapsed during the period	-	-	(300)	-	(300)
On options exercised during the period	459	-	(641)	-	(182)
Costs capitalized in respect of issuance of shares during the period	(2,447)	-	-	-	(2,447)
Movement in the period	30,597	-	6,149	-	36,746
At September 30, 2021	**184,331**	**22,248**	**11,864**	**5,194**	**223,637**

	September 30, 2021	December 31, 2020
	£000s	£000s
Authorized, allotted, called up and fully paid ordinary shares, par value £0.05	**4,489**	4,165
Number of shares in issue	**89,777,000**	83,306,259

The Group has only one class of share. All ordinary shares have equal voting rights and rank pari passu for the distribution of dividends.

On February 5, 2021 the Group announced a private placement of 2,022,218 of the Company's American Depositary Shares ("ADSs"), each representing three ordinary shares, at a price of US $22.50 per ADS, with new and existing institutional and accredited investors (the "Private Placement"). The aggregate gross proceeds of the Private Placement was US $45 million (approximately £33 million) before deducting approximately £2.4 million in placement agent fees and other expenses. The financing syndicate included Adage Capital Management LP, BVF Partners L.P., Consonance Capital, Great Point Partners, LLC, and other investors.

On October 15, 2021, the Company filed a registration statement on Form F-3 with the SEC to cover the offering, issuance and sale of securities from time to time in one or more offerings. The aggregate initial offering price is not to exceed $300,000,000, which includes a sale of up to a maximum aggregate offering price of $100,000,000 of ADSs that may be issued and sold under an Open Market Sale Agreement, dated October 15, 2021 with Jefferies LLC.

The Company also announced on October 15, 2021, its intention to cancel the admission of the Company's ordinary shares of nominal value £0.05 each trading on AIM, with effect from November 30, 2021. Shareholders approved the delisting on November 1, 2021. The last day of trading for the Company's ordinary shares on AIM will be November 29, 2021. The Company intends to retain the listing on the Nasdaq Global Market ('Nasdaq') of ADSs under ticker symbol SLN. The Nasdaq Global Market is expected to become the primary trading venue for the Company's equity securities.

Details of the shares issued by the Company during the nine months ended September 30, 2021 are as follows:

Number of shares in issue at January 1, 2020	78,370,265
Shares issued during the period	4,276,580
Options exercised at £0.05	496,666
Options exercised at £0.85	56,470
Options exercised at £1.00	60,000
Options exercised at £1.90	46,278
Number of shares in issue at December 31, 2020	83,306,259
Shares issued during the period	6,066,654
Options exercised at £0.05	59,114
Options exercised at £0.60	80,302
Options exercised at £1.06	25,000
Options exercised at £1.90	198,119
Number of shares in issue at June 30, 2021	89,735,448
Options exercised at £0.05	10,407
Options exercised at £0.60	31,145
Number of shares in issue at September 30, 2021	**89,777,000**

11. Related party transactions

Transactions between the Group and its subsidiaries, which are related parties, have been eliminated on consolidation and are not disclosed in this note.

During the nine months to September 30, 2021 the Group paid £nil (nine months to September 30, 2020: £75k) to Gladstone Partners Limited, a company controlled by Director Iain Ross. The amounts payable were settled before the relevant period ends.

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of financial condition and operating results together with our unaudited financial statements as of and for the three and nine months ended September 30, 2021 and the related notes to those financial statements included as Exhibit 99.1 to this Report on Form 6-K.

The statements in this discussion with respect to our plans and strategy for our business, including expectations regarding our future liquidity and capital resources and other non-historical statements, are forward-looking statements. These forward-looking statements are subject to numerous risks and uncertainties, including the risks and uncertainties described in Exhibit 99.1 to this Report on Form 6-K. Our actual results may differ materially from those contained in or implied by any forward-looking statements.

Overview

Silence Therapeutics plc ("we", "us", "our", "the Company" or "Silence") is a biotechnology company focused on discovering and developing novel molecules incorporating short interfering ribonucleic acid, or siRNA, to inhibit the expression of specific target genes thought to play a role in the pathology of diseases with significant unmet medical need. Our siRNA molecules are designed to harness the body's natural mechanism of RNA interference, or RNAi, by specifically binding to and degrading messenger RNA, or mRNA, molecules that encode specific targeted disease-associated proteins in a cell. By degrading the message that encodes the disease-associated protein, the production of that protein is reduced, and its level of activity is lowered. In the field of RNAi therapeutics, this reduction of disease-associated protein production and activity is referred to as "gene silencing." Our proprietary mRNAi GOLD™ (**G**alNAc **Ol**igonucleotide **D**iscovery) platform is a platform of precision engineered medicines designed to accurately target and 'silence' specific disease-associated genes in the liver, which represents a substantial opportunity. Using our mRNAi GOLD™ platform, we have generated siRNA product candidates both for our internal development pipeline as well as for out-licensed programs with third-party collaborators. In May 2021, we presented the first clinical data from our mRNAi GOLD platform that successfully translated the results from pre-clinical models into humans.

Our proprietary clinical programs include SLN360 designed to address the high and prevalent unmet need in reducing cardiovascular risk in people born with high levels of lipoprotein(a), or Lp(a), and SLN124 designed to address rare hematological disorders, including thalassemia and myelodysplastic syndrome, or MDS, and polycythemia vera, or PV. We are evaluating SLN360 in the APOLLO phase 1 single-ascending dose study in healthy individuals with high levels of Lp(a) $\geq$ 60 mg/dL. In August 2021, we announced complete enrollment in the SLN360 single-ascending dose study and we anticipate topline data in the first quarter of 2022. We are evaluating SLN124 in the GEMINI II phase 1 single-ascending dose studies in patients with thalassemia and MDS. We anticipate topline data from both studies in the third quarter of 2022. In May 2021, we reported positive topline results from the SLN124 GEMINI healthy volunteer study, which was the first clinical data from our mRNAi GOLD™ platform. The SLN124 healthy volunteer study demonstrated safety and proof-of-mechanism to support the ongoing SLN124 phase 1 studies in patients with thalassemia and MDS.

Our partnered pipeline includes ongoing research and development collaborations with leading pharmaceutical companies, such as AstraZeneca plc, or AstraZeneca, Mallinckrodt plc, or Mallinckrodt, Takeda Pharmaceutical Company Limited, or Takeda and Hansoh Pharmaceutical Group Company Limited or Hansoh. These collaborations collectively represent up to 14 pipeline programs and up to $6 billion in potential milestones plus royalties.

There are approximately 14,000 liver-expressed genes and only around one percent of them have been targeted by publicly known siRNAs. We aim to maximize the substantial opportunity of our mRNAi GOLD™ platform through a combination of building and advancing our proprietary and partnered pipelines. Through this hybrid model, we plan to significantly expand our portfolio of mRNAi GOLD™ platform programs by delivering 2-3 initial new drug applications per year from 2023.

Recent Corporate Highlights

We held a R&D Day on October 21, 2021 to provide updates on our mRNAi GOLD™ platform and pipeline. The updates included the following:

Proprietary Pipeline

SLN360

- The independent safety review committee recommended to extend the follow-up period in the single-ascending dose study from 150 days to 365 days to fully assess the duration of action, which may be longer than initially anticipated based on preclinical modelling. The therapeutic dose range has been established based on Cohorts 1-4 (optional Cohort 5 not needed) and the study can now proceed to the multiple-ascending dose phase.

SLN124

- We plan to pursue new polycythemia vera (PV) indication and start a phase 1 trial in the second half of 2022.
- We received the FDA Acceptance of the US IND in myelodysplastic syndrome (MDS) on October 20, 2021.
- The positive results from the healthy volunteer study reported in May 2021 was accepted for poster presentation at the American Society of Hematology (ASH) Annual Meeting being held December 11-14, 2021.

Partnered Pipeline

- On October 15, 2021, we announced a collaboration agreement with Hansoh, one of the leading biopharmaceutical companies in China, to develop siRNAs for three undisclosed targets leveraging Silence's proprietary mRNAi GOLD™ platform. Under the terms of the agreement, Hansoh will have the exclusive option to license rights to the first two targets in Greater China, Hong Kong, Macau and Taiwan following the completion of phase 1 studies. 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 studies. Hansoh will also have the exclusive option to license global rights to a third target at the point of IND filing. Hansoh will be responsible for all development activities post option exercise for the third target. Hansoh will make a $16 million upfront payment and Silence is eligible to receive up to $1.3 billion in additional development, regulatory and commercial milestones. Silence will also receive royalties tiered from low double-digit to mid-teens on Hansoh net product sales.
- In our Mallinckrodt collaboration for complement-mediated diseases, we are progressing IND-enabling studies for SLN501 C3 targeting program and expect to initiate a phase 1 study in the first half of 2022.

De-Listing from AIM

- On October 15, 2021, we announced our intention to cancel the admission of our ordinary shares of nominal value £0.05 each trading on AIM, with effect from November 30, 2021. Shareholders approved the delisting on November 1, 2021. Our last day of trading on AIM will be November 29, 2021. We will retain our listing on the Nasdaq Global Market of American Depositary Shares, of which each represents three Ordinary Shares, under ticker symbol “SLN”. We expect Nasdaq to become the primary trading venue for our equity securities.

Shelf Filing Registration

- On October 15, 2021, we filed a registration statement on Form F-3 to cover the offering, issuance and sale of our securities from time to time in one or more offerings, for an aggregate initial offering price not to exceed $300,000,000, which includes a prospectus supplement covering the offering, issuance and sale of up to a maximum aggregate offering price of $100,000,000 of our American Depositary Shares (“ADSs”) each representing three ordinary shares that may be issued and sold under the an Open Market Sale Agreement, dated October 15, 2021 with Jefferies LLC.

Upcoming Events and Anticipated Data Milestones

- Additional results from the SLN124 healthy volunteer study will be presented at ASH Annual Meeting being held December 11-14, 2021.
- Topline data from the SLN360 phase 1 single-ascending dose study in people with high Lp(a) is anticipated in the first quarter of 2022. The Company plans to start phase 2 development in the second half of 2022 pending regulatory discussions.

- Topline data from the SLN124 phase 1 single-ascending dose studies in people with thalassemia and MDS is anticipated in the third quarter of 2022.
- Silence plans to initiate a phase 1 study of SLN124 in PV patients in the second half of 2022.
- We anticipate initiating a phase 1 study of SLN501 in our Mallinckrodt collaboration for complement-mediated diseases in the first half of 2022.

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 (equivalent to £17.1 million as of the payment date) with a further £30.8 million ($40 million) 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.

We anticipate initiating work on five targets within the first three years of the collaboration, with AstraZeneca having the option to extend the collaboration to an additional five targets. AstraZeneca has agreed to pay us $10.0 million upon the exercise of each option to collaborate on an additional target. For each target selected, we will be eligible to receive up to $140.0 million in potential milestone payments upon the achievement of milestones relating to the initiation of specified clinical trials, the acceptance of specified regulatory filings and the first commercial sale in specified jurisdictions. For each target selected, we will also be eligible to receive up to $250.0 million in potential commercial milestone payments, upon the achievement of specified annual net sales levels, as well as tiered royalties as a percentage of net sales ranging from the high single digits to the low double digits.

We continue to advance the research and development workplans for each identified target as scheduled and agreed to with our collaboration partner.

Collaboration Agreement with Mallinckrodt

In July 2019, we entered into a collaboration agreement with Mallinckrodt Pharma IP Trading DAC, a wholly owned subsidiary of Mallinckrodt plc, to develop and commercialize RNAi drug targets designed to silence the complement cascade in complement-mediated disorders. Under the agreement, we granted Mallinckrodt an exclusive worldwide license to our C3 targeting program, SLN500, with options to license two additional complement-mediated disease targets from us. Mallinckrodt exercised options to license two additional complement targets from us in July 2020.

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

The collaboration provides for potential additional development and regulatory milestone payments in aggregate of up to $100 million for the initial C3 target and up to $140 million for each of the two optioned complement-mediated disease targets, with such milestones relating to the initiation of specified clinical trials in specified jurisdictions, and upon the receipt of regulatory approvals by specified authorities, in each case for multiple indications. We are also eligible to receive potential commercial milestone payments of up to $562.5 million upon the achievement of specified levels of annual net sales of licensed products for each program. We are also eligible to receive tiered, low double-digit to high-teen percentage royalties on net sales for licensed products for each program. We received a research milestone payment of $2 million in October 2019 upon the initiation of work for the first complement C3 target. In September 2020, we received another $2 million research milestone payment following the initiation of work on a second complement target. In February 2021, we initiated work on the third complement target which triggered another $2 million research milestone payment. In April 2021, we received another $2.0 million research milestone for the initiation of the toxicology study for the first identified target.

In connection with the execution of this agreement, Mallinckrodt made an upfront cash payment in 2019 of $20.0 million (equivalent to £16.4 million as of the payment date). Under a separate subscription agreement, Cache Holdings Limited, a wholly owned subsidiary of Mallinckrodt plc, concurrently subscribed for 5,062,167 new ordinary shares for an aggregate subscription price of $5.0 million (equivalent to £4.0 million as of the payment date).

We continue to advance the research and development workplans for each identified target as scheduled and agreed to with our collaboration partner.

Financial Operations Overview

Revenue

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

Under our collaboration agreement with AstraZeneca, we received an upfront cash payment of £17.1 million ($20.0 million) and an additional payment of £30.8 million ($40.0 million) in May 2021. We are also eligible to receive specified development and commercial milestone payments as well as tiered royalties on net sales, if any. We recognize the upfront payment and milestone payments over time, in accordance with IFRS 15. During the nine months ended September 30, 2021, we recognized a total of £1.8 million in revenue under this agreement.

Under our collaboration agreement with Mallinckrodt, we received an upfront cash payment of $20.0 million (£16.4 million as of the payment date) and are eligible to receive specified development, regulatory and commercial milestone payments. We received a milestone payment of $2.0 million (£1.7 million as of the payment date) in 2020 and 2 other milestone payments totaling $4.0 million (£2.9 million as of the payment date) in the first half of 2021. In addition to these potential payments, Mallinckrodt has agreed to fund some of our research personnel and preclinical development costs. We recognize the upfront payment, milestone payments, payments for personnel costs and other research funding payments over time, in accordance with IFRS 15. During the nine months ended September 30, 2021, we recognized a total of £6.4 million in revenue under this agreement.

We entered into a Technology Evaluation Agreement with Takeda on January 7, 2020 to explore the potential of our platform to generate siRNA molecules against a novel, undisclosed target controlled by Takeda. Under our collaboration agreement, during the nine months ended September 30, 2021 we received a milestone payment of £nil (nine months ended September 30, 2020: £0.4 million). We recognize the milestone payments over time, in accordance with IFRS 15. Our activities under the Technology Evaluation Agreement with Takeda were effectively complete as of September 30, 2021. We may negotiate to enter into an exclusive follow-on license and collaboration agreement covering the Takeda target at some point in the future.

In December 2018, we entered into a settlement and license agreement with Alnylam Pharmaceuticals Inc., or Alnylam, pursuant to which we settled outstanding patent litigation with Alnylam related to its RNAi product ONPATTRO. As part of the settlement, we license specified patents to Alnylam, and Alnylam pays us a tiered royalty of up to one percent of net sales of ONPATTRO in the EU. We are eligible to receive these royalties until 2023. We invoice Alnylam quarterly in arrears based on sales data for that quarter as reported to us by Alnylam. Royalty revenue is recognized based on the level of sales when the related sales occur. During the nine months ended September 30, 2021, we recognized a total of £0.3 million in royalty income from Alnylam.

Cost of Sales

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

Operating Expenses

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

Research and Development Expenses

The largest component of our total operating expenses since inception has been costs related to our research and development activities, including the preclinical and clinical development of our product candidates. We account for research and development costs on an accruals basis.

Our contracted research and development expense primarily consists of:

- costs incurred under agreements with CROs and investigative sites that conduct preclinical studies and clinical trials;
- costs related to manufacturing active pharmaceutical ingredients and drug products for preclinical studies and clinical trials; and
- costs for materials used for in-house research and development activities.

Our research and development personnel expense primarily consists of:

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

Other research and development expense primarily consists of:

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

The successful development of our product candidates is highly uncertain. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. Accordingly, we expect research and development costs to increase significantly for the foreseeable future as programs progress. However, we do not believe that it is possible at this time to accurately project total program-specific expenses through commercialization. We are also unable to predict when, if ever, material net cash inflows will commence from our product candidates to offset these expenses. Our expenditures on current and future preclinical and clinical development programs are subject to numerous uncertainties in timing and cost to completion.

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

- the scope, rate of progress, results and expenses of our ongoing and future clinical trials, preclinical studies and research and development activities;
- the potential need for additional clinical trials or preclinical studies requested by regulatory agencies;
- potential uncertainties in clinical trial enrollment rates or drop-out or discontinuation rates of patients;
- competition with other drug development companies in, and the related expense of, identifying and enrolling patients in our clinical trials and contracting with third-party manufacturers for the production of the drug product needed for our clinical trials;

- the achievement of milestones requiring payments under in-licensing agreements, if any;
- any significant changes in government regulation;
- the terms and timing of any regulatory approvals;
- the expense of filing, prosecuting, defending and enforcing patent claims and other intellectual property rights; and
- the ability to market, commercialize and achieve market acceptance for any of our product candidates, if they are approved.

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

Administrative Expenses

Administrative expenses consist of personnel costs, including salaries, bonuses, benefits, recruitment costs and share-based payment expense for personnel in executive, finance, business development and other support functions. Administrative expenses also include those costs associated with being a public company, such as general and D&O insurance, legal, audit, tax, public relations and investor relations services.

Finance and Other Income (Expense)

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

Taxation

We are subject to corporate taxation in the United Kingdom, United States and Germany. Due to the nature of our business, we have generated losses since inception. Our income tax credit recognized represents the sum of the research and development, or R&D, tax credits recoverable in the United Kingdom. The U.K. R&D tax credit, as described below, is fully refundable to us and is not dependent on current or future taxable income. As a result, we have recorded the entire benefit from the U.K. R&D tax credit as a credit to "Taxation."

As a company that carries out extensive research and development activities, we currently benefit from the U.K. research and development tax credit regime for small or medium-sized enterprises, or SMEs. Under the SME regime, we are able to surrender some of the trading losses that arise from qualifying R&D activities for a cash rebate of up to 33.35% of such qualifying R&D expenditures. Qualifying expenditures are net of any revenue contribution and largely comprise employment costs for research staff, materials, outsourced CRO costs and R&D consulting costs incurred as part of research projects, clinical trial and manufacturing costs, including outsourced CRO costs, employment costs for relevant staff and consumables incurred as part of research and development projects. Certain subcontracted qualifying research and development expenditures are eligible for a cash rebate of up to 21.68%. A large portion of costs relating to our research and development, clinical trials and manufacturing activities are eligible for inclusion within these tax credit cash rebate claims. We recognize research and development tax credits when receipt is probable.

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

Total estimated tax losses of £142.0 million as of September 30, 2021 were available for relief against our future profits. Unsurrendered U.K. tax losses may be carried forward indefinitely to be offset against future taxable profits, subject to numerous utilization criteria and restrictions. The amount that can be offset each year is limited to £5.0 million plus an incremental 50% of U.K. taxable profits. After accounting for tax credits receivable, we had accumulated tax losses for carry

forward in the United Kingdom of £84.1 million as of December 31, 2020. 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 £51.5 of accumulated tax losses as of December 31, 2020 related to our operations in Germany.

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 Three Months and Nine Months Ended September 30, 2021 and 2020

The following tables summarize the results of our operations for the three months and nine months ended September 30, 2021 and 2020.

Consolidated Income Statements (unaudited)

	Three months ended		Nine months ended	
£000s (except per share information)	September 30, 2021	September 30, 2020	September 30, 2021	September 30, 2020
Revenue	**3,156**	1,988	**9,001**	3,134
Cost of sales	**(2,052)**	(2,331)	**(5,414)**	(2,331)
Gross profit	**1,104**	(343)	**3,587**	803
Research and development costs	**(7,916)**	(3,468)	**(23,541)**	(13,647)
Administrative expenses	**(5,472)**	(2,666)	**(14,597)**	(7,826)
Other (losses)/gains - net	**-**	(3,091)	**-**	(3,091)
Operating loss	**(12,284)**	(9,568)	**(34,551)**	(23,761)
Finance and other expenses	**(64)**	(119)	**(86)**	(119)
Finance and other income	**296**	147	**8**	1,011
Loss for the period before taxation	**(12,052)**	(9,540)	**(34,629)**	(22,869)
Taxation	**2,123**	462	**4,653**	2,762
Loss for the period after taxation	**(9,929)**	(9,078)	**(29,976)**	(20,107)
Loss per ordinary equity share (basic and diluted)	**(11.1) pence**	(11.0) pence	**(33.8) pence**	(24.7) pence

Revenue

Revenue for the three-month period ended September 30, 2021 increased by £1.2 million from the same three-month period in 2020. The growth is a result of the further advancement of the partner programs, as well as introduction of additional programs with our partners. For the nine months ended September 30, 2021 revenue was £9.0 million (nine months ended September 30, 2020: £3.1 million). The increase was primarily due to the AstraZeneca and Mallinckrodt collaborations which delivered £1.8 million (nine months ended September 30, 2020: £nil) and £6.4 million (nine months ended September 30, 2020: £2.3 million) of revenue respectively in 2021.

Research and Development Expenses

The following table summarizes our research and development expenses for the nine months ended September 30, 2021 and 2020, based on their classification.

	Three months ended		Nine months ended	
	September 30, 2021 £000s	September 30, 2020 £000s	September 30, 2021 £000s	September 30, 2020 £000s
Research and development expenses				
Contracted development costs	**4,171**	1,576	**13,084**	7,573
Personnel costs	**3,268**	1,561	**9,284**	5,126
Other costs	**477**	331	**1,173**	948
Total	**7,916**	3,468	**23,541**	13,647

Research and development expenses for the three months ended September 30, 2021 were £7.9 million, compared to £3.5 million for the three months ended September 30, 2020. For the nine months ended September 30, 2021, research and development expenses were £23.5 million as compared to £13.6 million for the nine months ended September 30, 2020, an increase of £9.9 million. The largest contributor to the increase in R&D spend is contracted research and development expenses

which increased by £ 5.5 million due to the advancement of clinical studies and manufacturing of clinical supply. Personnel expenses (including payroll, consultants, share-based payment expense and recruitment fees), also increased by £4.2 million as a result of the advancement and addition of new R&D programs.

Administrative Expenses

Administrative expenses increased £2.8 million for the three months ended September 30, 2021 as compared to the same period in 2020. The increase is primarily due to the growth of the organization, as well as the increase in share-based payment expense. For the nine months ended September 30, 2021, administrative expenses were £14.6 million as compared to £7.8 million for the nine months ended September 30, 2020. Administrative expenses consist of personnel costs, allocated expenses and other expenses for outside professional services, including legal, audit, tax and accounting services and public relations and investor relations services. Personnel costs consist of salaries, bonuses, benefits, recruitment costs and share-based payment expense for personnel in executive, finance, business development and other support functions. Other administrative expenses include office space-related costs not otherwise allocated to research and development expense, costs of our information systems and costs for compliance with the day-to-day requirements of being a listed public company. We anticipate that our administrative expenses will continue to increase in the future to support our continued research and development activities of our product candidates.

Finance and Other Income (Expense)

Finance income/(expense) includes:

- interest income on our cash, cash equivalents and short-term deposits of £6 thousand for the three-months ended September 31, 2021 compared to £23 thousand for the three-months ended September 31, 2020. For the nine-month period ended September 30, 2021, interest income was £8 thousand compared to £86 thousand for the nine-months ended September 30, 2020. The decrease is primarily attributable to fewer instances of funds being placed on term deposits in 2021 primarily due a general decrease in interest rates being offered by Deposit Taking Institutions.

- net foreign exchange income was £226 thousand for the three-months ended September 31, 2021 compared to £5 thousand for the three-months ended September 31, 2020. For the nine-month period ended September 30, 2021, net foreign exchange loss was £86 thousand compared to £806 thousand for the nine-months ended September 30, 2020.; foreign exchange gains/losses relate to cash held in foreign currencies.

Taxation

We have recognized U.K. research and development tax credits of £2.1 million for the three months ended September 30, 2021 as compared to £0.5 million for the nine months ended September 30, 2020. For the nine-months ended September 40. 2021, we recognized £3.8 million for the nine months ended September 30, 2021 and an additional £0.9 million recognized and received as part of the full year 2020 submission. This compares to £2.8 million for the nine months ended September 30, 2020. We expect to receive the amount in respect of the full year 2021 in 2022.

Quantitative and Qualitative Disclosures about Market Risk

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

Interest Rate Risk

As of September 30, 2021, we had cash, cash equivalents and term deposits of £76.5 million (September 30, 2020: £43.9 million). Our exposure to interest rate sensitivity is impacted primarily by changes in the underlying U.K. bank interest rates. Our surplus cash and cash equivalents are invested in interest-bearing savings accounts and fixed term and fixed interest rate term deposits from time to time. We have not entered into investments for trading or speculative purposes in the year ended December 31, 2020 or the nine months ended September 30, 2021. Due to the conservative nature of our investment portfolio, which is predicated on capital preservation of investments with short-term maturities, an immediate one percentage point

change in interest rates would not have a material effect on the fair market value of our portfolio, and therefore we do not expect our operating results or cash flows to be significantly affected by changes in market interest rates.

Currency Risk

Our functional currency is U.K. pounds sterling, and our transactions are commonly denominated in that currency. However, we receive payments under our collaboration agreements in U.S. dollars and we incur a portion of our expenses in other currencies, primarily Euros, and are exposed to the effects of these exchange rates. We seek to minimize this exposure by maintaining currency cash balances at levels appropriate to meet foreseeable short to mid-term expenses in these other currencies. Where significant foreign currency cash receipts are expected, we consider the use of forward exchange contracts to manage our exchange rate exposure. A 10% increase in the value of the pound sterling relative to the U.S. dollar or Euro would not have had a material effect on the carrying value of our net financial assets and liabilities in foreign currencies at September 30, 2021.

Counterparty, Credit and Liquidity Risk

Our cash, cash equivalents and term deposits are on deposit with financial institutions with a credit rating equivalent to, or above, the main U.K. clearing banks. We invest our liquid resources based on the expected timing of expenditures to be made in the ordinary course of our activities. All financial liabilities are payable in the short term, meaning no more than three months, and we maintain adequate bank balances in either instant access or short-term deposits to meet those liabilities as they fall due. We believe we have had minimal credit risk relating to our trade receivables as of September 30, 2021 and 2020, which consisted solely of amounts due from AstraZeneca, Mallinckrodt and Alnylam.

Critical Accounting Policies, Judgments and Estimates

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

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

Revenue Recognition under Collaboration Agreements

During the nine months ended September 30, 2021 and the nine months ended September 30, 2020, a significant portion of our revenue from collaboration agreements was derived from our agreements with AstraZeneca (in 2021), Mallinckrodt (in 2020 and 2021) and Takeda (2020 through the six months ended June 30, 2021).

For the nine months ended September 30, 2021 and 2020, we determined actual costs and forecast costs for the remainder of the contract. We then 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 then multiplied this percentage by the consideration deemed probable, calculating the cumulative revenue to be recognized. When variable consideration increases due to a further milestone becoming probable, a catch-up in revenue is recorded to reflect efforts already expended by us up to that point.

AstraZeneca Research Collaboration, Option and License Agreement

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

AstraZeneca agreed to make an upfront cash payment of $60 million, of which $20 million was paid in May 2020 and the remaining $40 million was paid in May 2021. AstraZeneca also made an equity investment of $20 million in the Company. We have initially started working on two targets and anticipate initiating work on an additional three targets within the first three years of the collaboration, with AstraZeneca having the option to extend the collaboration to a further five targets. AstraZeneca would be obligated to pay us an option exercise payment of $10 million for each option exercised.

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

As there is only a single performance obligation per target under the collaboration agreement, 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 a Phase 1 clinical trial for which we will be reimbursed. Other variable elements of consideration will only begin to be recognized when the amounts are considered probable.

Mallinckrodt License and Collaboration Agreement

On July 18, 2019, Mallinckrodt obtained an exclusive worldwide license from us for an early-stage RNAi program targeting C3 in the complement cascade (known as SLN500), with options to license additional complement-mediated disease targets. The license of the intellectual property and the R&D services are not distinct, as Mallinckrodt cannot benefit from the intellectual property absent the R&D services, since R&D services are used to discover and develop a drug candidate and to enhance the value in the underlying intellectual property. 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 targets which represent material rights). We recognize revenue over the duration of the contract based on an input method based on cost to cost.

The agreement with Mallinckrodt has four elements of consideration:

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

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

As there is only a single performance obligation per target under the collaboration agreement, 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 a Phase 1 clinical trial for which we will be reimbursed. Other variable elements of consideration will only begin to be recognized when the amounts are considered probable.

Takeda Technology Evaluation Agreement

We entered into a Technology Evaluation Agreement with Takeda on January 7, 2020 to explore the potential of our platform to generate siRNA molecules against a novel, undisclosed target controlled by Takeda. Our activities under the Technology Evaluation Agreement with Takeda were effectively complete as of September 30, 2021. We may negotiate to enter into an exclusive follow-on license and collaboration agreement covering the Takeda target at some point in the future.

Recognition of Clinical Trial Expenses

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

Recent Accounting Pronouncements

We have reviewed new IFRS standards issued and updates to existing standards in the reporting period and concluded that none of the recent pronouncements are relevant to Silence Therapeutics plc (either because they relate to standards not relevant to Silence Therapeutics plc or because they have not yet become effective; and there is currently no preference for early adoption). The group did not have to change its accounting policies or make retrospective adjustments as a result.

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

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

Emerging Growth Company

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

- an exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting pursuant to the Sarbanes-Oxley Act of 2002, as amended;

- to the extent that we no longer qualify as a foreign private issuer, (i) reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and (ii) exemptions from the requirement to hold a non-binding advisory vote on executive compensation, including golden parachute compensation; and

- an exemption from compliance with the requirement that the Public Company Accounting Oversight Board has adopted regarding a supplement to the auditor's report providing additional information about the audit and the financial statements.

We will remain an emerging growth company until the earliest of (a) the last day of our fiscal year during which we have total annual gross revenue of at least $1.07 billion; (b) December 31, 2025; (c) the date on which we have, during the previous three-year period, issued more than $1.0 billion in non-convertible debt; or (d) the date on which we are deemed to be a "large accelerated filer" under the Securities Exchange Act of 1934, as amended, which would occur if the market value of our equity securities that are held by non-affiliates exceeds $700 million as of the last business day of our most recently completed second fiscal quarter. As of September 30, 2021, we did not exceed this threshold. Once we cease to be an emerging growth company, we will not be entitled to the exemptions provided in the JOBS Act.

Foreign Private Issuer

We report under the Securities Exchange Act of 1934, as amended, or the Exchange Act, as a non-U.S. company with foreign private issuer status. Even after we no longer qualify as an emerging growth company, as long as we continue to qualify as a foreign private issuer under the Exchange Act, we are exempt from certain provisions of the Exchange Act that are applicable to U.S. domestic public companies, including:

- the rules under the Exchange Act requiring domestic filers to issue financial statements prepared under U.S. GAAP;
- the sections of the Exchange Act regulating the solicitation of proxies, consents or authorizations in respect of a security registered under the Exchange Act;
- the sections of the Exchange Act requiring insiders to file public reports of their share ownership and trading activities and liability for insiders who profit from trades made in a short period of time; and
- the rules under the Exchange Act requiring the filing with the SEC of quarterly reports on Form 10-Q containing unaudited financial statements and other specified information, and current reports on Form 8-K upon the occurrence of specified significant events.

Notwithstanding these exemptions, we will file with the SEC, per foreign private issuer requirements.

We may take advantage of these exemptions until such time as we are no longer a foreign private issuer. We would cease to be a foreign private issuer at such time as more than 50% of our outstanding voting securities are held directly or indirectly by U.S. residents and any of the following three circumstances applies: (i) the majority of our executive officers or directors are U.S. citizens or residents, (ii) more than 50% of our assets are located in the United States or (iii) our business is administered principally in the United States.

Liquidity and Capital Resources

Overview

Since our inception, we have incurred significant operating losses. We anticipate that we will continue to incur losses for at least the next several years. 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 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.

As of September 30, 2021, we had cash, cash equivalents and term deposits of £76.5 million (December 31, 2020: £37.4 million).

We do not currently have any approved products and have never generated any revenue from product sales or otherwise. To date, we have financed our operations primarily through the issuances of our equity securities and from upfront, milestone and research payments under collaboration agreements with third parties.

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

Cash Flows

The following table summarizes the results of our cash flows for the nine months ended September 30, 2021 and 2020.

	Nine months ended	
	September 30, 2021 £000s	September 30, 2020 £000s
Net cash inflow/(outflow) from operating activities	**9,011**	(5,369)
Net cash inflow/(outflow) from investing activities	**4,224**	(10,352)
Net cash inflow from financing activities	**30,711**	15,534
Increase/(decrease) in cash and cash equivalents	**43,946**	(187)

Operating activities

The increase in net cash generated from operating activities of £9.0 million for the nine months ended September 30, 2021 from net cash outflow of £5.4 million for the nine months ended September 30, 2020 was primarily due to the $40 million (£30.8 million) upfront payment from AstraZeneca in the first half of 2021 partially offset by higher research, development and administrative costs.

Investing activities

Net cash inflow from investing activities was £4.2 million for the nine months ended September 30, 2021, compared to £10.4 outflow for the nine months ended September 30, 2020 which was primarily due to the purchase of short-term deposits. Short-term deposits for the nine months ended September 30, 2021 were £5.0 million.

Financing activities

The increase in net cash from financing activities to £30.7 million for the nine months ended September 30, 2021 (nine months ended September 30, 2020: £15.5 million), was due to the proceeds from the issuance of share capital. The only other financing activity for the nine months ended September 30, 2021 of £0.2 million (nine months ended September 30, 2020: £0.3 million) was the repayment of lease liabilities.

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 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 through the end of 2022.

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

- the scope, rate of progress and cost of our clinical trials, preclinical programs and other related activities;
- the extent of success in our early preclinical and clinical-stage research programs, which will determine the amount of funding required to further the development of our product candidates;
- the cost of manufacturing clinical supplies and establishing commercial supplies of our product candidates and any products that we may develop;
- the costs involved in filing and prosecuting patent applications and enforcing and defending potential patent claims;
- the outcome, timing and cost of regulatory approvals of our product candidates;

- the cost and timing of establishing sales, marketing and distribution capabilities; and
- the costs of hiring additional skilled employees to support our continued growth and the related costs of leasing additional office space.

Trend Information

Other than as disclosed elsewhere in this Report on Form 6-K, we are not aware of any trends, uncertainties, demands, commitments or events since December 31, 2020 that are reasonably likely to have a material adverse effect on our net revenues, income from continuing operations, profitability, liquidity or capital resources, or that would cause the disclosed financial information to be not necessarily indicative of future operating results or financial conditions.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and do not currently have, any off-balance sheet arrangements.

Contractual Obligations and Commitments

The following table summarizes our contractual commitments and obligations as of September 30, 2021 and December 31, 2020.

	September 30, 2021 £000s	December 31, 2020 £000s
Lease liability	**131**	341

We have agreed to make payments to CROs and manufacturers under various CRO and manufacturing agreements that generally provide for our ability to terminate on short notice. We have not included any such contingent payment obligations in the table above as the amount, timing and likelihood of such payments are not fixed or determinable.

RISK FACTORS

Investing in American Depositary Shares, or ADSs, representing our ordinary shares involves a high degree of risk. You should carefully consider the following risk factors and all other information contained in this Report on Form 6-K, including our unaudited financial statements and the related notes, and our other filings with the Securities and Exchange Commission, or the SEC, before investing in the ADSs. The risks and uncertainties described below are certain significant risk factors, currently known and specific to us, that we believe are relevant to an investment in the ADSs. If any of these risks materialize, our business, results of operations or financial condition could suffer, the price of the ADSs could decline and you could lose part or all of your investment. Additional risks and uncertainties not currently known to us or that we now deem immaterial may also harm us and adversely affect your investment in the ADSs.

Risks Associated with Our Business

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

- The approach we are taking to discover and develop drugs is novel and we may not be successful in our efforts to identify or discover potential drug product candidates to bring into clinical trials.
- If clinical trials of our product candidates fail to commence or, once commenced, fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities, or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.
- We have a history of net losses and we anticipate that we will continue to incur significant losses for the foreseeable future.
- We will need to raise additional capital, which may not be available on acceptable terms, or at all.
- We face competition from other companies that are working to develop novel drugs and technology platforms using technologies similar to ours. If these companies develop drugs more rapidly than we do or their technologies, including delivery technologies, are more effective, our ability to successfully commercialize drugs may be adversely affected.
- We rely on third parties to conduct some aspects of our manufacturing, research and development activities, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of research or clinical testing.
- If we are unable to obtain or protect intellectual property rights related to our current or future product candidates, we may not be able to compete effectively in our markets.
- An active trading market for our ADSs may not develop and you may not be able to resell your ADSs at or above the price you pay for them, if at all.
- We qualify as a foreign private issuer and, as a result, we will not be subject to U.S. proxy rules and will be subject to reporting obligations under the Securities Exchange Act of 1934, as amended, or the Exchange Act, that, to some extent, are more lenient and less frequent than those of a U.S. domestic public company.
- If equity research analysts do not publish research or reports, or publish unfavorable research or reports, about us, our business or our market, the price and trading volume of our ADSs could decline.
- If we are a passive foreign investment company, there could be adverse U.S. federal income tax consequences to U.S. Holders.

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

- The ongoing COVID-19 pandemic could adversely affect our operations, including at our clinical trial sites, as well as the business or operations of our contract research organizations, or CROs, or other third parties with whom we conduct business.

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.

In recent years, our operations have been primarily limited to developing our siRNA product platform, undertaking basic research around siRNA targets, conducting preclinical studies for our initial development programs and out-licensing some of our intellectual property rights. We have not yet completed any clinical trials for, nor have we obtained marketing regulatory approval for any product candidates. Consequently, any predictions about our future success or viability, or any evaluation of our business and prospects, may not be accurate.

We have incurred losses in each year since our inception. Our net losses were £33.5 million for the nine months ended September 30, 2021 and £19.0 million for the nine months ended September 30, 2020. Our net losses were £32.5 million for the year ended December 31, 2020 and £19.6 million for the year ended December 31, 2019. We have devoted most of our financial resources to research and development, including our preclinical and clinical development activities.

We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future, although these losses may fluctuate significantly between periods. We anticipate that our expenses will increase substantially as we continue the research and 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. 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 and planned future commercialization efforts. We expect that all of these additional expenses will cause our total expenses to substantially exceed our revenue over the next several years 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 and obtaining marketing approvals for product candidates that successfully complete clinical trials;

- establishing and maintaining supply and manufacturing relationships with third parties;

- 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, protecting and expanding 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 FDA, the European Medicines Agency, or EMA, the United Kingdom Medicines and Healthcare products Regulatory Agency, or MHRA, or other regulatory agencies to perform studies and trials in addition to those that we currently anticipate.

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

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

We have used substantial funds to develop our RNAi technologies and will require substantial funds to conduct further research and development, including preclinical testing and clinical trials of our product candidates, and to manufacture, market and sell any of our products that may be approved for commercial sale. Because the length of time or activities associated with successful development of our product candidates may be greater than we anticipate, we are unable to estimate the actual funds we will require to develop and commercialize them.

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

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

- significantly delay, scale back or discontinue the development or commercialization of any future product candidates;

- seek strategic alliances for research and development programs at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available;

- dispose of technology assets, or relinquish or license on unfavorable terms, our rights to technologies or any future product candidates that we otherwise would seek to develop or commercialize; and

- file for bankruptcy or cease operations altogether.

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

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

We expect that significant additional capital will be needed in the future to continue our planned operations, including expanded research and development activities. Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through any or a combination of securities offerings, debt financings, license and collaboration agreements and research grants and tax credits.

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

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

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

The approach we are taking with our research and development efforts may never lead to marketable products.

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

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

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

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

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

- our research methodology or that of any strategic collaborator may be unsuccessful in identifying potential product candidates that are successful in clinical development;

- potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval;

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

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

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

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

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

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

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

The success of our product candidates will depend on several factors, including, among other things, the following:

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

2. successfully conducting clinical trials;

3. receipt of marketing approvals from applicable regulatory authorities;

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

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

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

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

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

In clinical development, the risk of failure for product candidates is high. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive regulatory approval. 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, two of our product candidates are in Phase 1 clinical trials, and our other product candidates are pre-clinical. 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. Interim, "topline," and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to confirmation, audit and verification procedures that could result in material changes in the final data. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. Moreover, clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in clinical trials have nonetheless failed to obtain marketing approval for their products.

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

- delays in reaching an agreement with the FDA, EMA, MHRA or other regulatory authorities on final trial design;
- imposition of a clinical hold on our clinical trial operations or trial sites by the FDA or other regulatory authorities;
- delays in reaching agreement on acceptable terms with prospective CROs and clinical trial sites;
- inability to adhere to clinical trial requirements directly or with third parties such as CROs;
- delays in obtaining required institutional review board approval at each clinical trial site;
- delays in recruiting suitable patients to participate in a trial;
- delays in the testing, validation, manufacturing and delivery of the product candidates to the clinical sites;
- delays in having patients complete participation in a trial or return for post-treatment follow-up;
- delays caused by patients dropping out of a trial due to protocol procedures or requirements, product side effects or disease progression;
- clinical sites dropping out of a trial to the detriment of enrollment;
- time required to add new clinical sites;
- 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 due to the global lockdown as a result of the COVID-19 pandemic, further challenges of patient recruitment during the COVID-19 pandemic, as well as challenges regarding global clinical trial supply shipments, importation and customs clearances.

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

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

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

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

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

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

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

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

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

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

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

- the inability to meet any product specifications and quality requirements consistently;
- a delay or inability to procure or expand sufficient manufacturing capacity;
- manufacturing and product quality issues related to scale-up of manufacturing;
- costs and validation of new equipment and facilities required for scale-up;

- a failure to comply with applicable government regulations;
- the inability to negotiate manufacturing or supply agreements with third parties under commercially reasonable terms or at all;
- termination or non-renewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us;
- the reliance on a limited number of sources, such that if we were unable to secure a sufficient supply of these product components, we will be unable to manufacture and sell future product candidates in a timely fashion, in sufficient quantities or under acceptable terms; and
- the losses incurred by us if our insurance coverage is insufficient to cover any loss, contamination or damage of chemical materials, product components or products made by any of our contract manufacturing organizations, or 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 CMOs, as any disruption, such as a fire, natural hazards, pandemic, epidemic, or outbreak of an infectious disease at a CMO could significantly interrupt our manufacturing capability. If necessary to avoid future disruption, we may have to establish alternative manufacturing sources. This would require substantial capital on our part, which we may not be able to obtain on commercially acceptable terms or at all. Additionally, we may experience manufacturing delays as we build or locate replacement facilities and seek and obtain necessary regulatory approvals. If this occurs, we will be unable to satisfy manufacturing needs on a timely basis, if at all. Also, operating any new facilities may be more expensive than operating our current facility. Further, business interruption insurance may not adequately compensate us for any losses that may occur and we would have to bear the additional cost of any disruption. For these reasons, a significant disruptive event of the manufacturing facility could have drastic consequences, including placing our financial stability at risk.

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

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

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

Even if we obtain regulatory approval in the United States and the EU, the FDA and the EMA may still impose significant restrictions on the indicated uses or marketing of our product candidates or impose ongoing requirements for potentially costly post-approval studies or post-market surveillance. The holder of an approved new drug application, or NDA, in the United States, or a marketing authorization, or MA, in the EU is obligated to monitor and report adverse events, or AEs, and any failure of a product to meet the specifications in the NDA. The holder of an approved NDA or MA must also submit new or supplemental applications and obtain regulatory approval for 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, are subject to FDA review, in addition to other potentially applicable federal and state laws.

In addition, drug product manufacturers and their facilities are subject to payment of user fees and continual review and periodic inspections regulatory authorities for compliance with current good manufacturing practices, or cGMP, and adherence to commitments made in the NDA or MA. If we or a regulatory agency discovers previously unknown problems with a product such as AEs of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a

regulatory agency may impose restrictions relative to that product or the manufacturing facility, including requiring recall or withdrawal of the product from the market or suspension of manufacturing.

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

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

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

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

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

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs or biologics for relatively small patient populations as orphan drugs. In the United States, under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biological product intended to treat a rare disease or condition. Such diseases and conditions are those that affect fewer than 200,000 individuals in the United States, or if they affect more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and making a drug available in the United States for these types of diseases or conditions will be recovered from sales of the drug. However, orphan drug designation must be requested before submitting an NDA and there can be no assurance that any such designation will be granted. If the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by that agency. 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 of the 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 EU, orphan designation is intended to promote the development of medicinal products that are intended for (i) the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions affecting not more than five in 10,000 persons in, or that are intended for the diagnosis, prevention, or treatment of a life-threatening, seriously debilitating or serious and chronic condition when, without incentives, it is unlikely that sales in Europe would be sufficient to

justify the necessary investment, and (ii) there exists no satisfactory method of diagnosis, prevention or treatment of the condition that has been authorized in Europe or, if such method exists, that the medicinal product will be of significant benefit to those affected. In Europe, orphan designation entitles a party to a number of incentives, such as protocol assistance and scientific advice specifically for designated orphan medicines, and potential fee reductions depending on the status of the sponsor. European orphan medicines also benefit from ten years of market exclusivity, which precludes the EMA from approving another marketing application during this time period for the same drug and indication. This marketing exclusivity period can however, be reduced to six years if a drug no longer meets the criteria for orphan designation or if the drug is sufficiently profitable, such that market exclusivity is no longer justified.

Our product candidate SLN124 has received orphan drug designation from the EMA for the treatment of beta-thalassemia and from the FDA for the treatment of both beta-thalassemia in adults and MDS. Even though we have these designations, or if we obtain orphan drug exclusivity in the future for a product candidate for these or other indications, exclusivity may not effectively protect the product candidate from competition because different therapies can be approved for the same condition and the same therapies can be approved for different conditions but used off-label. Even after an orphan drug is approved, the FDA or EMA can subsequently approve the same 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 or similar indication containing a different active ingredient. In addition, if a subsequent drug is approved for marketing for the same or a similar indication as any of our product candidates that receive marketing approval, we may face increased competition and lose market share regardless of orphan drug exclusivity.

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

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

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

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

Because we have limited financial and human resources, we intend to leverage our existing licensing and collaboration agreements and may enter into new strategic collaboration agreements for the development and commercialization of our programs and potential product candidates in indications with potentially large commercial markets while focusing our internal development resources, and any future internal sales and marketing organization that we may establish, on research programs and product candidates intended for selected markets or patient populations, such as rare diseases. As a result, and even as we prioritize rare indications with expansion opportunities to large populations, we may forego or delay pursuit of other programs or product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation

decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through strategic collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate, or we may allocate internal resources to a product candidate in a therapeutic area in which it would have been more advantageous to enter into a collaboration arrangement.

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

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

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

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

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

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

Even if any of our product candidates receive marketing approval, they may fail to achieve the degree of market acceptance by physicians, patients, third party payors 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 payors and consumers, may not accept a product intended to improve therapeutic results based on RNAi technology. As a result, it may be more difficult for us to convince the medical community and third-party payors to accept and use our product, or to provide favorable reimbursement. 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 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.

We have never commercialized a product before and may lack the necessary expertise, personnel and resources to successfully commercialize a product, if approved, either on our own or with suitable collaborators.

To achieve commercial success for any product after approval, we would need to develop or acquire a sales and marketing organization, outsource these functions to third parties or enter into partnerships. There are risks involved in establishing our own sales and marketing capabilities, as well as with entering into arrangements with third parties to perform these services.

Even if any of our product candidates receive marking approval and we establish sales and marketing capabilities, we may fail to launch or to market our products effectively since we have limited organizational experience in the sales and marketing of products. In addition, recruiting and training a sales force is expensive and time-consuming, and could delay any product launch. In the event that any such launch is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel. Factors that may inhibit our efforts to commercialize our products on our own include our inability to recruit, train and retain effective market access and commercial personnel; the inability of commercial personnel to obtain access to or educate adequate numbers of physicians on the benefits of prescribing any future products; unforeseen costs and expenses associated with creating an independent market access and commercial organization; and costs of market access and commercialization above those anticipated by us.

If we enter into arrangements with third parties to perform market access and commercial services for any product, if approved, the revenue or the profitability of these revenues to us could be lower than if we were to commercialize such product ourselves. Such collaborative arrangements may place the commercialization of any approved products outside of our control and would make us subject to a number of risks including that we may not be able to control the amount or timing of resources that our collaborative partner devotes to our products or that our collaborator's willingness or ability to complete its obligations, and our obligations under our arrangements may be adversely affected by business combinations or significant changes in our collaborator's business strategy. We may not be successful in entering into arrangements with third parties to commercialize our therapies or may be unable to do so on terms that are favorable to us. Acceptable third parties may fail to devote the necessary resources and attention to commercialize our products, if approved, effectively.

If we do not establish commercial capabilities successfully, either on our own or in collaboration with third parties, we may not be successful in commercializing our products, which in turn would have a material adverse effect on our business, prospects, financial condition and results of operations.

Risks Related to Our Business Operations and Compliance with Government Regulations

The ongoing COVID-19 pandemic could adversely affect our operations, including at our clinical trial sites, as well as the business or operations of our CROs or other third parties with whom we conduct business.

Our business has been impacted and could be adversely affected by the effects of the rapidly evolving COVID-19 pandemic, which was declared by the World Health Organization as a global pandemic. The COVID-19 pandemic has resulted in travel and other restrictions in order to reduce the spread of the disease including in London and Berlin, where our European operations are focused and in New Jersey, where our U.S. operations are focused. Following executive orders and other health directives and recommendations in the state of New Jersey, the United Kingdom and Germany in 2020, we implemented work-from-home policies for all employees and continue to follow national, regional and local government

guidance and rules in the jurisdictions in which we operate. The effects of the executive order and our work-from-home policies may negatively impact productivity, disrupt our business and delay our clinical programs and timelines, the magnitude of which will depend, in part, on the length and severity of the restrictions and other limitations on our ability to conduct our business in the ordinary course. These and similar, and perhaps more severe, disruptions in our operations could negatively impact our business, operating results and financial condition. Our business, operations and clinical development timelines and plans could also be adversely affected by the COVID-19 pandemic if our CMOs, CROs and other service providers upon whom we rely experience delays in providing services.

In addition, our planned clinical trials may be affected by the COVID-19 pandemic. Clinical site initiation, patient enrollment and first dosing have been delayed due to prioritization of hospital resources toward the COVID-19 pandemic. Some patients may not be able to comply with clinical trial protocols if quarantines impede patient movement or interrupt healthcare services. Similarly, our ability to recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to the virus that causes COVID-19, may adversely impact our clinical trial operations. This may be particularly challenging in the context of trials that seek to enroll patients with underlying conditions such as cardiovascular disease or diabetes which increase the risk of serious morbidity and mortality related to COVID-19. In addition, it is possible that COVID-19 exposure or inoculation by any of the available COVID-19 vaccines may affect the response to one or more of our drug candidates or confound the interpretation of our clinical trial results in unknown ways in patients exposed to the virus prior to or following enrollment in clinical trials or future clinical trials. We continue to evaluate and adjust statistical plans for the potential effects of COVID-19 or of a COVID-19 vaccine on our clinical trial data but the impact may be difficult to fully assess or unknown until final analysis is complete.

The spread of COVID-19, which has caused a broad impact globally, may materially affect us economically. While the potential economic impact brought by, and the duration of, COVID-19 may be difficult to assess or predict, a widespread and lasting pandemic could result in prolonged significant disruption of global financial markets, reducing our ability to access capital, which could in the future negatively affect our liquidity. In addition, a recession or market correction resulting from the spread of COVID-19 could materially affect our business and the value of our ADSs.

The global pandemic of COVID-19 continues to rapidly evolve. The extent to which the COVID-19 pandemic impacts our business, our clinical development and regulatory efforts will depend on future developments that are highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of the disease, the duration of the outbreak, travel restrictions, quarantines, social distancing requirements, the unknown timing or effectiveness of any vaccine or treatment and business closures in the United States and other countries, business disruptions and the effectiveness of actions taken in the United States and other countries to contain and treat the disease. We do not yet know the full extent of potential delays or impacts on our business, our clinical and regulatory activities, healthcare systems or the global economy as a whole. However, these impacts could adversely affect our business, financial condition, results of operations and growth prospects.

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

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.

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. 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. Companies working on chemically synthesized siRNAs include, but are not limited to, Aligos Therapeutics, Alnylam Pharmaceuticals, Altimara Therapeutics, Amgen Inc., Arbutus Biopharma, Arcturus Therapeutics, Arrowhead Pharmaceuticals, Atalanta Therapeutics, Avidity Biosciences, Dicerna Pharmaceuticals, e-Therapeutics, Genevant Sciences, Nanopeptide Biotechnology, Nitto Biopharma, OliX Pharmaceuticals, Quark Pharmaceuticals, Sirnaomics, and Suzhou Ribo Life Sciences. With respect to our SLN360 product candidate targeting Lp(a), Ionis Pharmaceuticals and Akcea Therapeutics partnered with Novartis are developing Pelacarsen (TQJ230), a single-stranded antisense oligonucleotide therapeutic directed against Lp(a). Arrowhead Pharmaceuticals partnered with Amgen is developing Olpasiran (AMG 890), a different siRNA directed against Lp(a). Dicerna Pharmaceuticals partnered with Eli Lilly is developing LY3819469, another

siRNA directed against Lp(a). Eli Lilly is also developing an oral small molecule Lp(a) inhibitor LY3473329 with an undisclosed mechanism of action. We consider all four to be potentially competitive products. Abcentra is developing Orticumab, an antibody targeting oxidized LDL, which may reduce the pathogenicity of Lp(a) and is therefore also a potential competitor.

With respect to our SLN124 product candidate targeting TMPRSS6 for iron regulation, potential competitors include, but are not limited to, Bristol-Myers Squibb's Luspatercept (Reblozyl®), Ionis Pharmaceuticals' IONIS-TMPRSS6-LRx, Vifor Pharma's Vamifeport, Disc Medicine's matriptase-2 inhibitor, Protagonist's Rusfertide, Bluebird's Lentiglobin (Zynteglo®), Orchard Therapeutics' OTL-300, Vertex's CTX001, Sanofi's ST-400, Imara's IMR-687, Agios' Mitapivat, Phoenicia's Benserazide, Roivant's ARU-1801, Kymab's KY-1066, AstraZeneca/Astellas' Roxadustat, Geron's Imetelstat, Apogenix' Asunercept, Keros' KER-050, MedPacto's Vactosertib (TEW-7197), Lixte's LB-100, Syntrix's SX-682, MedPacto's Vactosertib (TEW-7197), Geron's Imetelstat, H3 Biomedicine's H3B-8800, Boehringer Ingelheim's BI-836858, and Astex's ASTX727. However, 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.

In addition to competition with respect to RNAi and with respect to specific products, we face substantial competition to discover and develop safe and effective means to deliver siRNAs to relevant cell and tissue types. Safe and effective means to deliver siRNAs to the relevant cell and tissue types may be developed by our competitors or other third parties in both the academic and corporate sectors, which could adversely affect our ability to successfully commercialize a competitive product. Some of our competitors have substantially greater resources than we do, and if our competitors are able to negotiate exclusive access to those delivery solutions developed by third parties, we may be unable to successfully commercialize our product candidates.

There has also been in the past, and there may again be in the future, instances of our competitors using developing product candidates for the same gene targets or indications that we are targeting once they are revealed to the public, in which case we may lose a competitive advantage or market share. Our competitors may also attempt to appropriate our technologies, which may force us to enforce our intellectual property rights through legal action, which may be costly and time consuming and may or may not ultimately prove to be effective.

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 employment with us at any time with no advance 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 September 30, 2021 we had 92 employees (September 30, 2020: 69). 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 keep pace with advances in technology, our business, financial condition and results of operations could be adversely affected.

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

We face potential product liability, and 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. 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. 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. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, product liability claims may result in, among other things:

- impairment of our business reputation;
- withdrawal of clinical trial participants;
- costs due to related litigation;
- distraction of management’s attention from our primary business;
- substantial monetary awards to patients or other claimants;
- the inability to commercialize our product candidates; and
- decreased demand for our product candidates, if approved for commercial sale.

We maintain product liability insurance relating to the use of our therapeutics in clinical trials. However, such insurance coverage may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive and in the future we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If and when we obtain marketing approval for product candidates, we intend to expand our insurance coverage to include the sale of commercial products; however, we may be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. On occasion, large judgments

have been awarded in class action lawsuits based on drugs that had unanticipated adverse effects. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business.

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

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees, consultants or contractors could include intentional failures to comply with governmental regulations, comply with healthcare fraud and abuse and anti-kickback laws and regulations in the United States, the United Kingdom and other jurisdictions, or failure to report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of, including improper trading based upon, information obtained in the course of clinical studies, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a code of business conduct and ethics and a robust compliance program, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

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

In the United States, there have been, and continue to be, legislative and regulatory developments regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities, and affect our ability to profitably sell any product candidates for which we obtain marketing approval. Additionally, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. While any proposed measures will require authorization through additional legislation to become effective, Congress and the current administration have each indicated that they will continue to seek new legislative 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.

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

Our business requires manipulating, analyzing and storing large amounts of data. We also maintain personally identifiable information about our employees. Our business therefore depends on the continuous, effective, reliable, and secure operation of our computer hardware, software, networks, internet servers, third party technology service providers and related infrastructure. To the extent that our hardware or software malfunctions or access to our data by internal research personnel is interrupted, our business could suffer. The integrity and protection of our employee and company data is critical to our business and employees have a high expectation that we will adequately protect their personal information. The regulatory environment governing information, security and privacy laws is increasingly demanding and continues to evolve, as further described below. Maintaining compliance with applicable security and privacy regulations may increase our operating costs. Although our computer and communications hardware is protected through physical and software safeguards, we are still vulnerable to fire, storm, flood, power loss, earthquakes, telecommunications failures, physical or software break-ins, software

viruses, accidental or malicious insider-action and similar events. These events could lead to the unauthorized access, disclosure and use of non-public information. The techniques used by criminal elements to attack computer systems are sophisticated, change frequently and may originate from less regulated and remote areas of the world and increasingly involve highly resourced threat actors such as organized criminals and nation states. As a result, we cannot provide assurance that our efforts to address these techniques proactively or implement adequate preventative measures will always be successful. If our computer systems are compromised, we could be subject to fines, damages, litigation and enforcement actions, and we could lose trade secrets, the occurrence of which could harm our business. In addition, any sustained disruption in internet systems or network access provided by other companies could harm our business.

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

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

In the EU, the collection and use of personal data (including health data) is governed by the provisions of the General Data Protection Regulation, or the GDPR, which became effective and enforceable across all then-current member states of the EU on May 25, 2018. The GDPR enhances data protection obligations for both processors and controllers of personal data, including by materially expanding the definition of what is expressly noted to constitute personal data, requiring additional disclosures about how personal data is to be used, imposing limitations on retention of personal data, creating mandatory data breach notification requirements in certain circumstances, and establishing onerous new obligations on services providers who process personal data simply on behalf of others, as well as obligations regarding the security and confidentiality of the personal data. The GDPR also imposes strict rules on the transfer of personal data out of the European Economic Area to third countries, including the United States. The GDPR has expanded its reach to include any business, regardless of its location, that processes personal data in relation to the offering of goods or services to individuals in the EU and/or the monitoring of their behavior. This expansion would incorporate any clinical trial activities in EU member states. The GDPR imposes special protections for "sensitive information" which includes health and genetic information of data subjects residing in the EU. The GDPR also grants individuals the opportunity to object to the processing of their personal information, allows them to request deletion of personal information in certain circumstances, and provides an express right to seek legal remedies in the event the individual believes his or her rights have been violated. Failure to comply with the requirements of the GDPR may result in fines of up to 4% of an undertaking's total global annual turnover for the preceding financial year, or €20,000,000, whichever is greater. In addition to administrative fines, a wide variety of other potential enforcement powers are available to competent authorities in respect of potential and suspected violations of the GDPR, including extensive audit and inspection rights, and powers to order temporary or permanent bans on all or some processing of personal data carried out by noncompliant actors. While we have taken steps to comply with the GDPR, and implementing legislation in applicable member states, including by seeking to establish appropriate lawful bases for the various processing activities we carry out as a controller, reviewing our security procedures, and entering into data processing agreements with relevant customers and business partners, we cannot guarantee that our efforts to achieve and remain in compliance have been, and/or will continue to be, fully successful.

Further, the United Kingdom's withdrawal from the EU, often referred to as Brexit, and ongoing developments in the United Kingdom have created uncertainty regarding data protection regulation in the United Kingdom. Following the United Kingdom's withdrawal from the EU on January 31, 2020, pursuant to the transitional arrangements agreed to between the United Kingdom and EU, the GDPR continued to have effect in law in the United Kingdom, and continued to do so until December 31, 2020 as if the United Kingdom remained a Member State of the EU for such purposes. Following December 31, 2020, and the expiry of those transitional arrangements, the data protection obligations of the GDPR continue to apply to United Kingdom-related processing of personal data in substantially unvaried form under the so-called "UK GDPR" (i.e., the GDPR as it continues to form part of law in the United Kingdom by virtue of section 3 of the European Union (Withdrawal) Act 2018, as amended (including by the various Data Protection, Privacy and Electronic Communications (Amendments, etc.) (EU Exit) Regulations)). However, going forward, there will be increasing scope for divergence in application, interpretation and enforcement of the data protection law as between the United Kingdom and EEA. Furthermore, the relationship between the United Kingdom and the EEA in relation to certain aspects of data protection law remains somewhat uncertain. For example, it is unclear whether transfers of personal data from the EEA to the United Kingdom will be permitted to take place on the basis of a future adequacy decision of the European Commission, or whether a "transfer mechanism," such as the Standard Contractual Clauses, will be required. For the meantime, under the post-Brexit trade and cooperation agreement between the European Union and the United Kingdom, or the Trade and Cooperation Agreement, it has been agreed that transfers of personal

data to the United Kingdom from EU Member States will not be treated as "restricted transfers" to a non-EEA country for a period of up to four months from January 1, 2021, plus a potential further two months extension, or the extended adequacy assessment period. This will also apply to transfers to the United Kingdom from EEA Member States, assuming those Member States accede to the relevant provision of the Trade and Cooperation Agreement. Although the current maximum duration of the extended adequacy assessment period is six months it may end sooner, for example, in the event that the European Commission adopts an adequacy decision in respect of the United Kingdom, or the United Kingdom amends the UK GDPR or makes certain changes regarding data transfers under the UK GDPR/Data Protection Act 2018 without the consent of the EU (unless those amendments or decisions are made simply to keep relevant United Kingdom laws aligned with the EU's data protection regime). If the European Commission does not adopt an 'adequacy decision' in respect of the United Kingdom prior to the expiry of the extended adequacy assessment period, from that point onwards the United Kingdom will be an "inadequate third country" under the GDPR and transfers of data from the EEA to the United Kingdom will require a "transfer mechanism," such as the Standard Contractual Clauses.

Additionally, as noted above, the United Kingdom has transposed the GDPR into United Kingdom domestic law by way of the UK GDPR with effect from January 2021, which could expose us to two parallel regimes, each of which potentially authorizes similar fines and other potentially divergent enforcement actions for certain violations (for example, the power to impose fines up to the greater of either 4% of total global annual revenue, or €20,000,000 (for the EU) or £17,500,000 (for the United Kingdom)). Also, following the expiry of the post-Brexit transitional arrangements, the United Kingdom Information Commissioner's Office is not able to be our "lead supervisory authority" in respect of any "cross border processing" for the purposes of the GDPR. For so long as we are unable to, or do not, designate a lead supervisory authority in an EEA member state, with effect from January 1, 2021, we are not able to benefit from the GDPR's "one stop shop" mechanism. Amongst other things, this would mean that, in the event of a violation of the GDPR affecting data subjects across the United Kingdom and the EEA, we could be investigated by, and ultimately fined by the United Kingdom Information Commissioner's Office and the supervisory authority in each and every EEA member state where data subjects have been affected by such violation. Other countries have also passed or are considering passing laws requiring local data residency and/or restricting the international transfer of data.

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

Brexit may adversely impact our ability to obtain regulatory approvals of our product candidates in the EU, result in restrictions or imposition of taxes and duties for importing our product candidates into the EU, and may require us to incur additional expenses in order to develop, manufacture and commercialize our product candidates in the EU.

After the United Kingdom left the EU on January 31, 2020, pursuant to the formal withdrawal arrangements agreed between the United Kingdom and the EU, the United Kingdom was subject to a transition period until December 31, 2020, or the Transition Period, during which EU rules continued to apply. The Trade and Cooperation Agreement, or the Trade and Cooperation Agreement, which outlines the future trading relationship between the United Kingdom and the European Union was agreed in December 2020.

Since a significant proportion of the regulatory framework in the United Kingdom applicable to our business and our product candidates is derived from EU directives and regulations, Brexit has had, and may continue to have, a material impact upon the regulatory regime with respect to the development, manufacture, importation, approval and commercialization of our product candidates in the United Kingdom or the EU. For example, Great Britain is no longer covered by the centralized procedures for obtaining EU-wide marketing authorization from the EMA and a separate marketing authorization will be required to market our product candidates in Great Britain. It is currently unclear whether the MHRA is sufficiently prepared to handle the increased volume of marketing authorization applications that it is likely to receive. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, could make it more difficult for us to commercialize our product candidates in the EU or in the United Kingdom and restrict our ability to generate revenue and achieve and sustain profitability. While the Trade and Cooperation Agreement provides for the tariff-free trade of medicinal products between the United Kingdom and the EU, there may be additional non-tariff costs to such trade which did not exist prior to the end of the Transition Period. Further, should the United Kingdom diverge from the EU from a regulatory perspective in relation to medicinal products, tariffs could be put into place in the future. We could therefore, both now and in the future,

face significant additional expenses (when compared to the position prior to the end of the Transition Period) to operate our business, which could significantly and materially harm or delay our ability to generate revenues or achieve profitability of our business. Any further changes in international trade, tariff and import/export regulations as a result of Brexit or otherwise may impose unexpected duty costs or other non-tariff barriers on us. These developments, or the perception that any of them could occur, may significantly reduce global trade and, in particular, trade between the impacted nations and the United Kingdom. It is also possible that Brexit may negatively affect our ability to attract and retain employees, particularly those from the EU, and make travel between our United Kingdom and German offices more difficult, time-consuming and expensive than previously was the case.

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

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

The uncertainty concerning the United Kingdom's legal, political and economic relationship with the EU after the Transition Period may be a source of instability in the international markets, create significant currency fluctuations, and/or otherwise adversely affect trading agreements or similar cross-border co-operation arrangements (whether economic, tax, fiscal, legal, regulatory or otherwise).

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

If the United Kingdom and the EU are unable to negotiate acceptable trading and customs terms or if other EU member states pursue withdrawal, barrier-free access between the United Kingdom and other EU member states or among the European Economic Area overall could be diminished or eliminated. The long-term effects of Brexit will depend on any agreements (or lack thereof) between the United Kingdom and the EU and, in particular, any arrangements for the United Kingdom to retain access to EU markets after the Transition Period.

Such a withdrawal from the EU is unprecedented, and it is unclear how the United Kingdom's access to the European single market for goods, capital, services and labor within the EU, or single market, and the wider commercial, legal and regulatory environment, will impact our U.K. operations and customers.

There may continue to be economic uncertainty surrounding the consequences of Brexit, following the Transition Period, which could adversely impact: customer confidence resulting in customers reducing their spending budgets on our products, our business, revenue, financial condition, results of operations, and the market price of our ADSs.

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

Our functional currency is pounds sterling, and our transactions are commonly denominated in that currency. However, we receive payments under our collaboration agreements in U.S. dollars and we incur a portion of our expenses in other currencies, primarily Euros. As a result, fluctuations in exchange rates, particularly between the pound sterling on the one hand and the U.S. dollar and Euro on the other hand, may adversely affect our reported results of operations and cash flows. Since the Brexit referendum in 2016, there has been a significant increase in the volatility of these exchange rates and an overall weakening of the pound sterling. 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 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.

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. Furthermore, even if they are unchallenged, 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 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 post-grant challenges, re-examination or opposition before the United States Patent Office or European Patent Office and in other jurisdictions. For example, re-examination of, or oppositions to, patents owned by us have previously been initiated, and while we believe these concluded proceedings did not result in a commercially relevant impact on the individual patents, any successful challenge of patents or any other patents owned by us could deprive us of rights necessary for the successful commercialization of any product candidates that we or our strategic alliance partners may develop. Since patent applications in the United States and most other countries are confidential for a period of time after filing, and some remain so until issued, we cannot be certain that we were the first to file any patent application related to a product candidate or a 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, previously known as an interference, which may now fall under the scope of an action known as a derivation proceeding, 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. Our defense of a patent or patent application in such a proceeding may not be successful and, even if successful, may result in substantial costs and distract 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, 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 employees 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 and independently develop substantially equivalent information and techniques. In addition, others may independently discover our trade secrets, proprietary know-how and information. For example, the FDA, as part of its transparency initiative, is currently considering whether to make additional information publicly available on a routine basis, including information that we may consider to be trade secrets or other proprietary information, and it is not clear at the present time how the FDA's disclosure policies may change in the future, if at all.

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

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

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

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. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our product candidates, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable patents, or until such patents expire. Similarly, if any third-party patents were held by a court of competent jurisdiction to cover aspects of our compositions, formulations, processes for manufacture or methods of use, including combination therapy, the holders of any such patents may be able to block our ability to develop and commercialize the applicable product candidate unless we obtained a license or until such patent expires. In either case, such a license may not be available on commercially reasonable terms or at all.

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

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

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

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

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

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

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

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

Risks Related to Our ADSs and Shares

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

While our ADSs have been listed on Nasdaq since September 8, 2020, there can be no assurance that an active trading market for the ADSs will be sustained. The lack of an active trading market may also reduce the fair market value of the ADSs. The price at which our ADSs trade on Nasdaq may or may not be correlated with the price at which our ordinary shares trade on AIM. As of November 30, 2021, our ordinary shares will no longer be listed on AIM.

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

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

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

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

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

Any such negative outcome could result in payments of substantial damages or fines, damage to our reputation or adverse changes to our business practices. Defending against litigation is costly and time-consuming, and could divert our management's and key employees' attention and our resources. Furthermore, during the course of litigation, there could be negative public announcements of the results of hearings, motions or other interim proceedings or developments, which could have a negative effect on the market price of our ADSs.

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

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

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

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

The dual listing of ordinary shares may adversely affect the liquidity and value of our ordinary shares and ADSs.

Our ordinary shares trade on AIM and our ADSs are listed on Nasdaq. The dual listing of ADSs and ordinary shares may dilute the liquidity of these securities in one or both markets and may adversely affect the development of an active trading market for our ADSs. The price of our ADSs could also be adversely affected by trading in our ordinary shares on AIM. As of November 30, 2021, our ordinary shares will no longer be listed on AIM.

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 63.2% of our issued and outstanding ordinary shares, based on the number of ordinary shares issued and outstanding as of September 30, 2021. 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 on Nasdaq and have held their shares for a longer period, they may be more interested in selling our company to an acquirer than other investors, or they may want us to pursue strategies that deviate from the interests of other shareholders.

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

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

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

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

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, regardless of whether or not we are an EGC we will be required to furnish a report by our senior management on our internal control over financial reporting, beginning with our annual report filed with the SEC for the year ending December 31, 2021, which we expect to file by April 2022. However, while we remain an EGC we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To prepare for eventual compliance with Section 404, including the attestation report required once we no longer qualify as an EGC, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants, adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented, and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404.

Further, being a U.S. listed company with ADS listed on Nasdaq and an English public company with ordinary shares admitted to trading on AIM impacts the disclosure of information and requires compliance with two sets of applicable rules. From time to time, this may result in uncertainty regarding compliance matters and result in higher costs necessitated by legal analysis of dual legal regimes, ongoing revisions to disclosure and adherence to heightened governance practices. As a result of the enhanced disclosure requirements of the U.S. securities laws, business and financial information that we report is broadly disseminated and highly visible to investors, which we believe may increase the likelihood of threatened or actual litigation, including by competitors and other third parties, which could, even if unsuccessful, divert financial resources and the attention of our management and key employees from our operations. As of November 30, 2021, our ADSs will no longer be listed on AIM.

We have identified material weaknesses in our internal control over financial reporting. If we are unable to remediate these material weaknesses, or if we identify additional material weaknesses in the future or otherwise fail to maintain an

effective system of internal controls, we may not be able to accurately or timely report our financial condition or results of operations, which may adversely affect our business.

In connection with the preparation of our financial statements for the year ended December 31, 2020, we identified material weaknesses in our internal control over our financial close and reporting process. A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of annual or interim financial statements will not be prevented or detected and corrected on a timely basis. The material weaknesses identified relate to controls to address timely reconciliation and analysis of certain key accounts, including those related to revenue recognition and the recognition and accrual of research and development related expenses such as CRO and CMO activities. We have concluded that these material weaknesses arose because, as a company that has recently become public on Nasdaq, the financial resources, business processes and related internal controls necessary to satisfy the accounting and financial reporting requirements of a publicly-listed company are still being developed and established.

We have and continue to identify additional controls to help remediate the material weaknesses described above. The current remediation plan include a more robust review process on the data and calculations to support the reconciliation and analysis of key accounts, an increase in the supervision and monitoring of the financial reporting processes and broadening the understanding of activities as it relates to financial accounting across the organization. We are expanding the level of accounting and controls knowledge and experience within the corporate accounting personnel to meet our financial reporting requirements, and are instituting a training program, when necessary, on proper internal control procedures over financial reporting. The remediation plan also includes implementing controls over calculations, analysis and conclusions associated with revenue and research and development related expenses more precisely. We have and will continue to allocate additional resources to the corporate accounting function, which may include the use of independent consultants with sufficient expertise to assist in the preparation and review of certain non-recurring transactions, timely review of the account reconciliations and the preparation of mid-year and year-end reporting.

We cannot assure you that the measures we have taken to date, and actions we may take in the future, will be sufficient to remediate the control deficiency that led to this material weakness in our internal control over financial reporting or that they will prevent or avoid potential future material weaknesses. In addition, neither our management nor an independent auditor has performed an evaluation of our internal control over financial reporting in accordance with the provisions of the Sarbanes-Oxley Act because no such evaluation has been required. Had we or our independent auditors performed an evaluation of our internal control over financial reporting in accordance with the provisions of the Sarbanes-Oxley Act, additional material weaknesses may have been identified. If we are unable to successfully remediate our existing or any future material weaknesses in our internal control over financial reporting, or identify any additional material weaknesses, the accuracy and timing of our financial reporting may be adversely affected, potentially resulting in restatements of our financial statements, we may be unable to maintain compliance with securities law requirements regarding timely filing of periodic reports and applicable Nasdaq listing requirements, investors may lose confidence in our financial reporting, and our share price may decline as a result.

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

We are an EGC as defined in the SEC's rules and regulations and we will remain an EGC until the earlier to occur of (1) the last day of 2025, (2) the last day of the fiscal year in which we have total annual gross revenues of at least $1.07 billion, (3) the last day of the fiscal year in which we are deemed to be a "large accelerated filer" under SEC rules, which means the market value of our equity securities that is held by non-affiliates exceeds $700 million as of the prior September 30th, and (4) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period. For so long as we remain an EGC, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not EGCs. These exemptions include:

- not being required to comply with the auditor attestation requirements of Section 404;
- not being required to comply with any requirement that has or may be adopted by the PCAOB regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;

- reduced disclosure obligations regarding executive compensation; and

- an exemption from the requirement to seek nonbinding shareholder advisory votes on executive compensation or golden parachute arrangements.

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

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

We report under the Exchange Act as a non-U.S. company with foreign private issuer status. Because we qualify as a foreign private issuer under the Exchange Act, we are exempt from certain provisions of the Exchange Act that are applicable to U.S. domestic public companies, including (i) the sections of the Exchange Act regulating the solicitation of proxies, consents or authorizations in respect of a security registered under the Exchange Act; (ii) the sections of the Exchange Act requiring insiders to file public reports of their stock ownership and trading activities and liability for insiders who profit from trades made in a short period of time; and (iii) the rules under the Exchange Act requiring the filing with the SEC of quarterly reports on Form 10-Q containing unaudited financial and other specified information, or current reports on Form 8-K upon the occurrence of specified significant events. In addition, foreign private issuers are not required to file their annual report on Form 20-F until 120 days after the end of each fiscal year, while U.S. domestic issuers that are accelerated filers are required to file their annual report on Form 10-K within 75 days after the end of each fiscal year. Foreign private issuers also are exempt from Regulation Fair Disclosure, aimed at preventing issuers from making selective disclosures of material information. As a result of the above, you may not have the same protections afforded to shareholders of companies that are not foreign private issuers.

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

As a foreign private issuer listed on Nasdaq, we are subject to corporate governance listing standards. However, Nasdaq rules permit a foreign private issuer like us to follow the corporate governance practices of its home country in lieu of certain Nasdaq corporate governance listing standards. Certain corporate governance practices in England, which is our home country, may differ significantly from Nasdaq corporate governance listing standards. For example, neither the corporate laws of England nor our articles of association require a majority of our directors to be independent; we may include non-independent directors as members of our nominations and remuneration committees; and our independent directors would not necessarily hold regularly scheduled meetings at which only independent directors are present. Until November 30, 2021, when our ordinary shares will no longer be listed on AIM, we are required to follow the AIM Rules for Companies published by London Stock Exchange plc, and have adopted the Corporate Governance Code published by the Quoted Companies Alliance. Therefore, our shareholders may be afforded less protection than they otherwise would have under Nasdaq corporate governance listing standards applicable to U.S. domestic issuers.

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

As a foreign private issuer, we are not required to comply with all of the periodic disclosure and current reporting requirements of the Exchange Act applicable to U.S. domestic issuers. If we lose our status as a foreign private issuer, we would be required to comply with the Exchange Act reporting and other requirements applicable to U.S. domestic issuers, which are more detailed and extensive than the requirements for foreign private issuers. We may also be required to make changes in our corporate governance practices in accordance with various SEC and Nasdaq rules. The regulatory and compliance costs to us under U.S. securities laws if we are required to comply with the reporting requirements applicable to a U.S. domestic issuer may be significantly higher than the cost we would incur as a foreign private issuer. As a result, we expect

that a loss of foreign private issuer status would increase our legal and financial compliance costs and would make some activities highly time consuming and costly. We also expect that if we were required to comply with the rules and regulations applicable to U.S. domestic issuers, it would make it more difficult and expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced coverage and/or incur substantially higher costs to obtain coverage. These rules and regulations could also make it more difficult for us to attract and retain qualified members of our board of directors.

Securities traded on AIM may carry a higher risk than securities traded on other exchanges, which may impact the value of your investment.

Our ordinary shares are currently traded, and until November 30, 2021 will continue to be traded on AIM. Investment in equities traded on AIM is sometimes perceived to carry a higher risk than an investment in equities quoted on exchanges with more stringent listing requirements, such as the main market of the London Stock Exchange, New York Stock Exchange or Nasdaq. This is because AIM imposes less stringent corporate governance and ongoing reporting requirements than those other exchanges. In addition, AIM requires only six-monthly, rather than quarterly, financial reporting. You should be aware that the value of our ordinary shares may be influenced by many factors, some of which may be specific to us and some of which may affect AIM companies generally, including the depth and liquidity of the market, our performance, a large or small volume of trading in our ordinary shares, legislative changes and general economic, political or regulatory conditions, and that the prices may be volatile and subject to extensive fluctuations. Therefore, the market price of our ordinary shares, the ADSs, or the ordinary shares underlying the ADSs, may not reflect the underlying value of our company.

Fluctuations in the exchange rate between the U.S. dollar and the British pound sterling may increase the risk of holding ADSs and ordinary shares.

The share price of our ordinary shares is quoted on AIM in British pence sterling, while our ADSs trade on Nasdaq in U.S. dollars. Fluctuations in the exchange rate between the U.S. dollar and the British pound sterling may result in differences between the value of our ADSs and the value of our ordinary shares, which may result in heavy trading by investors seeking to exploit such exchange rate differences. In addition, as a result of fluctuations in the exchange rate between the U.S. dollar and the British pound sterling, the U.S. dollar equivalent of the proceeds that a holder of the ADSs would receive upon the sale in the United Kingdom of any ordinary shares withdrawn from the depositary, and the U.S. dollar equivalent of any cash dividends paid in British pounds sterling on ordinary shares represented by the ADSs, could also decline.

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.

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 United Kingdom 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. You will receive these distributions in proportion to the number of our ordinary shares your ADSs represent. However, in accordance with the limitations set forth in the deposit agreement, it may be unlawful or impractical to make a distribution available to holders of ADSs. We have no obligation to register under U.S. securities laws any offering of ADSs, ordinary shares or other securities received through such distributions. We also have no obligation to take any other action to permit distribution on the ADSs, ordinary shares, rights or anything else to holders of the ADSs. This means that you may not receive the distributions we make on our ordinary shares or any value from them if it is unlawful or impractical to make them available to you. These restrictions may have an adverse effect on the value of your ADSs.

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

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

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

Under the Internal Revenue Code of 1986, as amended, or the Code, we will be a passive foreign investment company, or PFIC, for any taxable year in which (1) 75% or more of our gross income consists of passive income, or (2) 50% or more of the average quarterly value of our assets consists of assets that produce, or are held for the production of, passive income (including cash). For purposes of these tests, passive income includes dividends, interest, gains from the sale or exchange of investment property and certain rents and royalties. In addition, for purposes of the above calculations, a non-U.S. corporation that directly or indirectly owns at least 25% by value of the shares of another corporation is treated as if it held its proportionate share of the assets and received directly its proportionate share of the income of such other corporation. If we are a PFIC for

any taxable year during which a U.S. Holder holds our ADSs, the U.S. Holder may be subject to adverse tax consequences regardless of whether we continue to qualify as a PFIC, including ineligibility for any preferred tax rates on capital gains or on actual or deemed dividends, interest charges on certain taxes treated as deferred, and additional reporting requirements. A "U.S. Holder" is a beneficial owner of ordinary shares or ADSs who is eligible for the benefits of the Treaty and is (1) a citizen or individual resident of the United States; (2) a corporation, or other entity taxable as a corporation, created or organized in or under the laws of the United States, any state therein or the District of Columbia; (3) an estate the income of which is subject to U.S. federal income taxation regardless of its source; or (4) a trust if (a) a U.S. court is able to exercise primary supervision over the administration of the trust and one or more U.S. persons have authority to control all substantial decisions of the trust or (b) the trust has a valid election to be treated as a U.S. person under applicable U.S. Treasury Regulations.

Based on estimates of our income and assets, and certain assumptions with respect to the characterization of our assets as active or passive, we do not believe we were a PFIC for our taxable year ended December 31, 2020. 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.

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, 2020, we had cumulative carryforward tax losses of £135.6 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 activities, we benefit from the U.K. research and development tax credit regime under the scheme for small and medium-sized enterprises, or SMEs. Under the SME scheme, we are able to surrender some of our trading losses that arise from our qualifying research and development activities for a cash rebate of up to 33.35% of such qualifying research and development expenditures. We may not be able to continue to claim payable research and development tax credits in the future if we cease to qualify as an SME, based on size criteria concerning employee headcount, turnover and gross assets. Qualifying expenditures largely are comprised of employment costs for research staff, research materials, outsourced CRO costs and R&D consulting costs incurred as part of research projects. Specified subcontracted qualifying research expenditures are eligible for a cash rebate of up to 21.67%.

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%. We are the exclusive licensee or owner of one patent and several patent applications which, if issued, would cover our product candidates, and accordingly, future upfront fees, milestone fees, product revenues and royalties could be taxed at this tax rate. When taken in combination with the enhanced relief available on our research and development expenditures, we expect a long-term lower effective rate of corporation tax to apply to us. If, however, there are unexpected adverse changes to the U.K. research and development tax credit regime or the "patent box" regime, or for any reason we are unable to qualify for such advantageous tax legislation, or we are unable to use net operating loss and tax credit carryforwards and certain built-in losses to reduce future tax payments, our business, results of operations, and financial condition may be adversely affected. This may impact our ongoing requirement for investment and the timeframes within which additional investment is required.

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

We conduct business in the United Kingdom, Germany and the United States and file income tax returns in multiple jurisdictions. Our consolidated effective income tax rate could be materially adversely affected by several factors, including: changing tax laws, regulations and treaties, or the interpretation thereof; tax policy initiatives and reforms under consideration (such as those related to the Organisation for Economic Co-Operation and Development's, or OECD, Base Erosion and Profit Shifting, or BEPS, Project, the European Commission's state aid investigations and other initiatives); the practices of tax authorities in jurisdictions in which we operate; the resolution of issues arising from tax audits or examinations and any related

interest or penalties. Such changes may include (but are not limited to) the taxation of operating income, investment income, dividends received or (in the specific context of withholding tax) dividends paid.

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

A tax authority may disagree with tax positions that we have taken, which could result in increased tax liabilities. For example, Her 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 lengthy and costly and if we were unsuccessful in disputing the assessment, the implications could increase our anticipated effective tax rate, where applicable.

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

The Takeover Code applies, amongst other things, to an offer for a public company whose registered office is in the United Kingdom and whose securities are admitted to trading on a multilateral trading facility in the United Kingdom, which includes AIM. We are therefore currently subject to the Takeover Code.

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 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 unsubstantiated statements made in documents or to the media must be publicly corrected immediately.

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

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

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

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

We are incorporated under English law. The rights of holders of ordinary shares and, therefore, certain of the rights of holders of our ADSs, are governed by English law, including the provisions of the U.K. Companies Act 2006, or the Companies Act, and by our articles of association. These rights differ in certain respects from the rights of shareholders in typical U.S. corporations.

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

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

English law also generally provides shareholders with preemptive rights when new shares are issued for cash. However, it is possible for the articles of association, or for shareholders to pass a special resolution at a general meeting, being a resolution passed by at least 75% of the votes cast, to disapply preemptive rights. Such a disapplication of preemptive rights may be for a maximum period of up to five years from the date of adoption of the articles of association, if the disapplication is contained in the articles of association, or from the date of the shareholder special resolution, if the disapplication is by shareholder special

resolution, but not longer than the duration of the authority to allot shares to which the disapplication relates. In either case, this disapplication would need to be renewed by our shareholders upon its expiration (i.e., at least every five years). Typically, English public companies renew the disapplication of preemptive rights on an annual basis at their annual general meeting.

English law also generally prohibits a public company from repurchasing its own shares without the prior approval of shareholders by ordinary resolution, being a resolution passed by a simple majority of votes cast, and other formalities. Such approval may be for a maximum period of up to five years.

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

We are incorporated under English law. Substantially all of our assets are located outside the United States. The majority of our senior management and board of directors reside outside the United States. As a result, it may not be possible for investors to effect service of process within the United States upon such persons or to enforce judgments obtained in U.S. courts against them or us, including judgments predicated upon the civil liability provisions of the U.S. federal securities laws.

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

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

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

Our articles of association provide that the U.S. federal district courts are the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. Although such a provision has been determined to be enforceable under the laws of Delaware by the courts of Delaware, there is uncertainty as to whether other courts would enforce such provision, and the enforceability of similar choice of forum provisions in other companies' constitutive documents has been challenged in legal proceedings. 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.

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.

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

The deposit agreement governing our ADSs provides that owners and holders of ADSs irrevocably waive the right to a trial by jury in any legal proceeding arising out of or relating to the deposit agreement or the ADSs, including claims under

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

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

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