UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-Q

(Mark One)

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

For the quarterly period ended September 30, 2022
OR

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

For the transition period from to
Commission File Number: 001-38503

Iterum Therapeutics plc
(Exact name of registrant as specified in its charter)

Ireland	**98-1283148**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**

Fitzwilliam Court 1st Floor,
Leeson Close,
Dublin 2, Ireland
(Address of principal executive offices)
Not applicable
(Zip Code)

(+353) 1 669-4820

(Registrant's telephone number, including area code)

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

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Ordinary Shares, $0.01 par value per share	ITRM	The Nasdaq Stock Market LLC

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

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

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

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

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☒

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

As of October 31, 2022, the registrant had 12,233,374 ordinary shares, $0.01 par value per share, outstanding.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This Quarterly Report on Form 10-Q contains forward-looking statements that involve risks and uncertainties. All statements other than statements of historical facts contained in this Quarterly Report are forward-looking statements. In some cases, you can identify forward-looking statements by words such as "anticipate," "believe," "contemplate," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "seek," "should," "target," "will," "would," or the negative of these words or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- our use of cash reserves;
- the design, initiation, timing, progress and results of our preclinical studies and clinical trials, and our research and development programs including the ongoing Phase 3 clinical trial and non-clinical development being conducted in response to the Complete Response Letter (CRL) received from the U.S. Food and Drug Administration in July 2021 in connection with our New Drug Application (NDA) for oral sulopenem;
- our ability to resolve the issues set forth in the CRL and resubmit our NDA;
- our ability to retain the continued service of our key professionals and to identify, hire and retain additional qualified professionals;
- our ability to advance product candidates into, and successfully complete, clinical trials;
- the potential advantages of our product candidates;
- the timing or likelihood of regulatory filings and approvals, including with respect to the potential resubmission of our NDA for oral sulopenem;
- the commercialization of our product candidates, if approved;
- our manufacturing plans;
- our sales, marketing and distribution capabilities and strategy;
- market acceptance of any product we successfully commercialize;
- the pricing, coverage and reimbursement of our product candidates, if approved;
- the implementation of our business model, strategic plans for our business and product candidates;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and our ability to defend and enforce any such intellectual property rights;
- our ability to enter into strategic arrangements, collaborations and/or commercial partnerships in the United States and other territories and the potential benefits of such arrangements;
- our estimates regarding expenses, capital requirements and needs for additional financing;
- our expectations regarding how far into the future our cash on hand will fund our ongoing operations;
- our financial performance;
- developments relating to our competitors and our industry;
- the impact of COVID-19, including the responsive measures taken by governmental authorities and others, on our clinical trials, on regulatory approval, on future commercialization of, and future demand for, our products, available funding, our operations and the economy in general, which may precipitate or exacerbate other risks and/or uncertainties;
- our ability to maintain compliance with listing requirements of the Nasdaq Capital Market; and
- the outcome, impact, effects and results of our evaluation of corporate, strategic, financial and financing alternatives, including the terms, timing, structure, value, benefits and costs of any corporate, strategic, financial or financing alternative and our ability to complete one at all.

These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including those described in "Risk Factors" and elsewhere in this Quarterly Report. Moreover, we operate in a very competitive and rapidly changing environment, and new risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this Quarterly Report may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements.

You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur. We undertake no obligation to update publicly any forward-looking statements for any reason after the date of this Quarterly Report to conform these statements to new information, actual results or to changes in our expectations, except as required by law.

You should read this Quarterly Report and the documents that we have filed with the Securities and Exchange Commission (SEC), as exhibits to this Quarterly Report with the understanding that our actual future results, levels of activity, performance, and events and circumstances may be materially different from what we expect.

This Quarterly Report also contains industry, market and competitive position data from our own internal estimates and research as well as industry and general publications and research surveys and studies conducted by third parties. Industry publications, studies, and surveys generally state that they have been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. Our internal data and estimates are based upon information obtained from trade and business organizations and other contacts in the markets in which we operate and our management's understanding of industry conditions. While we believe that each of these studies and publications is reliable, we have not independently verified market and industry data from third-party sources. While we believe our internal company research is reliable and the market definitions are appropriate, neither such research nor these definitions have been verified by any independent source. The industry in which we operate is subject to a high degree of uncertainty and risks due to various factors, including those described in the section titled "Risk Factors".

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this Quarterly Report, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain, and investors are cautioned not to unduly rely upon these statements.

PART I—FINANCIAL INFORMATION

Item 1. Financial Statements (Unaudited).

ITERUM THERAPEUTICS PLC
Condensed Consolidated Balance Sheets
(In thousands except share and per share data)
(Unaudited)

	September 30, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 20,489	$ 27,446
Short-term investments	43,834	53,898
Current portion of restricted cash	30	—
Income taxes receivable	413	—
Prepaid expenses and other current assets	1,886	1,922
Total current assets	66,652	83,266
Intangible asset, net	2,148	3,435
Property and equipment, net	34	91
Restricted cash, less current portion	34	64
Other assets	2,687	4,653
Total assets	$ 71,555	$ 91,509
Liabilities and Shareholders' Equity		
Current liabilities:		
Accounts payable	$ 1,229	$ 878
Accrued expenses	3,732	1,165
Derivative liability	610	6,058
Current portion of long-term debt	—	1,627
Income taxes payable	—	221
Other current liabilities	1,938	2,992
Total current liabilities	7,509	12,941
Long-term debt, less current portion	9,298	6,930
Royalty-linked notes	20,917	17,968
Other liabilities	1,282	3,436
Total liabilities	$ 39,006	$ 41,275
Commitments and contingencies (Note 15)		
Shareholders' equity:		
Undesignated preferred shares, $0.01 par value per share: 100,000,000 shares authorized at September 30, 2022 and December 31, 2021; no shares issued at September 30, 2022 and December 31, 2021	—	—
Ordinary shares, $0.01 par value per share: 20,000,000 shares authorized at September 30, 2022 and December 31, 2021, 12,233,374 shares issued at September 30, 2022; 12,185,018 shares issued at December 31, 2021	122	122
Additional paid-in capital	450,264	428,605
Accumulated deficit	(417,837)	(378,493)
Total shareholders' equity	$ 32,549	$ 50,234
Total liabilities and shareholders' equity	$ 71,555	$ 91,509

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

ITERUM THERAPEUTICS PLC
Condensed Consolidated Statements of Operations and Comprehensive Loss
(In thousands, except share and per share data)
(Unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Operating expenses:				
Research and development	$ (4,353)	$ (1,845)	$ (11,777)	$ (7,010)
General and administrative	(2,681)	(3,029)	(10,680)	(10,698)
Total operating expenses	(7,034)	(4,874)	(22,457)	(17,708)
Operating loss	(7,034)	(4,874)	(22,457)	(17,708)
Interest expense, net	(636)	(849)	(2,441)	(4,781)
Adjustments to fair value of derivatives	(4,834)	9,783	2,498	(64,526)
Cancellation of share options	(17,350)	—	(17,350)	—
Other income, net	175	33	606	167
Total other income / (expense), net	(22,645)	8,967	(16,687)	(69,140)
(Loss) / income before income taxes	(29,679)	4,093	(39,144)	(86,848)
Income tax benefit / (expense)	570	(352)	(200)	(534)
Net (loss) / income and comprehensive (loss) / income	(29,109)	3,741	(39,344)	(87,382)
Net (loss) / income attributable to ordinary shareholders	$ (29,109)	$ 3,741	$ (39,344)	$ (87,382)
Net (loss) / income per share attributable to ordinary shareholders – basic	$ (2.38)	$ 0.31	$ (3.22)	$ (8.40)
Net (loss) / income per share attributable to ordinary shareholders – diluted	$ (2.38)	$ 0.28	$ (3.22)	$ (8.40)
Weighted average ordinary shares outstanding – basic	12,233,374	12,182,002	12,217,188	10,403,889
Weighted average ordinary shares outstanding – diluted	12,233,374	13,483,807	12,217,188	10,403,889

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

ITERUM THERAPEUTICS PLC
Condensed Consolidated Statements of Cash Flows
(In thousands, except share and per share data)
(Unaudited)

	Nine Months Ended September 30,	
	2022	**2021**
Cash flows from operating activities:		
Net loss	$ (39,344)	$ (87,382)
Adjustments to reconcile net loss to cash used in operating activities:		
Depreciation	74	331
Amortization of intangible asset	1,287	—
Share-based compensation expense	4,301	2,352
Cancellation of share options expense	17,350	—
Interest on short-term investments	(81)	(136)
Non-cash loss on short-term investments	468	353
Amortization of debt discount and deferred financing costs	1,748	3,636
Interest on exchangeable notes - non-cash	615	873
Adjustments to fair value of derivatives	(2,498)	64,526
Other	1,914	2,311
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(1,742)	1,516
Accounts payable	351	(540)
Accrued expenses	2,577	(137)
Income taxes	(620)	(397)
Other liabilities	(608)	(689)
Net cash used in operating activities	(14,208)	(13,383)
Cash flows from investing activities:		
Purchases of property, plant and equipment	(17)	(48)
Purchases of short-term investments	(36,031)	(60,081)
Proceeds from sale of short-term investments	45,627	10,000
Net cash (used in) / provided by investing activities	9,579	(50,129)
Cash flows from financing activities:		
Repayments of long-term debt	(2,251)	(4,887)
Proceeds from issuance of ordinary shares, net of transaction costs	—	89,643
Net cash (used in) / provided by financing activities	(2,251)	84,756
Effect of exchange rates on cash and cash equivalents	(77)	(14)
Net (decrease) / increase in cash, cash equivalents and restricted cash	(6,957)	21,230
Cash, cash equivalents and restricted cash, at beginning of period	27,510	14,816
Cash, cash equivalents and restricted cash, at end of period	$ 20,553	$ 36,046
Supplemental Disclosure of Cash Flow Information:		
Income tax paid - US	$ 821	$ 397
Interest paid	$ 22	$ 361

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

1. Basis of Presentation

Iterum Therapeutics plc (the Company) was incorporated under the laws of the Republic of Ireland in June 2015 as a limited company and re-registered as a public limited company on March 20, 2018. The Company maintains its registered office at Fitzwilliam Court, 1st Floor, Leeson Close, Dublin 2, Ireland. The Company commenced operations in November 2015. The Company licensed global rights to its novel anti-infective compound, sulopenem, from Pfizer Inc. (Pfizer). The Company is a clinical-stage pharmaceutical company dedicated to developing and commercializing sulopenem to be potentially the first oral penem available in the United States and the first and only oral and intravenous (IV) branded penem available globally.

The Company is subject to risks and uncertainties common to early-stage companies in the pharmaceutical industry, including, but not limited to, the ability to secure additional capital to fund operations, failure to achieve regulatory approval, failure to successfully develop and commercialize its product candidates, development by competitors of new technological innovations, dependence on key personnel, protection of proprietary technology and compliance with government regulations. Product candidates currently under development will require additional research and development efforts, including regulatory approval prior to commercialization.

Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales.

The accompanying condensed consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America (GAAP) and include the accounts of the Company and its subsidiaries.

In accordance with Accounting Standards Update (ASU) 2014-15, *Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern (Subtopic 205-40)*, the Company has evaluated whether there are conditions and events, considered in aggregate, that raise substantial doubt about the Company's ability to continue as a going concern within one year of the date of issue of these quarterly condensed consolidated financial statements.

Since inception, the Company has devoted substantially all of its efforts to research and development, recruiting management and technical staff, and raising capital, and has financed its operations through the issuance and sale of ordinary shares and convertible preferred shares, debt raised under financing arrangements with Silicon Valley Bank (SVB) including the Paycheck Protection Program loan (PPP loan), a sub-award from the Trustees of Boston University under the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X) program and the proceeds of a private placement (Private Placement) and subsequent rights offering (Rights Offering) pursuant to which the Company's wholly owned subsidiary, Iterum Therapeutics Bermuda Limited (Iterum Bermuda) issued and sold $51,808 aggregate principal amount of 6.500% Exchangeable Senior Subordinated Notes due 2025 (Exchangeable Notes) and $104 aggregate principal amount of Limited Recourse Royalty-Linked Subordinated Notes (the RLNs and, together with the Exchangeable Notes, the Securities), which Securities were sold in units consisting of an Exchangeable Note in the original principal amount of $1,000 and 50 RLNs (the Units). The Company has not generated any product revenue. The Company has incurred operating losses since inception, including net losses of $39,344 and $87,382 for the nine months ended September 30, 2022 and 2021, respectively, and a net loss of $91,564 for the year ended December 31, 2021. The Company had an accumulated deficit of $417,837 as of September 30, 2022 and expects to continue to incur net losses for the foreseeable future. Management believes that its cash and cash equivalents balance of $20,489 and short-term investments balance of $43,834 at September 30, 2022 are sufficient to fund operations into 2024. In making this assessment management have considered the planned operations of the company and the ability to adjust its plans if required.

In addition, in parallel, the Company is evaluating its corporate, strategic, financial and financing alternatives, with the goal of maximizing value for its stakeholders. These alternatives could potentially include the licensing, sale or divestiture of the Company's assets or proprietary technologies, a sale of the Company, a merger or other business combination or another strategic transaction involving the Company. The evaluation of corporate, strategic, financial and financing alternatives may not result in any particular action or any transaction being pursued, entered into or consummated, and there is no assurance as to the timing, sequence or outcome of any action or transaction or series of actions or transactions.

The Company's shareholders approved a reverse share split of the Company's ordinary shares on June 15, 2022, which became effective on August 17, 2022, (the Reverse Share Split). As of 5:00 p.m. Eastern Standard Time on August 17, 2022, every fifteen ordinary shares of $0.01 each (nominal value) in the authorized and unissued and authorized and issued share capital of the Company were consolidated into one ordinary share of $0.15 each (nominal value), and the nominal value of each ordinary share was subsequently reduced from $0.15 to $0.01 nominal value per share. No fractional shares were issued to any shareholders in connection with the Reverse Share Split. Shareholders who were otherwise entitled to receive a fractional ordinary share instead received a cash payment in an amount equal to the net cash proceeds attributable to the sale of such fractional entitlement following aggregation and sale by the Company on behalf of each of the relevant shareholders of the Company's ordinary shares, on the basis of prevailing market prices at such time. As the par value per share of the Company's shares remained at $0.01 per share following the Reverse Share Split, the difference between the total share capital at (par value) prior to the Reverse Share Split and the total share capital (par value) after the Reverse Share Split, has been reclassified as additional paid-in-capital on a retroactive basis. The number of ordinary shares reserved for issuance upon exercise of the Exchangeable Notes, outstanding share options and warrants or upon the vesting of outstanding restricted share units, was adjusted and proportionately decreased and the exercise price of all share options, Exchangeable Notes and warrants was proportionately increased. Additionally, the number of shares that may be the subject of future grants under our share plans was proportionally decreased. Accordingly, all historical share and per share information related to the issued and outstanding ordinary shares, the Exchangeable Notes, share options, restricted share units, warrants and shares reserved for future issuance under the Company's share plans have been adjusted to reflect the Reverse Share Split for all prior periods presented.

Interim Financial Information

The condensed consolidated balance sheet at December 31, 2021 was derived from audited financial statements, but does not include all disclosures required by GAAP. The accompanying unaudited condensed consolidated financial statements as of September 30, 2022 and for the three and nine months ended September 30, 2022 and 2021 have been prepared by the Company pursuant to the rules and regulations of the Securities and Exchange Commission (SEC) for interim financial statements. Certain information and footnote disclosures normally included in financial statements prepared in accordance with GAAP have been condensed or omitted pursuant to such rules and regulations. These condensed consolidated financial statements should be read in conjunction with the Company's audited consolidated financial statements and the notes thereto for the year ended December 31, 2021, included in the Company's Annual Report on Form 10-K filed with the SEC on March 28, 2022. In the opinion of management, all adjustments, consisting only of normal recurring adjustments necessary for a fair statement of the Company's financial position as of September 30, 2022, and results of operations for the three and nine months ended September 30, 2022 and 2021, and cash flows for the nine months ended September 30, 2022 and 2021 have been made. The results of operations for the three and nine months ended September 30, 2022 are not necessarily indicative of the results of operations that may be expected for the year ending December 31, 2022.

2. Summary of Significant Accounting Policies

There have been no material changes in the Company's significant accounting policies, other than the adoption of accounting pronouncements as described below, as compared to the significant accounting policies described in the Company's Annual Report on Form 10-K for the year ended December 31, 2021.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of expenses during the reporting period. Significant estimates and assumptions reflected in these condensed consolidated financial statements include, but are not limited to, the valuation of share-based compensation awards, the valuation of the RLNs and the Derivative liabilities, which consist of embedded features in the Exchangeable Notes, and the accrual for research and development expenses. The Company bases its estimates on historical experience, known trends and other market-specific or other relevant factors that it believes to be reasonable under the circumstances. On an ongoing basis, management evaluates its estimates as there are changes in circumstances, facts and experience. Actual results could differ materially from those estimates. The Company has contemplated the impact of COVID-19 within its financial statements and is not aware of any specific event or circumstance that would require the Company to update estimates or judgments or revise the carrying value of any assets or liabilities.

Specifically, management has estimated variables in the discounted cash flow analysis (DCF) to value derivative instruments (see Note 3 - Fair Value of Financial Assets and Liabilities).

Cash and Cash Equivalents

The Company's cash and cash equivalents consist of cash balances and highly liquid investments with maturities of three months or less at the date of purchase. Accounts held at U.S. financial institutions are insured by the Federal Deposit Insurance Corporation up to $250, while accounts held at Irish financial institutions are insured under the Deposit Guarantee Scheme up to $98 (€100).

(In thousands, except share and per share data)

Cash accounts with any type of restriction are classified as restricted cash. If restrictions are expected to be lifted in the next twelve months, the restricted cash account is classified as current. Included within restricted cash on the Company's condensed consolidated balance sheet is a certificate of deposit for $30 as of September 30, 2022 which is being held by a third party bank as collateral for the irrevocable letter of credit issued in March 2018 to secure an office lease. Also included within restricted cash on the Company's condensed consolidated balance sheet is $17 as of September 30, 2022 relating to the warrants issued on June 5, 2020 pursuant to the securities purchase agreement (June 3, 2020 SPA) from the June 3, 2020 registered direct offering (June 3, 2020 Offering), $6 as of September 30, 2022 relating to the warrants issued on July 2, 2020 pursuant to the securities purchase agreement (June 30, 2020 SPA) from the June 30, 2020 registered direct offering (June 30, 2020 Offering) and $11 as of September 30, 2022 relating to warrants issued in the underwritten offering in October 2020 (October 2020 Offering). These restricted cash amounts are unchanged from December 31, 2021. On the closing date of each of the June 3, 2020 Offering, June 30, 2020 Offering and the October 2020 Offering, each investor deposited $0.01 per warrant issued being the nominal value of the underlying ordinary share represented by each warrant. This amount will be held in trust by the Company pending a decision by the relevant investor to exercise the warrant by means of a "cashless exercise" pursuant to the terms of the warrant, in which case the $0.01 will be used to pay up the nominal value of the ordinary share issued pursuant to the warrant. Upon the exercise of the warrants other than by means of a "cashless exercise", the amount held in trust will be returned to the relevant investor in accordance with the terms of the applicable purchase agreement or prospectus.

Concentration of Credit Risk

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash and cash equivalents and short-term investments. The Company has most of its cash, cash equivalents and short-term investments at two accredited financial institutions in the United States and Ireland, in amounts that exceed federally insured limits. The Company does not believe that it is subject to unusual credit risk beyond the normal credit risk associated with commercial banking relationships.

Net Loss Per Ordinary Share

Basic and diluted net loss per ordinary share is determined by dividing net loss attributable to ordinary shareholders by the weighted-average ordinary shares outstanding during the period in accordance with Accounting Standard Codification (ASC) 260, *Earnings per Share*. For the periods presented, the following ordinary shares underlying the options, unvested restricted share units, unvested performance restricted share units, warrants and the Exchangeable Notes have been excluded from the calculation because they would be anti-dilutive.

	Three Months Ended		Nine Months Ended	
	September 30, 2022	September 30, 2021	September 30, 2022	September 30, 2021
Options to purchase ordinary shares	329,799	—	329,799	951,426
Unvested restricted share units	128,096	—	128,096	85,684
Unvested performance restricted share units	—	—	—	1,733
Warrants	480,186	—	480,186	480,186
Exchangeable Notes	1,270,094	—	1,270,094	1,199,819
Total	2,208,175	—	2,208,175	2,718,848

Segment and Other Information

The Company determines and presents operating segments based on the information that is internally provided to the Chief Executive Officer, Chief Financial Officer and Chief Medical Officer, who together are considered the Company's chief operating decision maker, in accordance with ASC 280, *Segment Reporting*. The Company has determined that it operates as a single business segment, which is the development and commercialization of innovative treatments for drug resistant bacterial infections.

The distribution of total operating expenses by geographical area was as follows:

	Three Months Ended September 30,		Nine Months Ended September 30,	
Operating expenses	**2022**	**2021**	**2022**	**2021**
Ireland	$ 5,675	$ 3,056	$ 15,302	$ 11,166
U.S.	1,352	1,817	7,129	6,495
Bermuda	7	1	26	47
Total	$ 7,034	$ 4,874	$ 22,457	$ 17,708

(In thousands, except share and per share data)

The distribution of long-lived assets by geographical area was as follows:

Long-lived assets	September 30, 2022	December 31, 2021
Ireland	$ 4,572	$ 7,601
U.S.	297	578
Total	$ 4,869	$ 8,179

Income Taxes

On March 27, 2020, the Coronavirus Aid, Relief, and Economic Security Act (CARES Act) was signed into law in the United States to provide certain relief as a result of the COVID-19 pandemic. In addition, governments around the world have enacted or implemented various forms of tax relief measures in response to the economic conditions in the wake of COVID-19. Neither the enactment of the CARES Act nor changes to income tax laws or regulations in other jurisdictions had a significant impact on the Company's income tax provision for the three and nine months ended September 30, 2022 and 2021, or to the Company's net deferred tax assets as of September 30, 2022.

Recently Adopted Accounting Pronouncements

In August 2020, the Financial Accounting Standards Board (FASB) issued ASU 2020-06, *Debt—Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging—Contracts in Entity's Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity's Own Equity,* which reduces the number of accounting models for convertible instruments and allows more contracts to qualify for equity classification. The ASU is effective for annual and interim periods in fiscal years beginning after December 15, 2021. The new standard became effective for the Company on January 1, 2022 and did not have a material impact on the Company's condensed consolidated financial statements.

In May 2021, the FASB issued ASU 2021-04, *Earnings Per Share (Topic 260), Debt—Modifications and Extinguishments (Subtopic 470-50), Compensation—Stock Compensation (Topic 718), and Derivatives and Hedging—Contracts in Entity's Own Equity (Subtopic 815-40): Issuer's Accounting for Certain Modifications or Exchanges of Freestanding Equity-Classified Written Call Options,* which clarifies an issuer's accounting for modifications or exchanges of freestanding written call options that remain equity-classified after modification. The ASU 2021-04 is effective for all entities for interim and annual periods in fiscal years beginning after December 15, 2021. The new standard became effective for the Company on January 1, 2022 and did not have a material impact on the Company's condensed consolidated financial statements.

In July 2021, the FASB issued ASU 2021-05, *Leases (Topic 842): Lessors – Certain Leases with Variable Lease Payments*, which requires a lessor to classify a lease with entirely or partially variable payments that do not depend on an index or rate as an operating lease if a different classification would result in a commencement date selling loss (Day 1 loss). For entities that have adopted ASU 2016-02, *Leases*, as of July 19, 2021, ASU 2021-05 is effective for annual and interim periods in fiscal years beginning after December 15, 2021 for public business entities and annual periods in fiscal years beginning after December 15, 2021 and interim periods in fiscal years beginning after December 15, 2022 for all other entities. The new standard became effective for the Company on January 1, 2022 and did not have a material impact on the Company's condensed consolidated financial statements.

3. Fair Value of Financial Assets and Liabilities

The following table presents information about the Company's financial assets that were carried at fair value on a recurring basis on the condensed consolidated balance sheet as of September 30, 2022 and December 31, 2021 and indicates the fair value hierarchy of the valuation inputs utilized to determine such fair value.

September 30, 2022				
Assets	**Total**	**Level 1**	**Level 2**	**Level 3**
Short-term investments	$ 43,834	43,834	—	—

December 31, 2021				
Assets	**Total**	**Level 1**	**Level 2**	**Level 3**
Short-term investments	$ 53,898	53,898	—	—

See Note 4 for details on the short-term investments. The carrying amounts reported in the condensed consolidated balance sheets for prepaid expenses and other current assets, accounts payable, accrued expenses and other current liabilities approximate their fair value based on the short-term maturity of these instruments.

(In thousands, except share and per share data)

The following table presents information about the Company's debt, Exchangeable Notes, Derivative liability and RLNs. The Company's long-term debt was carried at amortized cost on the condensed consolidated balance sheet as of December 31, 2021 and indicates the fair value hierarchy of the valuation inputs utilized to determine the approximate fair value:

September 30, 2022 Liabilities	Book Value	Approximate Fair Value	Level 1	Level 2	Level 3
Exchangeable Notes					
Long-term exchangeable note	$ 9,298	$ 10,722	—	10,722	—
Derivative liability - exchange option and change of control	610	610	—	—	610
Revenue Futures					
Royalty-linked notes	20,917	20,917	—	—	20,917
Total	$ 30,825	$ 32,249	—	10,722	21,527

December 31, 2021 Liabilities	Book Value	Approximate Fair Value	Level 1	Level 2	Level 3
Debt					
Current portion of long-term debt	$ 1,627	$ 1,627	—	1,627	—
Exchangeable Notes					
Long-term exchangeable note	6,930	9,495	—	9,495	—
Derivative liability - exchange option and change of control	6,058	6,058	—	—	6,058
Revenue Futures					
Royalty-linked notes	17,968	17,968	—	—	17,968
Total	$ 32,583	$ 35,148	—	11,122	24,026

The book value of the current portion of long-term debt approximates its fair value due to the short-term nature of the balance.

The fair value of long-term Exchangeable Notes was determined using DCF analysis using the fixed interest rate outlined in the indenture governing the Exchangeable Notes (Exchangeable Notes Indenture), without consideration of transaction costs, which represents a Level 2 basis of fair value measurement.

The Level 3 liabilities held as of September 30, 2022 consist of the embedded exchange option and change of control premium contained in the Exchangeable Notes (see Note 10 - Debt) and a separate financial instrument, that was issued as part of the Units, the RLNs (see Note 11 – Royalty-Linked Notes). The exchange option and change of control premium met the criteria requiring these to be bifurcated and accounted for separately from the host debt in accordance with ASC 815-15, *Derivatives and Hedging; Embedded Derivatives*. The exchange option and change of control premium are presented as a Derivative liability upon issuance of the Exchangeable Notes under the Private Placement and Rights Offering and are subsequently remeasured to fair value at the end of each reporting period. At any time on or after January 21, 2021, subject to specified limitations, the Exchangeable Notes are exchangeable for the Company's ordinary shares, cash or a combination of ordinary shares and cash, at an exchange rate of 85.7456 shares per $1,000 principal and interest on the Exchangeable Notes (equivalent to an exchange price of approximately $11.6624 per ordinary share) as of August 17, 2022, which was adjusted from an initial exchange rate of 66.666 shares per $1,000 principal and interest on the Exchangeable Notes (equivalent to an initial exchange price of $15.00 per ordinary share) and is subject to further adjustment pursuant to the terms of the Exchangeable Notes Indenture. Beginning on January 21, 2021 to September 30, 2022, certain noteholders of $39,201 aggregate principal amount of Exchangeable Notes have exchanged their notes for an aggregate of 3,592,555 of the Company's ordinary shares, which included accrued and unpaid interest relating to such notes. The aggregate principal amount of Exchangeable Notes outstanding as of September 30, 2022 was $12,607. The fair value of the exchange option at September 30, 2022 amounted to $312.

In the event of a fundamental change that is not a liquidation event (Fundamental Change), under the Exchangeable Notes Indenture, the Company will be required to pay each holder of an Exchangeable Note the greater of three times the outstanding principal amount of such Exchangeable Note and the consideration that would be received by the holder of such Exchangeable Note, in connection with such Fundamental Change, if the holder had exchanged its note for ordinary shares immediately prior to the consummation of such Fundamental Change, plus any accrued and unpaid interest. The Derivative liability, representing the change of control feature, was recorded at a fair value of $298 at September 30, 2022.

(In thousands, except share and per share data)

The fair value of each component of the Derivative liability was determined using the binomial option pricing model, and in the case of the change of control component, in combination with a DCF analysis, without consideration of transaction costs, which represents a Level 3 basis of fair value measurement. The key inputs to valuing the Derivative liability as of September 30, 2022 include the terms of the Exchangeable Notes Indenture, the Company's share price and market capitalization, the expected annual volatility of the Company's ordinary shares, management's assumption regarding the probability of a Fundamental Change pursuant to the terms of the Exchangeable Notes Indenture, and the risk-free interest rate. Fair value measurements are highly sensitive to changes in these inputs and significant changes in these inputs could result in a significantly higher or lower fair value.

The following table presents the changes in fair value of the Company's Derivative liability for the nine months ended September 30, 2022:

	September 30, 2022
Balance at December 31, 2021	$ 6,058
Conversion of Exchangeable Notes	—
Adjustment to fair value	(5,448)
Balance at period end	$ 610

The following summary table shows the assumptions used in the binomial option pricing model to estimate the fair value of the Derivative liabilities:

	September 30, 2022	December 31, 2021
Share price	$ 1.62	$ 5.88
Market capitalization	$ 19,818,066	$ 71,647,911
Volatility	100 %	130 %
Risk-free interest rate	4.30 %	1.00 %
Dividend rate	0 %	0 %

The additional significant assumption used in the DCF model to estimate the fair value of the change of control feature at September 30, 2022 was management's assumption regarding the probability of a Fundamental Change pursuant to the terms of the Exchangeable Notes Indenture.

The RLN liability is carried at fair value on the condensed consolidated balance sheet as of September 30, 2022 (see Note 11 – Royalty-Linked Notes). The total fair value of $20,917 was determined using DCF analysis, without consideration of transaction costs, which represents a Level 3 basis of fair value measurement. The key inputs to valuing the RLNs were the terms of the indenture governing the RLNs (the RLN Indenture), the expected cash flows to be received by holders of the RLNs based on management's revenue forecasts of U.S. sulopenem sales and a risk-adjusted discount rate to derive the net present value of expected cash flows. The RLNs will be subject to a maximum return amount, including all principal and payments and certain default interest in respect of uncurable defaults, of $160.00 (or 4,000 times the principal amount of such note). The discount rate applied to the model was 20%. Fair value measurements are highly sensitive to changes in these inputs and significant changes in these inputs could result in a significantly higher or lower fair value.

There have been no transfers of assets or liabilities between the fair value measurement levels.

4. Short-term Investments

The Company classifies its short-term investments as available for sale. Short-term investments comprise highly liquid investments with minimum "A-" rated securities and as at period-end consist of corporate entity commercial paper and U.S. Treasury and Agency Bonds with maturities of more than three months at the date of purchase. Short-term investments as of September 30, 2022 have a weighted average maturity of 0.41 years. The investments are reported at fair value with unrealized gains or losses recorded in the condensed consolidated statements of operations and comprehensive loss. Any differences between the cost and fair value of investments are represented by unrealized gains or losses. The fair value of short-term investments is represented by Level 1 fair value measurements – quoted prices in active markets for identical assets.

The following table represents the Company's available for sale short-term investments by major security type as of September 30, 2022 and December 31, 2021:

September 30, 2022					Maturity by period	
Available for sale	Cost Total	Unrealized gains	Unrealized (losses)	Fair Value Total	Less than 1 year	1 to 5 years
Commercial paper	$ 27,271	134	(138)	27,267	27,267	—
U.S. Treasury and Agency Bonds	16,988	9	(430)	16,567	16,567	—
Total	$ 44,259	$ 143	$ (568)	$ 43,834	$ 43,834	$ -

(In thousands, except share and per share data)

December 31, 2021					Maturity by period	
Available for sale	Cost Total	Unrealized gains	Unrealized (losses)	Fair Value Total	Less than 1 year	1 to 5 years
Commercial paper	$ 37,549	17	(570)	36,996	31,833	5,163
U.S. Treasury and Agency Bonds	16,984	6	(88)	16,902	—	16,902
Total	$ 54,533	23	(658)	53,898	31,833	22,065

5. Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consist of the following:

	September 30, 2022	December 31, 2021
Prepaid insurance	$ 866	$ 624
Prepaid research and development expenses	495	—
Other prepaid assets	111	56
Research and development tax credit receivable	249	840
Interest receivable	81	290
Short-term deposits	32	37
Value added tax receivable	52	75
Total	$ 1,886	$ 1,922

6. Intangible Asset, net

Intangible asset and related accumulated amortization are as follows:

	September 30, 2022	December 31, 2021
Gross intangible asset	$ 5,148	$ 5,148
Less: accumulated amortization	(3,000)	(1,713)
	$ 2,148	$ 3,435

On December 10, 2021, the Company entered into an amendment to an agreement with a supplier whereby advance payments made from June 2016 to January 2020 are being set against a reservation fee for a tableting facility for the period from January 1, 2021 to December 31, 2023. This reservation right is being amortized over the three year term of the amended agreement.

7. Property and Equipment, net

Property and equipment and related accumulated depreciation are as follows:

	September 30, 2022	December 31, 2021
Leasehold improvements	$ 148	$ 148
Furniture and fixtures	120	120
Laboratory equipment	—	86
Computer equipment	40	23
	308	377
Less: accumulated depreciation	(274)	(286)
	$ 34	$ 91

Depreciation expense was $74 for the nine months ended September 30, 2022 and $391 for the year ended December 31, 2021.

(In thousands, except share and per share data)

8. Leases

The Company has entered into a number of operating leases, primarily for office space and commercial property. These leases have remaining terms which range from 1.1 years to 5.75 years. The renewal option on one lease was exercised in February 2022 for an additional period of three years, extending this lease term to June 2025. The renewal option on another lease was derecognized in June 2022 as it is no longer reasonably certain that the option will be exercised, resulting in a reduction in the remaining term from 16 to six years. In September 2020, the Company entered into a sublease agreement for a commercial unit that extends through September 2023. In November 2021, the Company entered into a 12-month lease, with a rolling extension, for office space, and in May 2022, the Company entered into a 6-month lease for office space, which was extended to November 2023 and has elected not to apply the measurement and recognition requirements of ASC 842 to these short-term leases as any renewal term exercised or considered reasonably certain of exercise by the Company does not extend more than 12 months from the end of the previously determined lease term. Certain leases contain variable lease payments, including payments based on an index or rate. Variable lease payments based on an index or rate are initially measured using the index or rate in effect at lease commencement. Certain agreements contain both lease and non-lease components. The Company has elected to separately account for these components in determining the lease liabilities and right-of-use assets. The Company's lease agreements generally do not provide an implicit borrowing rate; therefore, an internal incremental borrowing rate was determined based on information available at lease commencement date for the purposes of determining the present value of lease payments. The Company used the incremental borrowing rate on January 1, 2019 for all leases that commenced prior to that date. All operating lease expenses are recognized on a straight-line basis over the lease term. The Company recognized $234 and $644 of operating lease costs for right-of-use assets during the three and nine months ended September 30, 2022 and $259 and $827 of operating lease costs for right-of-use assets during the three and nine months ended September 30, 2021. The Company recognized $55 and $176 of rental expenses on the short term lease during the three and nine months ended September 30, 2022. The Company recognized $75 and $223 of sublease income during the three and nine months ended September 30, 2022 and $77 and $241 of sublease income during the three and nine months ended September 30, 2021.

Information related to the Company's right-of-use assets and related lease liabilities is as follows:

	Three Months Ended September 30, 2022	Three Months Ended September 30, 2021	Nine Months Ended September 30, 2022	Nine Months Ended September 30, 2021
Cash paid for operating lease liabilities	$ 165	$ 156	$ 608	$ 689

	September 30, 2022	December 31, 2021
Weighted-average remaining lease term	5.24 years	13.97 years
Weighted-average discount rate	5.6 %	7.0 %

Right-of-use assets and lease liabilities for the Company's operating leases were recorded in the condensed consolidated balance sheet as follows, representing the Company's right to use the underlying asset for the lease term ("Other assets") and the Company's obligation to make lease payments ("Other current liabilities" and "Other liabilities"):

	September 30, 2022	December 31, 2021
Other assets	$ 1,856	$ 3,741
Other current liabilities	$ 305	$ 464
Other liabilities	1,282	3,436
Total lease liabilities	$ 1,587	$ 3,900

(In thousands, except share and per share data)

Future lease payments included in the measurement of lease liabilities on the condensed consolidated balance sheet as of September 30, 2022 for the following five fiscal years and thereafter were as follows:

Due in 12 month period ended September 30,		
2023	$	380
2024		385
2025		348
2026		269
2027		269
Thereafter		135
	$	1,786
Less imputed interest		(199)
Total lease liabilities	$	1,587

9. Accrued Expenses

Accrued expenses consist of the following:

	September 30, 2022	December 31, 2021
Accrued payroll and bonus expenses	$ 1,580	$ 771
Accrued clinical trial costs	971	45
Accrued professional fees	891	16
Accrued other expenses	245	256
Accrued manufacturing expenses	45	77
Total	$ 3,732	$ 1,165

10. Debt

Secured Credit Facility

On April 27, 2018, the Company's subsidiaries, Iterum Therapeutics International Limited, Iterum Therapeutics US Holding Limited and Iterum Therapeutics US Limited (the Borrowers), entered into a loan and security agreement (Loan and Security Agreement) with SVB pursuant to which SVB agreed to lend the Borrowers up to $30,000 in two term loans. $15,000 of the secured credit facility was funded on closing. A second draw of up to $15,000 was available to the Company through October 31, 2019, upon satisfaction of either of the following: (i) the achievement by the Company of both non-inferiority and superiority primary endpoints from its Phase 3 uncomplicated urinary tract infection (uUTI) trial, as well as reporting satisfactory safety data from the trial, or (ii) the achievement of non-inferiority primary endpoints from both its Phase 3 uUTI and complicated urinary tract infection (cUTI) trials, as well as reporting satisfactory safety data from the trials. The Company did not satisfy the conditions for the second draw above before the deadline of October 31, 2019.

Required monthly amortization payments for the initial $15,000 draw commenced on November 1, 2019 and total principal repayments of $1,552 were made during the nine months ended September 30, 2022. Interest accrued at a floating per annum rate equal to the greater of (i) 8.31%; or (ii) 3.89% above the Wall Street Journal prime rate, and was payable monthly in arrears. All outstanding principal, plus a 4.20% final interest payment, were due and paid on March 1, 2022 (the maturity date), effectively terminating the Loan and Security Agreement. The final payment fee of $630, which represented 4.2% of the funded loan, was accreted using the effective interest method over the life of the loan as interest expense.

In connection with the initial $15,000 draw, the Company issued SVB and Life Sciences Fund II LLC (LSF) warrants to purchase an aggregate of 19,890 Series B convertible preferred shares (which converted into warrants to purchase 1,326 ordinary shares upon the Company's initial public offering (IPO)) at an exercise price of $282.75 per share. These warrants will expire on April 27, 2028.

The loan proceeds were allocated based on the relative fair values of the debt instrument and the warrant instrument. The fair value of the warrants and the closing costs were recorded as debt discounts and were amortized using the effective interest rate method over the term of the loan. The effective annual interest rate of the outstanding debt was approximately 12.51% on March 1, 2022. The Company did not recognize any interest expense related to the Loan and Security Agreement during the three months ended September 30, 2022, and the Company recognized $16 of interest expense related to the Loan and Security Agreement during the nine months ended September 30, 2022 including $6 related to the accretion of the debt discounts and deferred financing costs during the nine months ended September 30, 2022. The Company recognized $116 and $490 of interest expense related to the Loan and Security Agreement during the three and nine months ended September 30, 2021, respectively, including $28 and $130 related to the accretion of the debt discounts and deferred financing costs during the three and nine months ended September 30, 2021, respectively. All outstanding amounts were repaid on March 1, 2022, effectively terminating the Loan and Security Agreement.

In connection with the Private Placement, Iterum Bermuda was joined as a party to the Loan and Security Agreement as a borrower and the Loan and Security Agreement was amended on January 16, 2020 to, among other things, modify the definition of subordinated debt to include the RLNs and Exchangeable Notes.

2025 Exchangeable Notes

On January 21, 2020, the Company completed a Private Placement pursuant to which its wholly owned subsidiary, Iterum Bermuda issued and sold $51,588 aggregate principal amount of Exchangeable Notes and $103 aggregate principal amount of RLNs, to a group of accredited investors. On September 8, 2020, the Company completed a Rights Offering pursuant to which Iterum Bermuda issued and sold $220 aggregate principal amount of Exchangeable Notes and $0.5 aggregate principal amount of RLNs, to existing shareholders. The Securities were sold in Units with each Unit consisting of an Exchangeable Note in the original principal amount of $1,000 and 50 RLNs. The Units were sold at a price of $1,000 per Unit.

At any time on or after January 21, 2021, subject to specified limitations, the Exchangeable Notes are exchangeable for the Company's ordinary shares, cash or a combination of ordinary shares and cash, at the Company's election, at an exchange rate of 85.7456 shares per $1,000 principal and interest on the Exchangeable Notes (equivalent to an exchange price of approximately $11,6624 per ordinary share) as of August 17, 2022, which exchange rate was adjusted from an initial exchange rate of 66.666 shares per $1,000 principal and interest on the Exchangeable Notes (equivalent to an initial exchange price of $15.00 per ordinary share) and is subject to further adjustment pursuant to the terms of the Exchangeable Notes Indenture. Any accrued and unpaid interest being exchanged will be calculated to include all interest accrued on the Exchangeable Notes being exchanged to, but excluding, the exchange settlement date. Beginning on January 21, 2021 to September 30, 2022, certain noteholders of $39,201 aggregate principal amount of Exchangeable Notes have completed a non-cash exchange of their notes for an aggregate of 3,592,555 of the Company's ordinary shares, which included accrued and unpaid interest relating to such notes. The aggregate principal amount of Exchangeable Notes outstanding as of September 30, 2022 was $12,607.

In addition, the Exchangeable Notes will become due and payable by the Company upon the occurrence of a Fundamental Change as defined in the Exchangeable Notes Indenture. The Company will be required to pay each holder of the Exchangeable Notes the greater of three times the outstanding principal amount of such Exchangeable Note and the consideration that would be received by the holder of such Exchangeable Note in connection with such Fundamental Change if the holder had exchanged its note for ordinary shares immediately prior to the consummation of such Fundamental Change, plus any accrued and unpaid interest.

The Company evaluates its debt and equity issuances to determine if those contracts, or embedded components of those contracts, qualify as derivatives under ASC 815-15, *Derivatives and Hedging*, requiring separate recognition in the Company's financial statements. The Company evaluated the accounting for the issuance of the Exchangeable Notes and concluded that the embedded exchange option and change of control feature are considered a Derivative liability under ASC 815-15 requiring bifurcation, from the Exchangeable Notes, as it does not qualify for the scope exceptions for contracts in an entity's own equity given the terms of the Exchangeable Notes. The exchange option and change of control feature are accounted for as a Derivative liability, under ASC 815-15, and are required to be separated and recorded as a single liability, which is revalued at each reporting period with the resulting change in fair value reflected in adjustments to fair value of derivatives in the condensed consolidated statements of operations and comprehensive loss.

The fair value of the Derivative liability related to the Private Placement on January 21, 2020 was $27,038, and the fair value of the Derivative liability related to the Rights Offering on September 8, 2020 was $82, both of which were recorded as a reduction to the book value of the host debt contract. This debt discount is being amortized to interest expense over the term of the debt using the effective interest method. Transaction costs amounting to $2,848 were allocated to the exchange option. These costs are reflected in financing transaction costs in the condensed consolidated statements of operations and comprehensive loss for the year ended December 31, 2020. Transaction costs amounting to $2,814 were allocated to the debt host and capitalized in the host debt book value.

In circumstances where the embedded exchange option in a convertible instrument is required to be bifurcated, and there are other embedded derivative instruments in the convertible instrument that are required to be bifurcated, the derivative instruments are accounted for as a single, compound derivative instrument. The classification of derivative instruments, including whether such instruments should be recorded as liabilities or as equity, is reassessed at the end of each reporting period. Derivative instrument liabilities are classified in the balance sheet as current or non-current based on whether or not settlement of the derivative instrument is expected within twelve months of the balance sheet date.

The Company determined that all other features of the Exchangeable Notes were clearly and closely associated with a debt host and did not require bifurcation as a Derivative liability. The initial value of the Exchangeable Notes on inception, net of transaction costs, was $9,891.

(In thousands, except share and per share data)

The Company recognized $205 and $615 of interest expense related to the Exchangeable Notes during the three and nine months ended September 30, 2022 and $205 and $873 of interest expense related to the Exchangeable Notes during the three and nine months ended September 30, 2021. The Company recognized $591 and $1,753 related to the amortization of the debt discounts and deferred financing costs during the three and nine months ended September 30, 2022 and $591 and $2,302 related to the amortization of the debt discounts and deferred financing costs during the three and nine months ended September 30, 2021. These amounts are recorded in interest expense, net in the condensed consolidated statements of operations and comprehensive loss for the three and nine months ended September 30, 2022 and September 30, 2021. The balance of the Exchangeable Notes as of September 30, 2022 is as follows:

	September 30, 2022	
	Principal	Accrued Interest
January 2020 $1,000 Exchangeable Notes exchangeable into ordinary shares at $11.6624 per share, 6.5% interest, due January 31, 2025 (2025 Exchangeable Notes)	$ 51,588	$ 4,855
September 2020 $1,000 Exchangeable Notes exchangeable into ordinary shares at $11.6624 per share, 6.5% interest, due January 31, 2025 (2025 Exchangeable Notes)	220	18
Conversion of $1,000 Exchangeable Notes exchangeable into ordinary shares at $11.6624 per share, 6.5% interest, due January 31, 2025 (2025 Exchangeable Notes)	(39,201)	(2,697)
2025 Exchangeable Notes, net	12,607	2,176
Unamortized discount and debt issuance costs	(5,485)	—
2025 Exchangeable Notes, net	$ 7,122	$ 2,176

Payment Protection Program

On April 3, 2020, the U.S. Small Business Administration (SBA) launched the Paycheck Protection Program, which was established following the signing of the CARES Act on March 27, 2020. On April 30, 2020, our wholly owned subsidiary, Iterum Therapeutics US Limited (Iterum US Limited), entered into the PPP loan with SVB under the Paycheck Protection Program, pursuant to the Company receiving a PPP loan of $744 with a fixed 1% annual interest rate and a maturity of two years. Under the terms of the agreement, there were no payments due by the Company until the SBA remitted the forgiveness amount to Iterum US Limited or until after the 10 months after the end of the six-month period beginning April 30, 2020 (the Deferral Period). Following the Deferral Period, equal monthly repayments of principal and interest were due to fully amortize the principal amount outstanding on the PPP loan by the maturity date. The SBA forgave $340 of the loan in November 2020 and monthly amortization payments on the remaining loan balance of $404 began in December 2020. No principal repayments were made during the three months ended September 30, 2022 and principal repayments of $69 were made during the nine months ended September 30, 2022 and total principal repayments of $77 and $231 were made during the three and nine months ended September 30, 2021, respectively. The Company recognized $0 of interest expense related to the loan agreement during the three and nine months ended September 30, 2022 and $1 and $2 of interest expense related to the loan agreement during the three and nine months ended September 30, 2021, respectively. All outstanding amounts were repaid on March 17, 2022, effectively terminating the PPP loan.

Scheduled principal payments on outstanding debt, including principal amounts owed to RLN holders (see Note 11 – Royalty-Linked Notes), as of September 30, 2022, for the following five fiscal years and thereafter were as follows:

Year Ending September 30, (unaudited)	
2023	$ —
2024	—
2025	12,607
2026	—
2027	—
Thereafter	104
Total	$ 12,711

(In thousands, except share and per share data)

11. Royalty-Linked Notes

Liability Related to Sale of Future Royalties

On January 21, 2020, as part of the Private Placement, the Company issued 2,579,400 RLNs to a group of accredited investors. On September 8, 2020, as part of the Rights Offering, the Company issued 11,000 RLNs to existing shareholders. The RLNs will entitle the holders thereof to payments, at the applicable payment rate, based solely on a percentage of the Company's net revenues from U.S. sales of specified sulopenem products earned through December 31, 2045, but will not entitle the holders thereof to any payments unless the Company receives FDA approval for one or more specified sulopenem products prior to December 31, 2025 and the Company earns net revenues on such product. If any portion of the principal amount of the outstanding RLNs, equal to $0.04 per RLN, has not been paid as of the end date on December 31, 2045 (or December 31, 2025, in the event that the Company has not yet received FDA approval with respect to one or more specified sulopenem products by such date), Iterum Bermuda must pay the unpaid portion of the principal amount. The RLNs will earn default interest if the Company breaches certain obligations under the RLN Indenture (but do not otherwise bear interest) and will be subject to a maximum return amount, including all principal and payments and certain default interest in respect of uncurable defaults, of $160.00 (or 4,000 times the principal amount of such note). The RLNs will be redeemable at the Company's option, subject to the terms of the RLN Indenture.

In accordance with exceptions allowed under ASC 815-10, *Derivatives and Hedging*, this transaction was initially accounted for as a debt liability under ASC 470, *Debt*. Subsequent to the listing of the RLNs on the Bermuda Stock Exchange in January 2021, the RLNs are accounted for as a derivative and are remeasured to fair value at each reporting date. The Company has no obligation to pay any amount to the noteholders until the net revenue of the specified products are earned. In order to record the amortization of the liability, the Company was required to estimate the total amount of future net revenue to be earned in each period under the RLN Indenture and the payments that will be passed through to the noteholders over the life of the RLN Indenture.

The note proceeds from both the Private Placement and subsequent Rights Offering were allocated based on the relative fair value of the debt instrument, less transaction costs amounting to $1,239, as debt discounts. The Company imputed interest on the amortized cost of the liability using an estimated effective interest rate of 31.7% up to the date of the change in measurement. Payments to the noteholders in each period, related to future sales of sulopenem, would offset the liability. Subsequent to recognition of the RLN in accordance with ASC 815, *Derivatives and Hedging*, in January 2021, the fair value of the RLN is determined using DCF analysis, without consideration of transaction costs, which represents a Level 3 basis of fair value measurement. The Company periodically assesses the revenue forecasts of the specified sulopenem products and the related payments.

Subsequent to the listing of the RLNs on the Bermuda Stock Exchange in January 2021, the Company recognized the remaining unaccreted interest balance of $1,204 related to debt discounts and deferred financing costs under ASC 470, *Debt,* in the condensed consolidated statements of operations and comprehensive loss for the nine months ended September 30, 2021. The balance of the RLNs as of September 30, 2022 is as follows:

	September 30, 2022
Total liability related to the sale of future royalties, on inception	$ 10,990
Liability related to the sale of future royalties, arising from the Rights Offering	51
Amortization of discount and debt issuance costs	3,666
Adjustments to fair value	6,210
Total liability related to the sale of future royalties at September 30, 2022	20,917
Current Portion	—
Long-term Portion	$ 20,917

(In thousands, except share and per share data)

12. Shareholders' Equity

The following tables present a reconciliation of the Company's beginning and ending balances in shareholders' equity for the nine months ended September 30, 2022 and 2021:

	Total Shareholders' Equity
Shareholders' equity at January 1, 2022	$ 50,234
Share-based compensation expense	4,301
Cancellation of share options expense	17,350
Issuance of ordinary shares, net	8
Net loss	(39,344)
Shareholders' equity at September 30, 2022	$ 32,549

	Total Shareholders' (Deficit) / Equity
Shareholders' deficit at January 1, 2021	$ (50,559)
Share-based compensation expense	2,352
Issuance of ordinary shares, net	68,161
Issuance of warrants for ordinary shares	6,199
Exercise of warrants for ordinary shares	15,289
Issuance of ordinary shares on conversion of Exchangeable Notes	98,388
Net loss	(87,382)
Shareholders' equity at September 30, 2021	$ 52,448

The Company's capital structure consists of ordinary shares and undesignated preferred shares. Under Irish law, the Company is prohibited from allotting shares without consideration. Accordingly, at least the nominal value of the shares issued underlying any warrant, restricted share award, restricted share unit, performance share award, bonus share or any other share based grant must be paid pursuant to the Irish Companies Act 2014 (Irish Companies Act).

Ordinary Shares

On February 3, 2021, the Company entered into an underwriting agreement (the Underwriting Agreement) pursuant to which it issued and sold 2,318,840 ordinary shares, $0.01 nominal value per share, at a public offering price per share of $17.25 (the February 2021 Underwritten Offering). The February 2021 Underwritten Offering closed on February 8, 2021. Pursuant to the Underwriting Agreement, the Company granted the underwriter an option for a period of 30 days to purchase up to an additional 347,826 ordinary shares on the same terms and conditions, which the underwriter exercised in full on February 10, 2021. This exercise increased the total number of ordinary shares sold by the Company in the offering to 2,666,666 shares, which resulted in aggregate gross proceeds of $46,000 and net proceeds of $42,119 after deducting underwriting discounts and commissions and other offering expenses.

On February 9, 2021, the Company completed a registered direct offering (the February 2021 Registered Direct Offering), pursuant to which the Company issued and sold an aggregate of 1,166,666 ordinary shares, $0.01 nominal value per share, at a purchase price per share of $30.00, for aggregate gross proceeds of $35,000 and net proceeds of $32,235 after deducting placement agent fees and other offering expenses. The closing date of the February 2021 Registered Direct Offering was February 12, 2021. The Company offered the ordinary shares in the June 3, 2020 Offering, June 30, 2020 Offering, February 2021 Underwritten Offering and February 2021 Registered Direct Offering pursuant to its universal shelf registration statement on Form S-3, which was declared effective on July 16, 2019 (File No. 333-232569).

Beginning on January 21, 2021 to September 30, 2022, certain noteholders of $39,201 aggregate principal amount of Exchangeable Notes have exchanged their notes for an aggregate of 3,592,555 of the Company's ordinary shares, which included accrued and unpaid interest relating to such notes. The aggregate principal amount of Exchangeable Notes outstanding as of September 30, 2022 was $12,607.

At the Company's extraordinary general meeting of shareholders on January 28, 2021, the Company's shareholders approved an increase of 10,000,000 ordinary shares of $0.01 par value each to the number of authorized ordinary shares and the Company's Articles of Association were amended accordingly. The Company has authorized ordinary shares of 20,000,000 ordinary shares of $0.01 par value each as of September 30, 2022. The holders of ordinary shares are entitled to one vote for each share held. The holders of ordinary shares currently have no preemptive or other subscription rights, and there are no redemption or sinking fund provisions with respect to such shares.

(In thousands, except share and per share data)

Warrants to purchase Ordinary Shares

In connection with the initial drawdown under the Loan and Security Agreement, the Company issued SVB and LSF warrants to purchase an aggregate of 19,890 Series B convertible preferred shares (which converted into warrants to purchase 1,326 ordinary shares upon the Company's IPO) at an exercise price of $282.75 per share. These warrants will expire on April 27, 2028. No warrants had been exercised as of September 30, 2022.

In connection with the June 3, 2020 Offering completed on June 5, 2020, pursuant to the June 3, 2020 SPA, in a concurrent private placement, the Company issued and sold to institutional investors warrants to purchase up to 99,057 ordinary shares. Upon closing, the warrants became exercisable immediately at an exercise price of $24.30 per ordinary share, subject to adjustment in certain circumstances, and will expire on December 5, 2025. Warrants to purchase 13,868 ordinary shares, amounting to 7% of the ordinary shares issued under the June 3, 2020 SPA, were issued to designees of the placement agent on the closing of the June 3, 2020 Offering. Upon closing, the warrants issued to such designees were exercisable immediately at an exercise price of $31.5465 per ordinary share and will expire on June 3, 2025. No warrants had been exercised as of September 30, 2022.

In connection with the June 30, 2020 Offering completed on July 2, 2020, pursuant to the June 30, 2020 SPA, in a concurrent private placement, the Company has also issued and sold to institutional investors warrants to purchase up to 112,422 ordinary shares. Upon closing, the warrants became exercisable immediately at an exercise price of $21.30 per ordinary share, subject to adjustment in certain circumstances, and will expire on January 2, 2026. Warrants to purchase 15,739 ordinary shares, amounting to 7% of the ordinary shares issued under the June 30, 2020 SPA, were issued to designees of the placement agent on closing of the June 30, 2020 Offering. Upon closing, the warrants issued to such designees were exercisable immediately at an exercise price of $27.7965 per ordinary share and will expire on June 30, 2025. As of September 30, 2022, warrants issued in connection with the June 30, 2020 Offering had been exercised for 84,317 ordinary shares, for net proceeds of $1,796.

In connection with the October 2020 Offering, the Company issued and sold warrants to purchase up to 1,346,153 ordinary shares. Upon closing, the warrants became exercisable immediately at an exercise price of $9.75 per ordinary share, subject to adjustment in certain circumstances, and will expire on October 27, 2025. Warrants to purchase 125,641 ordinary shares, which represents a number of ordinary shares equal to 7.0% of the aggregate number of ordinary shares and pre-funded warrants sold in the October 2020 Offering, were issued to designees of the placement agent on closing of the October 2020 Offering. Upon closing, the warrants issued to such designees became exercisable immediately at an exercise price of $12.1875 per ordinary share and expire on October 22, 2025. As of September 30, 2022, warrants issued in connection with the October 2020 Offering had been exercised for 1,392,701 ordinary shares, for net proceeds of $13,885.

In connection with the February 2021 Underwritten Offering, the Company issued to the underwriter's designees warrants to purchase 162,318 ordinary shares, amounting to 7.0% of the aggregate number of ordinary shares sold in the February 2021 Underwritten Offering which closed on February 8, 2021. The warrants issued to such designees have an exercise price of $21.5625 per ordinary share, were exercisable upon issuance and will expire on February 3, 2026. As of September 30, 2022, warrants issued in connection with the February 2021 Underwritten Offering had been exercised for 25,333 ordinary shares, for net proceeds of $546.

The Company has classified the warrants as equity in accordance with ASC 815. The fair value of the warrants was valued at issuance using the Black-Scholes option pricing model with the following assumptions:

	February 8, 2021
Volatility	120 %
Expected term in years	4.99
Dividend rate	0 %
Risk-free interest rate	0.48 %
Share price	$ 23.10
Fair value of warrants issued	$ 19.05

In connection with the February 2021 Underwritten Offering, the Company granted the underwriter an option for a period of 30 days to purchase an additional 347,826 ordinary shares. Upon the underwriter's exercise of its option, on February 10, 2021, the Company issued warrants to purchase an additional 24,347 ordinary shares to the underwriter's designees, amounting to 7.0% of the aggregate number of additional ordinary shares sold pursuant to the underwriter's option. The warrants issued to such designees have an exercise price of $21.5625 per ordinary share, were exercisable upon issuance and will expire on February 3, 2026. No warrants had been exercised as of September 30, 2022.

(In thousands, except share and per share data)

The Company has classified the warrants as equity in accordance with ASC 815. The fair value of the warrants was valued at issuance using the Black-Scholes option pricing model with the following assumptions:

	February 10, 2021
Volatility	120 %
Expected term in years	4.98
Dividend rate	0 %
Risk-free interest rate	0.46 %
Share price	$ 40.95
Fair value of warrants issued	$ 34.80

In connection with the February 2021 Registered Direct Offering which closed on February 12, 2021, warrants to purchase 81,666 ordinary shares, amounting to 7.0% of the aggregate number of ordinary shares issued under the securities purchase agreement, were issued to designees of the placement agent upon closing. The warrants issued to such designees were exercisable upon issuance at an exercise price of $37.50 per ordinary share and will expire on February 9, 2026. No warrants had been exercised as of September 30, 2022.

The Company has classified the warrants as equity in accordance with ASC 815. The fair value of the warrants was valued at issuance using the Black-Scholes option pricing model with the following assumptions:

	February 12, 2021
Volatility	120 %
Expected term in years	4.99
Dividend rate	0 %
Risk-free interest rate	0.50 %
Share price	$ 33.90
Fair value of warrants issued	$ 27.60

Undesignated Preferred Shares

The Company has authorized 100,000,000 undesignated preferred shares of $0.01 par value each as of September 30, 2022. The Company's Board of Directors is authorized by the Company's Articles of Association to determine the rights attaching to the undesignated preferred shares including rights of redemption, rights as to dividends, rights on winding up and conversion rights. There were no designated preferred shares in issue as of September 30, 2022 or December 31, 2021.

13. Share-Based Compensation

On November 18, 2015, the Company's Board of Directors adopted and approved the 2015 Equity Incentive Plan (the 2015 Plan), which authorized the Company to grant up to 14,895 ordinary shares in the form of incentive share options, nonstatutory share options, share appreciation rights, restricted share awards, restricted share units and other share awards. The types of share-based awards, including the rights, amount, terms, and exercisability provisions of grants are determined by the Company's Board of Directors. The purpose of the 2015 Plan was to provide the Company with the flexibility to issue share-based awards as part of an overall compensation package to attract and retain qualified personnel. On May 18, 2017, the Company amended the 2015 Plan to increase the number of ordinary shares available for issuance under the 2015 Plan by 14,640 shares to 29,535 shares.

On March 14, 2018, the Company's Board of Directors adopted and approved the 2018 Equity Incentive Plan (the 2018 Plan), which became effective upon the execution and delivery of the underwriting agreement related to the Company's IPO in May 2018. Since adopting the 2018 Plan, no further grants will be made under the 2015 Plan. The ordinary shares underlying any options that are forfeited, cancelled, repurchased or are otherwise terminated by the Company under the 2015 Plan will not be added back to the ordinary shares available for issuance.

The 2018 Plan originally authorized the Company to grant up to 67,897 ordinary shares in the form of incentive share options, nonstatutory share options, share appreciation rights, restricted share awards, restricted share units, performance share awards, performance cash awards and other share awards. The types of share-based awards, including the amount, terms, and exercisability provisions of grants are determined by the Company's Board of Directors. The ordinary shares underlying any options that are forfeited, cancelled, repurchased or are otherwise terminated by the Company under the 2018 Plan are added back to the ordinary shares available for issuance under the 2018 Plan.

On December 5, 2018, pursuant to powers delegated to it by the Board of Directors of the Company, the Compensation Committee approved an increase in the number of ordinary shares available to be granted pursuant to the 2018 Plan by 4% of the total number of shares of the Company's issued share capital on December 31, 2018, being 38,272 ordinary shares.

(In thousands, except share and per share data)

On February 14, 2020, pursuant to powers delegated to it by the Board of Directors of the Company, the Compensation Committee approved, by written resolution, an increase of 39,650 ordinary shares to the number of ordinary shares available to be granted pursuant to the 2018 Plan, being just under 4% of the total number of the Company's ordinary shares outstanding on December 31, 2019, in accordance with the terms of the 2018 Plan.

On June 10, 2020, at the Company's annual general meeting of shareholders, the shareholders approved and adopted an amended and restated 2018 Plan which, among other things included an increase of 150,000 ordinary shares to the number of ordinary shares reserved for issuance under the 2018 Plan.

On June 23, 2021, at the Company's annual general meeting of shareholders, the shareholders approved an amendment to the amended and restated 2018 Plan to increase the number of ordinary shares reserved for issuance under the amended and restated 2018 Plan by 1,000,000 ordinary shares to 1,295,819 ordinary shares.

On November 24, 2021, the Company's Board of Directors adopted and approved the 2021 Inducement Equity Incentive Plan (the 2021 Inducement Plan) reserving 333,333 of its ordinary shares to be used exclusively for grants of awards to individuals that were not previously employees or directors of the Company (or following such individuals' bona fide period of non-employment with the company), as a material inducement to such individuals' entry into employment with the company within the meaning of Rule 5635(c)(4) of the Nasdaq Listing Rules. The terms and conditions of the 2021 Inducement Plan are substantially similar to the 2018 Plan.

Share Options

Unless specified otherwise in an individual option agreement, share options granted under the 2015 Plan, the 2018 Plan and the 2021 Inducement Plan generally have a ten year term and a four year vesting period. The vesting requirement is conditioned upon a grantee's continued service with the Company during the vesting period. Once vested, all awards are exercisable from the date of grant until they expire. The option grants are non-transferable. Vested options generally remain exercisable for 90 days subsequent to the termination of the option holder's service with the Company. In the event of an option holder's disability or death while employed by or providing service to the Company, the exercisable period extends to twelve months or eighteen months, respectively.

The fair value of options granted are estimated using the Black-Scholes option-pricing model. The inputs for the Black-Scholes model require management's significant assumptions. The risk-free interest rate was based on a normalized estimate of the 7-year U.S. treasury yield. The Company has estimated the expected term utilizing the "simplified" method for awards that qualify as "plain vanilla". The Company does not have sufficient company-specific historical and implied volatility information and it therefore estimates its expected share volatility based on historical volatility information of reasonably comparable guideline public companies and itself. The Company expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded share price. Expected dividend yield is based on the fact that the Company has never paid cash dividends and the Company's future ability to pay cash dividends on its shares may be limited by the terms of any future debt or preferred securities. The Company has elected to account for forfeitures as they occur.

The Company granted 161,628 and 908,094 share options to employees and directors during the nine months ended September 30, 2022 and 2021, respectively, under the 2018 Plan and 6,332 share options to employees during the nine months ended September 30, 2022 under the 2021 Inducement Plan. No share options were granted to employees or directors under the 2021 Inducement Plan during the nine months ended September 30, 2021. There were 301,623 and 915,504 unvested employee and director share options outstanding as of September 30, 2022 and September 30, 2021, respectively. Total expense recognized related to employee share options was $135 and $3,498 for the three and nine months ended September 30, 2022 and $1,663 and $2,104 for the three and nine months ended September 30, 2021. Total unamortized compensation expense related to employee share options was $1,094 and $22,385 as of September 30, 2022 and September 30, 2021, respectively, which is expected to be recognized over a remaining weighted average vesting period of 1.88 years and 3.68 years as of September 30, 2022 and September 30, 2021, respectively.

The range of assumptions that the Company used to determine the grant date fair value of employee and director options granted were as follows:

	Nine months ended	
	September 30, 2022	**September 30, 2021**
Volatility	100% - 130%	120%-130%
Expected term in years	5.50 - 6.25	5.50 - 6.25
Dividend rate	0%	0%
Risk-free interest rate	1.9% - 3.96%	0.9% - 1.32%
Share price	$1.59 - $6.72	$8.40 - $30.15
Fair value of option on grant date	$1.25 - $5.95	$7.50 - $26.25

The following table summarizes total share option activity for all Company plans:

	Equity Plans	Inducement Plan	Total
Options outstanding December 31, 2021	948,639	120,000	1,068,639
Granted	161,628	6,332	167,960
Exercised	—	—	—
Cancelled	(906,800)	—	(906,800)
Forfeited	—	—	—
Expired	—	—	—
Options outstanding September 30, 2022	203,467	126,332	329,799

The following table summarizes the number of options outstanding and the weighted-average exercise price as of September 30, 2022:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Life in Years	Aggregate Intrinsic Value (in thousands)
Options outstanding December 31, 2021	1,068,639	$ 30.12	9.42	$ —
Granted	167,960	$ 3.24		
Exercised	—			
Forfeited	—			
Cancelled	(906,800)	$ 33.16		
Options outstanding September 30, 2022	329,799	$ 8.07	9.29	$ —
Exercisable at September 30, 2022	28,176	$ 38.58	7.41	$ —

On July 7, 2022, certain of the Company's executive officers and employees agreed to the surrender and cancellation of certain previously granted share options for an aggregate of 906,800 ordinary shares in order to make additional shares available under the 2018 Plan. Total expense recognized in connection with the cancellation of these employee share options was $17,350 for both the three and nine months ended September 30, 2022, and was recorded in other income and expense as Cancellation of Share Options.

Restricted Share Units (RSUs)

The Company granted 57,432 and 89,688 RSUs to employees and directors during the nine months ended September 30, 2022 and 2021, respectively, under the 2018 Plan.

The following table summarizes the number of RSUs granted covering an equal number of the Company’s ordinary shares for all of our plans:

	Equity Plans	Inducement Plan	Total
RSUs outstanding December 31, 2021	85,684	33,333	119,017
Granted	57,432	—	57,432
Shares vested	(48,353)	—	(48,353)
Forfeited	—	—	—
RSUs outstanding September 30, 2022	94,763	33,333	128,096

The table below shows the number of RSUs outstanding covering an equal number of the Company’s ordinary shares and the weighted-average grant date fair value of the RSUs outstanding as of September 30, 2022:

	Number of Shares	Weighted Average Grant Date Fair Value per Share
RSUs outstanding December 31, 2021	119,017	$ 19.16
Granted	57,432	$ 3.17
Shares vested	(48,353)	$ 23.64
Forfeited	—	
RSUs outstanding September 30, 2022	128,096	$ 10.31

(In thousands, except share and per share data)

The fair value of the RSUs is determined on the date of grant based on the market price of the Company's ordinary shares on that date. The fair value of RSUs is expensed ratably over the vesting period, which is generally one year for directors and two years for our employees under our 2018 Plan and four years for our employees under our 2021 Inducement Plan. Total expense recognized related to the RSUs was $287 and $803 for the three and nine months ended September 30, 2022 and $304 and $668 for the three and nine months ended September 30, 2021. Total unamortized compensation expense related to the RSUs was $712 and $1,467 as of September 30, 2022 and September 30, 2021, respectively, which is expected to be recognized over a remaining average vesting period of 1.27 and 1.35 years as of September 30, 2022 and September 30, 2021, respectively.

No RSUs that are subject to certain performance-based vesting conditions (Performance RSUs) were awarded to employees or directors during the three and nine months ended September 30, 2022 and 2021, respectively.

The fair value of Performance RSUs is expensed evenly over the vesting period. Due to the expiration of the Performance RSUs during the three months ended September 30, 2021, a credit of $455 and $420 was recognized for the three and nine months ended September 30, 2021. All Performance RSUs were fully expensed as of September 30, 2021.

The Company's share-based compensation expense was classified in the condensed consolidated statements of operations and comprehensive loss as follows:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
	(unaudited)		(unaudited)	
Research and development expense	$ 118	$ 570	$ 1,258	$ 748
General and administrative expense	304	942	3,043	1,604

There was a total of $1,806 and $23,852 unamortized share-based compensation expense for options and RSUs as of September 30, 2022 and September 30, 2021, respectively, which is expected to be recognized over a remaining average vesting period of 1.71 years and 3.58 years as of September 30, 2022 and September 30, 2021, respectively.

14. Income Taxes

In accordance with ASC 270, *Interim Reporting,* and ASC 740, *Income Taxes,* at the end of each interim period, the Company is required to determine the best estimate of its annual effective tax rate and then apply that rate in providing for income taxes on a current year-to-date (interim period) basis. For the nine months ended September 30, 2022 and 2021, the Company recorded an income tax expense of $200 and $534, respectively.

Deferred tax assets and deferred tax liabilities are recognized based on temporary differences between the financial reporting and tax bases of assets and liabilities using statutory rates. Management of the Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets, including the Company's history of losses and determined that it is more-likely-than-not that these net deferred tax assets will not be realized. As of September 30, 2022 and December 31, 2021, the Company has net operating loss carryforwards in Ireland which result in tax benefits of approximately $35,054 and $33,218, respectively, for which a full valuation allowance has been recognized. The net operating loss carryforwards do not expire, but are carried forward indefinitely. Realization of these deferred tax assets is dependent on the generation of sufficient taxable income. If the Company demonstrates consistent profitability in the future, the evaluation of the recoverability of these deferred tax assets may change and the remaining valuation allowance may be released in part or in whole. While management expects to realize the deferred tax assets, net of valuation allowances, changes in estimates of future taxable income or in tax laws may alter this expectation.

15. Commitments and Contingencies

License Agreement

On November 18, 2015, the Company entered into a license agreement with Pfizer for the worldwide exclusive rights to research, develop, manufacture and commercialize sulopenem (the Pfizer License).

As part of the Pfizer License, the Company is obligated to pay Pfizer potential future regulatory milestone payments as well as sales milestones upon achievement of net sales ranging from $250.0 million to $1.0 billion for each product type. The Company is also obligated to pay Pfizer royalties ranging from a single-digit to mid-teens percentage based on marginal net sales of each licensed product.

Royalty-Linked Notes

On January 21, 2020, as part of the Private Placement, the Company issued 2,579,400 RLNs to a group of accredited investors. On September 8, 2020, as part of the Rights Offering, the Company issued 11,000 RLNs to existing shareholders. The RLNs will entitle the holders thereof to payments, at the applicable payment rate, based solely on a percentage of the Company's net revenues from U.S. sales of specified sulopenem products earned through December 31, 2045, but will not entitle the holders thereof to any payments unless the Company receives FDA approval for one or more specified sulopenem products prior to December 31, 2025 and the Company earns net revenues on such product. If any portion of the principal amount of the outstanding RLNs, equal to $0.04 per RLN, has not been paid as of the end date on December 31, 2045 (or December 31, 2025, in the event that the Company has not yet received FDA approval with respect to one or more specified sulopenem products by such date), Iterum Bermuda must pay the unpaid portion of the principal amount. The RLNs will earn default interest if the Company breaches certain obligations under the RLN Indenture (but do not otherwise bear interest) and will be subject to a maximum return amount, including all principal and payments and certain default interest in respect of uncurable defaults, of $160.00 (or 4,000 times the principal amount of such note). The RLNs will be redeemable at the Company's option, subject to the terms of the RLN Indenture.

Legal Proceedings

On August 5, 2021, a putative class action lawsuit was filed against the Company, its Chief Executive Officer and Chief Financial Officer in the United States District Court for the Northern District of Illinois. The complaint purports to be brought on behalf of shareholders who purchased the Company's securities between November 30, 2020 and July 26, 2021. The complaint generally alleges that the defendants violated Sections 10(b) and/or 20(a) of the Securities Exchange Act of 1934 and Rule 10b-5 promulgated thereunder by making purportedly material misstatements or omissions concerning the Company's submission of its New Drug Application (NDA) to the FDA for marketing approval of oral sulopenem for the treatment of uUTIs in patients with a quinolone non-susceptible pathogen and the likelihood of such approval. The complaint seeks, among other things, unspecified damages, attorneys' fees, expert fees and other costs. The court appointed a lead plaintiff and approved plaintiff's selection of lead counsel on November 3, 2021.

On January 26, 2022, plaintiff filed an amended complaint which includes allegations similar to those made in the original complaint and seeks similar relief.

On April 8, 2022, the Company filed a motion to dismiss with the court seeking dismissal of all claims asserted. Oral argument on the motion to dismiss occurred on August 17, 2022. The next status conference is scheduled for December 7, 2022. The Company denies any and all allegations of wrongdoing and believes the defendants have valid defenses against these claims and, therefore, intends to vigorously defend against this lawsuit.

Other Contingencies

Liabilities for loss contingencies arising from claims, assessments, litigation, fines, penalties and other sources are recorded when it is probable that a liability has been incurred and the amount can be reasonably estimated. At each reporting date the Company evaluates whether or not a potential loss amount or a potential loss range is probable and reasonably estimable under the provisions of the authoritative guidelines that address accounting for contingencies. The Company expenses costs as incurred in relation to such legal proceedings. The Company has no contingent liabilities in respect of legal claims arising in the ordinary course of business.

Under the terms of their respective employment agreements, each of the named executive officers is eligible to receive severance payments and benefits upon a termination without "cause" or due to "permanent disability", or upon "resignation for good reason", contingent upon the named executive officer's continued performance for the Company.

16. Condensed Consolidating Financial Statements

On January 21, 2020, the Company completed a Private Placement pursuant to which its wholly owned subsidiary, Iterum Bermuda, issued and sold $51,588 aggregate principal amount of Exchangeable Notes and $103 aggregate principal amount of RLNs to a group of accredited investors. On September 8, 2020, the Company completed a Rights Offering pursuant to which Iterum Bermuda issued and sold $220 aggregate principal amount of Exchangeable Notes and $0.5 aggregate principal amount of RLNs to existing shareholders. The Securities were sold in Units with each Unit consisting of an Exchangeable Note in the original principal amount of $1,000 and 50 RLNs. As of September 30, 2022, $12,607 aggregate principal amount of Exchangeable Notes and all RLNs remained outstanding.

The Units were issued by Iterum Bermuda, which was formed on November 6, 2019 and is a 100% owned "finance subsidiary" of the Company under Rule 3-10 of Regulation S-X with no independent function and no assets or operations other than those related to the issuance, administration and repayment of the Exchangeable Notes and RLNs. Iterum Therapeutics plc, as the parent company, has no independent assets or operations, and its operations are conducted solely through its subsidiaries. The assets, liabilities and results of operations of the Company, Iterum Bermuda and Iterum Therapeutics International Limited, Iterum Therapeutics US Holding Limited and Iterum Therapeutics US Limited (the Subsidiary Guarantors) are not materially different than the corresponding amounts presented in the condensed consolidated financial statements of this Quarterly Report on Form 10-Q. The Company and the Subsidiary Guarantors have provided a full and unconditional guarantee of Iterum Bermuda's obligations under the Exchangeable Notes and the RLNs, and each of the guarantees constitutes the joint and several obligations of the applicable guarantor. The Subsidiary Guarantors are 100% directly or indirectly owned subsidiaries of the Company. There are no significant restrictions upon the Company's or the Subsidiary Guarantors' ability to obtain funds from their subsidiaries by dividend or loan. None of the assets of Iterum Bermuda or the Subsidiary Guarantors represent restricted net assets pursuant to Rule 4-08(e)(3) of Regulation S-X.

17. Subsequent Events

On October 7, 2022, the Company entered into a sales agreement with H.C. Wainwright & Co., LLC (HC Wainwright), as agent, pursuant to which the Company may offer and sell ordinary shares, nominal value $0.01 per share, for aggregate gross sales proceeds of up to $16.0 million (not to exceed 4,478,180 ordinary shares as of the date of filing of this Form 10-Q), from time to time through HC Wainwright by any method permitted that is deemed to be an "at the market offering" as defined in Rule 415 (a)(4) promulgated under the Securities Act of 1933, as amended.

Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations.

You should read the following discussion and analysis of our financial condition and results of operations together with our condensed consolidated financial statements and the related notes and the other financial information included elsewhere in this Quarterly Report on Form 10-Q. Some of the information contained in this discussion and analysis or set forth elsewhere in this Quarterly Report on Form 10-Q, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this Quarterly Report on Form 10-Q, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis. Unless otherwise stated herein, all ordinary shares, exchange rates for the Exchangeable Notes, equity awards, warrants and per share amounts have been adjusted to reflect the 1-for-15 reverse share split which became effective on August 17, 2022, for all prior periods presented.

Overview

We are a clinical stage pharmaceutical company dedicated to developing and commercializing sulopenem to be potentially the first oral branded penem available in the United States and the first and only oral and intravenous (IV) branded penem available globally. Penems, including thiopenems and carbapenems, belong to a class of antibiotics more broadly defined as ß-lactam antibiotics, the original example of which was penicillin, but which now also includes cephalosporins. Sulopenem is a potent, thiopenem antibiotic delivered intravenously which is active against bacteria that belong to the group of organisms known as gram-negatives and cause urinary tract and intra-abdominal infections. We have also developed sulopenem in an oral tablet formulation, sulopenem etzadroxil-probenecid, which we refer to herein as oral sulopenem. We believe that sulopenem and oral sulopenem have the potential to be important new treatment alternatives to address growing concerns related to antibacterial resistance without the known toxicities of some of the most widely used antibiotics, specifically fluoroquinolones.

During the third quarter of 2018, we initiated three clinical trials in our Phase 3 development program which included: a Phase 3 uncomplicated urinary tract infection (uUTI) clinical trial, known as Sulopenem for Resistant Enterobacteriaceae (SURE) 1, comparing oral sulopenem to oral ciprofloxacin in women with uUTI, a Phase 3 complicated urinary tract infection (cUTI) clinical trial known as SURE 2, comparing IV sulopenem followed by oral sulopenem to IV ertapenem followed by oral ciprofloxacin in adults with cUTI and a Phase 3 complicated intra-abdominal infection (cIAI) clinical trial known as SURE 3, comparing IV sulopenem followed by oral sulopenem to IV ertapenem followed by a combination of oral ciprofloxacin and oral metronidazole in adults with cIAI. We designed one Phase 3 clinical trial in each indication based on our end of Phase 2 meeting with the U.S. Food and Drug Administration (FDA) and feedback from the European Medicines Agency (EMA). We conducted the Phase 3 clinical trials under Special Protocol Assessment (SPA) agreements from the FDA. In December 2019, we announced that sulopenem did not meet the primary endpoint of statistical non-inferiority compared to the control therapy for the cIAI trial. In the second quarter of 2020, we announced the results of our Phase 3 clinical trials in cUTI and uUTI. In the cUTI trial, sulopenem did not meet the primary endpoint of statistical non-inferiority compared to the control therapies with the difference in response rates driven almost entirely by higher rates of asymptomatic bacteriuria on the sulopenem IV to oral sulopenem arm relative to the ertapenem IV to oral ciprofloxacin arm, only evident at the test of cure visit. The rates of patients receiving additional antibiotics or with residual cUTI symptoms were similar between therapies. Similarly, in the uUTI trial, sulopenem did not meet the primary endpoint of statistical non-inferiority compared to ciprofloxacin in the population of patients with baseline pathogens susceptible to ciprofloxacin driven to a large degree by a greater amount of asymptomatic bacteriuria in the sulopenem treated patients at the test of cure visit relative to those receiving ciprofloxacin. However, in the uUTI trial, in the population of patients with baseline pathogens resistant to quinolones, sulopenem achieved the related primary endpoint by demonstrating statistical significance in the overall response rate by treatment arm in the ciprofloxacin-resistant population, providing evidence of a treatment effect in patients with uUTI. Based on discussions with the FDA at a pre-New Drug Application (NDA) meeting in September 2020 and previous correspondence with the FDA, we submitted an NDA for oral sulopenem for the treatment of uUTIs in patients with a quinolone non-susceptible pathogen in the fourth quarter of 2020 and the FDA accepted the application for review in January 2021. We received a Complete Response Letter (CRL) from the FDA on July 23, 2021 in respect of our NDA. The CRL provided that the FDA had completed its review of the NDA and had determined that it could not approve the NDA in its present form. The CRL further provided that additional data are necessary to support approval of oral sulopenem for the treatment of adult women with uUTIs caused by designated susceptible microorganisms proven or strongly suspected to be non-susceptible to a quinolone and recommended that we conduct at least one additional adequate and well-controlled clinical trial, potentially using a different comparator drug. In July 2022 we reached an agreement with the FDA under the SPA process on the design, endpoints and statistical analysis of a Phase 3 clinical trial for oral sulopenem for the treatment of uUTIs and we commenced enrollment in that clinical trial, known as REnewed ASsessment of Sulopenem in uUTI caused by Resistant Enterobacterales (REASSURE), in October 2022. The study is designed as a non-inferiority trial comparing oral sulopenem and Augmentin® (amoxicillin/clavulanate) in the Augmentin® susceptible population. Additionally, though not an approvability issue, the FDA recommended in its CRL that we conduct additional non-clinical Pharmacokinetics and Pharmacodynamics (PK/PD) studies to support dose selection for the proposed treatment indication(s). We have commenced additional non-clinical PK/PD investigations to support the dosing regimen selected for oral sulopenem, as recommended by the FDA.

Since our inception, we have incurred significant operating losses. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of oral sulopenem and sulopenem. As of September 30, 2022, we had an accumulated deficit of $417.8 million. We expect to continue to incur significant expenses for the foreseeable future as we conduct ongoing Phase 3 clinical and non-clinical work to support a potential resubmission of the NDA for approval of oral sulopenem. In addition, if we obtain marketing approval for oral sulopenem, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. We may also incur expenses in connection with the further clinical development of IV sulopenem and clinical development of sulopenem in additional indications, the establishment of additional sources for the manufacture of sulopenem tablets and, if relevant, IV vials or the in-license or acquisition of additional product candidates. Additionally, we have incurred and expect to incur additional costs associated with operating as a public company, including significant legal, accounting, investor relations and other expenses that we did not incur as a private company.

Until such time as we can obtain marketing approval for oral sulopenem, sulopenem or any future product candidate and generate significant revenue from product sales, if ever, we expect to finance our operations through a combination of equity offerings, debt financings, collaboration agreements, other third-party funding, strategic alliances, licensing arrangements, marketing and distribution arrangements or government funding. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on favorable terms, or at all. If we fail to raise capital or enter into such agreements as, and when, needed, we may have to significantly delay, scale back or discontinue the development and commercialization of our sulopenem program, or otherwise change our strategy.

Because of the numerous risks and uncertainties associated with product development, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

As of September 30, 2022, we had cash, cash equivalents, restricted cash and short-term investments of $64.4 million. We believe that our existing cash, cash equivalents and short-term investments as of September 30, 2022 should be sufficient to fund our operating expenses into 2024, based on our current operating plan. However, this estimate is based on assumptions that may prove to be wrong, and our operating plans may change as a result of many factors and various risks and uncertainties.

We are currently evaluating our corporate, strategic, financial and financing alternatives, with the goal of maximizing value for our stakeholders while prudently managing our resources. These alternatives could potentially include the licensing, sale or divestiture of our assets or proprietary technologies, a sale of our company, a merger or other business combination or another strategic transaction involving us. The evaluation of corporate, strategic, financial and financing alternatives may not result in any particular action or any transaction being pursued, entered into or consummated, and there is no assurance as to the timing, sequence or outcome of any action or transaction or series of actions or transactions.

COVID-19 Global Pandemic

In December 2019, an outbreak of COVID-19 was reported in Wuhan, China. On March 11, 2020, the World Health Organization declared COVID-19 a global pandemic and on March 13, 2020, prior U.S. President Donald J. Trump declared the virus a national emergency. This highly contagious disease has spread to most of the countries in the world and throughout the United States, creating a serious impact on customers, workforces, and suppliers, disrupting economies and financial markets, and potentially leading to a world-wide economic downturn. It has caused a disruption of the normal operations of many businesses, including the temporary closure or scale-back of business operations and/or the imposition of either quarantine or remote work or meeting requirements for employees, either by government order or on a voluntary basis. The pandemic may impact the ability of our strategic partners to operate and fulfill their contractual obligations, and result in an increase in their costs and cause delays in performance. We may experience an impact to the timelines of our ongoing and any additional clinical and non-clinical development for sulopenem due to the worldwide spread of COVID-19. These effects, and the direct effect of the virus and any potential disruption on our operations, may negatively impact our ability to meet our strategic targets. Our employees, in many cases, are working remotely in part due to safety concerns and using various technologies to perform their functions. We feel we have sufficient office and IT resources to allow employees to return to office work or work from home indefinitely based on the latest government advice. Additionally, the disruption and volatility in the global and domestic capital markets may increase the cost of capital and limit our ability to access capital. Both the health and economic aspects of COVID-19 are highly fluid and the future course of each is uncertain. For these reasons and other reasons that may come to light if the coronavirus pandemic and associated protective or preventative measures expand, we may experience a material adverse effect on our business operations and financial condition; however, its ultimate impact is highly uncertain and subject to change.

We cannot foresee if and when the COVID-19 pandemic will be effectively contained, nor can we predict the severity and duration of its impact. COVID-19 has not yet had a significant impact on the Company's day to day operations but there can be no assurance that the continued spread of COVID-19 and the responsive measures taken to date will not impact the ongoing Phase 3 clinical trial being conducted in response to the CRL to support a potential resubmission of our NDA. Additionally, the COVID-19 pandemic could impact the FDA's regulatory review process, including delays in meetings related to planned or completed clinical trials and ultimately the review and approval of our product candidates. The FDA's review of any resubmitted NDA for the approval of oral sulopenem for the treatment of uUTI may be delayed due to COVID-19, including an inability to schedule, or delays in scheduling, meetings and inspections. Additionally, the COVID-19 pandemic may negatively impact our ability to initiate or complete future clinical trials, disrupt our regulatory and commercialization activities, and result in other adverse effects on our business and operations.

Management is actively monitoring the global situation and its possible effects on our financial condition, liquidity, suppliers, industry, and operations including manufacturing, clinical trials and workforce. Given the evolution of the COVID-19 pandemic and the global responses to curb its spread, we are not able to estimate the adverse effects of the COVID-19 pandemic on our results of operations, financial condition, or liquidity.

Components of Our Results of Operations

Operating Expenses

Research and Development Expenses

Research and development expenses consist primarily of costs incurred in connection with the development of our sulopenem program, which include:

•expenses incurred under agreements with contract research organizations (CROs), contract manufacturing organizations (CMOs), as well as investigative sites and consultants that conduct our clinical trials, preclinical studies and other scientific development services;

•manufacturing scale-up expenses and the cost of acquiring and manufacturing preclinical and clinical trial materials and commercial materials, including manufacturing validation batches and reservation fees;

•employee-related expenses, including salaries, related benefits, travel and share-based compensation expense for employees engaged in research and development functions;

•costs related to compliance with regulatory requirements, including the preparation and support of regulatory filings;

•facilities costs, depreciation and other expenses, which include rent under operating lease agreements and utilities; and

•payments made in cash, equity securities or other forms of consideration under third-party licensing agreements.

We expense research and development costs as incurred. Advance payments we make for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses. We recognize external development costs based on an evaluation of the progress to completion of specific tasks using information provided to us by our service providers.

The successful development and commercialization of oral sulopenem and/or sulopenem is highly uncertain. At this time, we cannot reasonably estimate or know the nature, timing and costs of the efforts that will be necessary to complete the clinical development of our sulopenem program or when, if ever, material net cash inflows may commence from any of our product candidates. This uncertainty is due to the numerous risks and uncertainties associated with product development and commercialization, including the uncertainty of:

•the impact of the COVID-19 pandemic on the economy and our business generally including the impact the pandemic may have on our ability to efficiently conduct the ongoing Phase 3 clinical trial to support a potential resubmission of our NDA for oral sulopenem, timing of regulatory review, potential approval and commercialization of any future products, including sulopenem for the treatment of uUTI;

•the scope, progress, outcome and costs of our clinical trials and other research and development activities;

•successful patient enrollment in, and the initiation and completion of, clinical trials;

•our ability to apply for regulatory approval, including the potential resubmission of our NDA for oral sulopenem, and the timing or likelihood of any such filings and approvals;

•the timing, receipt and terms of any marketing approvals from applicable regulatory authorities;

•establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;

•development and timely delivery of commercial drug formulations (i) that can be used in our clinical trials and (ii) that are available for commercial launch;

•obtaining, maintaining, defending and enforcing patent claims and other intellectual property rights;

•significant and changing government regulation;

•launching commercial sales of our product candidates, if and when approved, whether alone or in collaboration with others; and

•maintaining a continued acceptable safety profile of the product candidates following approval.

We may never succeed in achieving regulatory approval for any of our product candidates. For example, in the results of our cIAI clinical trial, sulopenem did not meet the primary endpoint of statistical non-inferiority compared to the control therapy for the cIAI trial. In the second quarter of 2020, we announced the results of our Phase 3 clinical trials of sulopenem for the treatment of cUTI and uUTI. In the cUTI trial, sulopenem did not meet the primary endpoint of statistical non-inferiority compared to the control therapies with the difference in response rates driven almost entirely by higher rates of asymptomatic bacteriuria on the sulopenem IV to oral sulopenem arm relative to the ertapenem IV to oral ciprofloxacin arm, only evident at the test of cure visit; the rates of patients receiving additional antibiotics or with residual cUTI symptoms were similar between therapies. Similarly, in the uUTI trial, sulopenem did not meet the primary endpoint of statistical non-inferiority compared to ciprofloxacin in the population of patients with baseline pathogens susceptible to ciprofloxacin driven to a large degree by a greater amount of asymptomatic bacteriuria in the sulopenem treated patients at the test of cure visit relative to those receiving ciprofloxacin. However, in the uUTI trial, in the population of patients with baseline pathogens resistant to quinolones, sulopenem achieved the related primary endpoint by demonstrating statistical significance in the overall response rate by treatment arm in the ciprofloxacin-resistant population, providing evidence of a treatment effect in patients with uUTI. Notwithstanding failure to meet the endpoints described above, in all three Phase 3 clinical trials, at all timepoints measured, the clinical response to sulopenem and/or oral sulopenem was similar to the comparator regimen (non-inferior), except in the instance of the quinolone non-susceptible population in the Phase 3 uUTI trial in which oral sulopenem was statistically superior. Based on discussions with the FDA at a pre-NDA meeting in September 2020 and previous correspondence with the FDA, we submitted an NDA for oral sulopenem for the treatment of uUTIs in patients with a quinolone non-susceptible pathogen in the fourth quarter of 2020 and the FDA accepted the application for review in January 2021. We received a CRL from the FDA on July 23, 2021, for our NDA. The CRL provided that additional data are necessary to support approval of oral sulopenem for the treatment of adult women with uUTIs caused by designated susceptible microorganisms proven or strongly suspected to be non-susceptible to a quinolone and recommended that we conduct at least one additional adequate and well-controlled clinical trial, potentially using a different comparator drug. In July 2022 we reached an agreement with the FDA under the SPA process on the design, endpoints and statistical analysis of a Phase 3 clinical trial for oral sulopenem for the treatment of uUTIs and we commenced enrollment in that clinical trial, known as REASSURE, in October 2022. The study is designed as a non-inferiority trial comparing oral sulopenem and Augmentin® (amoxicillin/clavulanate) in the Augmentin® susceptible population. Additionally, though not an approvability issue, the FDA recommended in its CRL that we conduct additional non-clinical PK/PD studies to support dose selection for the proposed treatment indication(s). We have commenced additional non-clinical PK/PD investigations to support the dosing regimen selected for oral sulopenem, as recommended by the FDA. There can be no assurance that we will be in a position to resolve the matters set forth in the CRL, that we will be able to complete the ongoing Phase 3 clinical trial and non-clinical studies intended to support a resubmission of our NDA or that any data generated by such clinical and non-clinical investigation will be adequate to support resubmission or approval of our NDA.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries, related benefits and share-based compensation expense for personnel in executive, finance, market research and administrative functions. General and administrative expenses also include director compensation, travel expenses, insurance, professional fees for legal, patent, consulting, accounting and audit services, pre-commercialization activities and market preparation expenses.

Following receipt of the CRL in the third quarter of 2021, in order to reduce operating expenses and conserve cash resources, we halted any remaining pre-commercial activities for oral sulopenem and plan to limit spending to essential costs required in connection with the potential resubmission of the NDA. If and when we believe regulatory approval of oral sulopenem and/or sulopenem appears likely, we anticipate an increase in payroll and expenses as a result of our preparation for commercial operations.

Interest Expense, Net

Interest expense, net consists of interest accrued and amortization of debt costs with respect to the 6.500% Exchangeable Senior Subordinated Notes due 2025 (Exchangeable Notes) and Limited Recourse Royalty-Linked Subordinated Notes (RLNs) issued in 2020 (through January 2021), realized and unrealized gains and losses on our short-term investments, interest earned on our cash and cash equivalents, which are generally invested in money market accounts, interest earned on our investments in marketable securities and interest incurred and amortization of debt costs on our loan from Silicon Valley Bank (SVB) (fully repaid in March 2022) and interest incurred on our note received under the Payment Protection Program (the PPP loan) (fully repaid in March 2022). Interest on the Exchangeable Notes is not payable until maturity of the instrument unless exchanged prior to maturity in accordance with the terms of the indenture governing the Exchangeable Notes (Exchangeable Notes Indenture) at which time any accrued and unpaid interest becomes due and payable.

Adjustments to Fair Value of Derivatives

Derivative liabilities, which consist of embedded features in the Exchangeable Notes, are revalued at each balance sheet date and the change in fair value during the reporting period is recorded in the condensed consolidated statements of operations as adjustments to fair value of derivatives.

Other Income, Net

Other income, net consists of realized and unrealized foreign currency gains and losses incurred in the normal course of business based on movement in the applicable exchange rates and sub-lease income from a sub-lease agreement for a commercial unit.

Provision for Income Taxes

We recognize income taxes under the asset and liability method. Deferred income taxes are recognized for differences between the financial reporting and tax bases of assets and liabilities at enacted statutory tax rates in effect for the years in which the differences are expected to reverse. The effect on deferred taxes of a change in tax rates is recognized in income in the period that includes the enactment date. In evaluating our ability to recover our deferred tax assets, we consider all available positive and negative evidence including past operating results, the existence of cumulative income in the most recent fiscal years, changes in the business in which we operate and our forecast of future taxable income. In determining future taxable income, we are responsible for assumptions utilized including the amount of Irish, U.S. and other foreign pre-tax operating income, the reversal of temporary differences and the implementation of feasible and prudent tax planning strategies. These assumptions require significant judgment about the forecasts of future taxable income and are consistent with the plans and estimates that we are using to manage the underlying business.

Valuation allowances are provided if it is more likely than not that some portion or all of the deferred tax assets will not be realized. We account for uncertain tax positions using a more-likely-than-not threshold for recognizing and resolving uncertain tax positions. The evaluation of uncertain tax positions is based on factors including, but not limited to, changes in tax law, the measurement of tax positions taken or expected to be taken in tax returns, the effective settlement of matters subject to audit, new audit activity and changes in facts or circumstances related to a tax position. We evaluate our tax positions on a quarterly basis. Our policy is to accrue for potential interest and penalties related to tax matters in income tax expense.

Critical Accounting Estimates

Our condensed consolidated financial statements are prepared in accordance with generally accepted accounting principles in the United States. The preparation of our condensed consolidated financial statements and related disclosures requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenue, costs and expenses, and the disclosure of contingent assets and liabilities in our financial statements. We believe that our critical accounting policies described under the heading “Management’s Discussion and Analysis of Financial Condition and Results of Operations – Critical Accounting Policies and Significant Judgments and Estimates” in our Annual Report on Form 10-K filed with the SEC on March 28, 2022, involve the most judgment and complexity. Accordingly, we believe the policies set forth in such Annual Report on Form 10-K are critical to fully understanding and evaluating our financial condition and results of operations. If actual results or events differ materially from the estimates, judgments and assumptions used by us in applying these policies, our reported financial condition and results of operations could be materially affected. There have been no significant changes to our critical accounting estimates from those described in our Annual Report on Form 10-K filed with the SEC on March 28, 2022.

Results of Operations

Comparison of the three months ended September 30, 2022 and 2021

The following table summarizes our operating loss and (loss) / income before income taxes for the three months ended September 30, 2022 and 2021 (in thousands):

	Three Months Ended September 30,		
	2022	2021	Change
Operating expenses:			
Research and development	$ (4,353)	$ (1,845)	$ (2,508)
General and administrative	(2,681)	(3,029)	348
Total operating expenses	(7,034)	(4,874)	(2,160)
Operating loss	(7,034)	(4,874)	(2,160)
Total other income / (expense), net	(22,645)	8,967	(31,612)
(Loss) / income before income taxes	$ (29,679)	$ 4,093	$ (33,772)

Research and Development Expenses (in thousands)

	Three Months Ended September 30, 2022	2021	Change
CRO and other preclinical and clinical trial expenses	$ 2,363	$ 408	$ 1,955
Personnel related (including share-based compensation)	841	744	97
Chemistry, manufacturing and control (CMC) related expenses	857	365	492
Consulting fees	292	328	(36)
Total research and development expenses	$ 4,353	$ 1,845	$ 2,508

The increase in CRO and other preclinical and clinical trial expenses of $2.0 million million was primarily due to an increase in costs incurred to support the activities for our REASSURE trial, which began enrollment in October 2022, in support of the potential resubmission of our NDA. Personnel related costs increased by $0.1 million primarily as a result of an increase in headcount. Personnel related costs for the three months ended September 30, 2022 and 2021 included share-based compensation expense of $0.2 million and $0.6 million, respectively. CMC related expenses increased by $0.5 million primarily as a result of the intangible asset amortization charge. Consulting fees of $0.3 million were flat to the prior year.

General and Administrative Expenses (in thousands)

	Three Months Ended September 30, 2022	2021	Change
Personnel related (including share-based compensation)	$ 906	$ 1,576	$ (670)
Facility related and other	749	851	(102)
Professional and consulting fees	1,026	602	424
Total general and administrative expenses	$ 2,681	$ 3,029	$ (348)

Personnel related costs decreased by $0.7 million primarily as a result of a decrease in share-based compensation expense. Personnel related costs for the three months ended September 30, 2022 and 2021 included share-based compensation expense of $0.2 million and $0.9 million, respectively. Facility related and other costs decreased by $0.1 million primarily as a result of a decrease in rent expense. Facility related and other costs for the three months ended September 30, 2022 and 2021 included share-based compensation expense of $0.1 million and $0.1 million, respectively, for directors. Professional and consulting fees increased by $0.4 million primarily as a result of an increase in legal fees associated with the lawsuit filed in August 2021, partially offset by pre-commercialization activities carried out in 2021 prior to receipt of the CRL.

Total Other Income / (Expense), net

The following table summarizes our total other income/(expense), net for the three months ended September 30, 2022 and 2021 (in thousands):

	Three Months Ended September 30, 2022	2021	Change
Interest expense, net	$ (636)	$ (849)	$ 213
Adjustments to fair value of derivatives	(4,834)	9,783	(14,617)
Cancellation of share options	(17,350)	—	(17,350)
Other income, net	175	33	142
Total other income / (expense), net	$ (22,645)	$ 8,967	$ (31,612)

Interest Expense, Net

Interest expense, net decreased by $0.2 million for the three months ended September 30, 2022 primarily as a result of a reduction in interest expense associated with our credit facility with SVB, which was repaid in full in March 2022.

Adjustments to Fair Value of Derivatives

Adjustments to the fair value of the Derivative liability were $4.8 million for the three months ended September 30, 2022. This non-cash adjustment related to an increase in the fair value of the RLNs due to the newly issued patent for the bilayer tablet which provides patent protection at least until 2039, partially offset by a decrease in the value of the derivative components associated with the Exchangeable Notes, primarily as a result of a decrease in the price of our ordinary shares and our market capitalization during the period. Adjustments to the fair value of derivatives were $9.8 million for the three months ended September 30, 2021. This non-cash adjustment related to a decrease in the value of the derivative components associated with the Exchangeable Notes, primarily as a result of a decrease in the price of our ordinary shares and our market capitalization during the period, partially offset by an increase in the fair value of the RLNs.

Cancellation of Share Options

On July 7, 2022, certain of the Company's executive officers and employees agreed to the surrender and cancellation of certain previously granted share options in order to make available additional shares under the Company's Amended and Restated 2018 Equity Incentive Plan. Total expense recognized in connection with the cancellation of these employee share options was $17,350 for three months ended September 30, 2022.

Other Income, Net

Other income, net consists of realized and unrealized foreign currency gains incurred in the normal course of business based on movement in the applicable exchange rates and sub-lease income from a sub-lease agreement for a commercial unit. The increase of $0.1 million is primarily related to an increase in unrealized foreign currency gains due to the strength of the US dollar.

Comparison of the nine months ended September 30, 2022 and 2021

The following table summarizes our operating loss and loss before income taxes for the nine months ended September 30, 2022 and 2021 (in thousands):

	Nine Months Ended September 30,		
	2022	2021	Change
Operating expenses:			
Research and development	$ (11,777)	$ (7,010)	$ (4,767)
General and administrative	(10,680)	(10,698)	18
Total operating expenses	(22,457)	(17,708)	(4,749)
Operating loss	(22,457)	(17,708)	(4,749)
Total other income / (expense), net	(16,687)	(69,140)	52,453
Loss before income taxes	$ (39,144)	$ (86,848)	$ 47,704

Research and Development Expenses (in thousands):

	Nine Months Ended September 30,		
	2022	2021	Change
CRO and other preclinical and clinical trial expenses	$ 4,812	$ 1,789	$ 3,023
Personnel related (including share-based compensation)	3,674	1,623	2,051
Chemistry, manufacturing and control (CMC) related expenses	2,313	1,025	1,288
Consulting fees	978	2,573	(1,595)
Total research and development expenses	$ 11,777	$ 7,010	$ 4,767

The increase in CRO and other preclinical and clinical trial expenses of $3.0 million was primarily due to an increase in costs incurred to support the activities for our ongoing Phase 3 clinical trial known as REASSURE, which commenced enrollment in October 2022, in support of the potential resubmission of our NDA. Personnel related costs increased by $2.1 million primarily as a result of an increase in headcount to support our REASSURE trial. Personnel related costs for the nine months ended September 30, 2022 and 2021 included share-based compensation expense of $1.3 million and $0.7 million, respectively. CMC related expenses increased by $1.3 million primarily as a result of the intangible asset amortization charge. The decrease in consulting fees of $1.6 million was primarily due to a decrease in consultants used for research and development activities in the nine months ended September 30, 2022. Consulting fees for the nine months ended September 30, 2021 primarily related to consultants used during the FDA review of our NDA for oral sulopenem.

General and Administrative Expenses (in thousands)

	Nine Months Ended September 30,		
	2022	2021	Change
Personnel related (including share-based compensation)	$ 5,281	$ 3,161	$ 2,120
Facility related and other	2,781	2,531	250
Professional and consulting fees	2,618	5,006	(2,388)
Total general and administrative expenses	$ 10,680	$ 10,698	$ (18)

Personnel related costs increased by $2.1 million primarily as a result of an increase in headcount. Personnel related costs for the nine months ended September 30, 2022 and 2021 included share-based compensation expense of $2.6 million and $1.5 million, respectively. Facility related and other costs increased by $0.3 million primarily as a result of an increase in directors fees and share-based compensation for directors. Facility related and other costs for the nine months ended September 30, 2022 and 2021 included share-based compensation expense of $0.4 million and $0.2 million, respectively, for directors. Professional and consulting fees decreased by $2.4 million primarily as a result of pre-commercialization activities carried out in 2021 prior to receipt of the CRL and a decrease in consultants used to support our general and administrative functions, partially offset by an increase in legal fees associated with the lawsuit filed in August 2021.

Total Other Income / (Expense), Net

The following table summarizes our total other income / (expense), net for the nine months ended September 30, 2022 and 2021 (in thousands):

	Nine Months Ended September 30,		
	2022	2021	Change
Interest expense, net	$ (2,441)	$ (4,781)	$ 2,340
Adjustments to fair value of derivatives	2,498	(64,526)	67,024
Cancellation of share options	(17,350)	-	(17,350)
Other income, net	606	167	439
Total other income / (expense), net	$ (16,687)	$ (69,140)	$ 52,453

Interest Expense, Net

Interest expense, net decreased by $2.3 million for the nine months ended September 30, 2022 primarily as a result of a decrease in the amortization of the debt discounts and deferred financing costs relating to the RLNs which were listed, and therefore fully amortized, - in January 2021, a decrease in interest accruing on our Exchangeable Notes and a decrease in the amortization of the debt discounts and deferred financing costs relating to them due to the reduction in the Exchangeable Notes outstanding balance and a reduction in interest expense associated with our credit facility with SVB, which was repaid in full in March 2022, partially offset by an increase in unrealized losses on our short-term investments.

Adjustments to Fair Value of Derivatives

Adjustments to the fair value of the Derivative liability were $2.5 million for the nine months ended September 30, 2022. This non-cash adjustment related to a decrease in the value of the derivative components associated with the Exchangeable Notes, primarily as a result of a decrease in the price of our ordinary shares and our market capitalization during the period, partially offset by an increase in the fair value of the RLNs due to the newly issued patent for the bilayer tablet which provides patent protection at least until 2039. Adjustments to the fair value of derivatives were $64.5 million for the nine months ended September 30, 2021. This non-cash adjustment related to an increase in the value of derivative components associated with the Exchangeable Notes which were exchanged in the first half of 2021 and an increase in the fair value of our RLNs, partially offset by a decrease in the value of the derivative components associated with the Exchangeable Notes, primarily as a result of a decrease in the price of our ordinary shares and our market capitalization during the period.

Cancellation of Share Options

On July 7, 2022, certain of the Company's executive officers and employees agreed to the surrender and cancellation of certain previously granted share options in order to make available additional shares under the Company's Amended and Restated 2018 Equity Incentive Plan. Total expense recognized in connection with the cancellation of these employee share options was $17,350 for nine months ended September 30, 2022.

Other Income, Net

Other income, net consists of realized and unrealized foreign currency gains incurred in the normal course of business based on movement in the applicable exchange rates and sub-lease income from a sub-lease agreement for a commercial unit. The increase of $0.4 million is primarily related to an increase in unrealized foreign currency gains due to the strength of the US dollar.

Liquidity and Capital Resources

Since our inception, we have incurred significant operating losses and negative cash flows from our operations. We have generated limited revenue to date from a funding arrangement with the Trustees of Boston University under the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X) program. We have funded our operations to date primarily through the issuance of ordinary and convertible preferred shares, warrants, debt raised under financing arrangements with SVB including the PPP loan, a sub-award from the Trustees of Boston University under the CARB-X program and the proceeds of the private placement which closed in January 2020 (the Private Placement) and the subsequent rights offering (the Rights Offering) pursuant to which our wholly owned subsidiary, Iterum Therapeutics Bermuda Limited (Iterum Bermuda), issued and sold $51.8 million aggregate principal amount of Exchangeable Notes and $0.1 million aggregate principal amount of RLNs. Through September 30, 2022, we had received cash proceeds of $198.2 million from sales of our Series A and Series B preferred shares and ordinary shares, $15.0 million from the first drawdown of our SVB loan, net proceeds of $45.0 million from the Private Placement and the Rights Offering, $0.7 million from the drawdown of our PPP loan, combined net proceeds of $8.6 million from the registered direct offering in June 2020 (June 3, 2020 Offering) and the registered direct offering in June 2020 (June 30, 2020 Offering) and $1.8 million from the exercise of warrants issued in the June 30, 2020 Offering, net proceeds of $15.5 million from the underwritten offering in October 2020 (October 2020 Offering) and $13.9 million from the exercise of warrants issued in the October 2020 Offering, net proceeds of $42.1 million from the underwritten offering in February 2021 (February 2021 Underwritten Offering) and $0.5 million from the exercise of warrants issued in the February 2021 Underwritten Offering and net proceeds of $32.2 million from the registered direct offering in February 2021 (February 2021 Registered Direct Offering).

As of September 30, 2022, we had cash, cash equivalents, restricted cash and short-term investments of $64.4 million.

We filed a universal shelf registration statement on Form S-3 with the SEC, which was declared effective on October 17, 2022 (File No. 333-267795), and pursuant to which we registered for sale up to $100.0 million of any combination of debt securities, ordinary shares, preferred shares, subscription rights, purchase contracts, units and/or warrants from time to time and at prices and on terms that we may determine. On October 7, 2022, we entered into a sales agreement (the Sales Agreement), with H.C. Wainwright & Co., LLC (HC Wainwright), as agent, pursuant to which we may offer and sell ordinary shares, nominal value $0.01 per share, for aggregate gross sales proceeds of up to $16.0 million (not to exceed 4,478,180 ordinary shares as of the date of filing this Form 10-Q), from time to time through HC Wainwright by any method permitted that is deemed to be an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended.

Secured Credit Facility

On April 27, 2018, our subsidiaries, Iterum Therapeutics International Limited, Iterum Therapeutics US Holding Limited and Iterum Therapeutics US Limited (Borrowers), entered into a loan and security agreement with SVB (Loan and Security Agreement) pursuant to which SVB agreed to lend the Borrowers up to $30.0 million in two term loans. $15.0 million of the secured credit facility was funded on closing. A second draw of up to $15.0 million was available to us through October 31, 2019, upon satisfaction of either of the following: (i) the achievement by us of both non-inferiority and superiority primary endpoints from our Phase 3 uUTI trial, as well as reporting satisfactory safety data from the trial, or (ii) the achievement of non-inferiority primary endpoints from both our Phase 3 uUTI and cUTI trials, as well as reporting satisfactory safety data from the trials. We did not satisfy the conditions for the second draw above before the deadline of October 31, 2019.

Required monthly amortization payments for the initial $15.0 million draw commenced on November 1, 2019 and total principal repayments of $1,552 were made during the nine months ended September 30, 2022. Interest accrued at a floating per annum rate equal to the greater of (i) 8.31%; or (ii) 3.89% above the Wall Street Journal prime rate, and was payable monthly in arrears. All outstanding principal, plus a 4.20% final interest payment, were due and paid on March 1, 2022 (the maturity date), effectively terminating the Loan and Security Agreement. The final payment fee of $0.6 million which represented 4.2% of the funded loan, was accreted using the effective interest method over the life of the loan as interest expense.

In connection with the initial $15.0 million draw, we issued SVB and Life Sciences Fund II LLC (LSF) warrants to purchase an aggregate of 19,890 Series B convertible preferred shares (which converted into warrants to purchase 1,326 ordinary shares upon our IPO) at an exercise price of $282.75 per share. These warrants will expire on April 27, 2028.

In connection with the Private Placement, Iterum Bermuda was joined as a party to the Loan and Security Agreement as a borrower and the Loan and Security Agreement was amended on January 16, 2020 to, among other things, modify the definition of subordinated debt to include the RLNs and Exchangeable Notes.

2025 Exchangeable Notes and Royalty-Linked Notes

On January 21, 2020, we completed the Private Placement pursuant to which our wholly owned subsidiary, Iterum Bermuda issued and sold $51.6 million aggregate principal amount of Exchangeable Notes and $0.1 million aggregate principal amount of RLNs, to a group of accredited investors. On September 8, 2020, we completed the Rights Offering pursuant to which Iterum Bermuda issued and sold $0.2 million aggregate principal amount of Exchangeable Notes and $0.04 million aggregate principal amount of RLNs, to existing shareholders. The Exchangeable Notes and RLNs were sold in Units with each Unit consisting of an Exchangeable Note in the original principal amount of $1,000 and 50 RLNs. The Units were sold at a price of $1,000 per Unit. At any time on or after January 21, 2021, subject to specified limitations, the Exchangeable Notes are exchangeable for our ordinary shares, cash or a combination of ordinary shares and cash, at an exchange rate of 85.7456 shares per $1,000 principal and interest on the Exchangeable Notes (equivalent to an exchange price of approximately $11.6624 per ordinary share) as of August 17, 2022, which exchange rate was adjusted from an initial exchange rate of 66.666 shares per $1,000 of principal and interest on the Exchangeable Notes (equivalent to an initial exchange price of approximately $15.00 per ordinary share), and is subject to further adjustment pursuant to the terms of the Exchangeable Notes Indenture. The Exchangeable Notes will mature on January 31, 2025. Beginning on January 21, 2021 to September 30, 2022, certain noteholders of $39.2 million aggregate principal amount of Exchangeable Notes have exchanged their notes for an aggregate of 3,592,555 of our ordinary shares, which included accrued and unpaid interest relating to such notes. The aggregate principal amount of Exchangeable Notes outstanding as of September 30, 2022 was $12.6 million. The RLNs entitle holders to payments based on a percentage of our net revenues from potential U.S. sales of specified sulopenem products subject to the terms and conditions of the indenture governing the RLNs (the RLN Indenture). Pursuant to the RLN Indenture, the payments on the RLNs will be up to either 15% or 20% of net revenues from U.S. sales of such products, depending on the indication approved by the FDA. The aggregate amount of payments on each RLN is capped at $160.00 (or 4,000 times the principal amount of such RLN). Iterum Bermuda received net proceeds from the sale of the Units of $45.0 million, after deducting placement agent fees and offering expenses.

Registered Direct Offerings

On June 3, 2020, we entered into the securities purchase agreement (June 3, 2020 SPA) with certain institutional investors pursuant to which we issued and sold, in the June 3, 2020 Offering, an aggregate of 198,118 ordinary shares, $0.01 nominal value per share, at a purchase price per share of $25.2375, for aggregate gross proceeds to us of $5.0 million and net proceeds of $4.3 million after deducting fees payable to the placement agent and other offering expenses payable by us. We offered the ordinary shares in the June 3, 2020 Offering pursuant to our universal shelf registration statement on Form S-3, which was declared effective on July 16, 2019 (File No. 333-232569) (the 2019 Shelf Registration Statement). Pursuant to the June 3, 2020 SPA, in a concurrent private placement, we issued and sold to the June 3 Purchasers warrants to purchase up to 99,057 ordinary shares. Upon closing, the warrants became exercisable immediately at an exercise price of $24.30 per ordinary share, subject to adjustment in certain circumstances, and will expire on December 5, 2025. The closing date of the June 3, 2020 Offering was June 5, 2020. Warrants to purchase 13,868 ordinary shares, amounting to 7% of the ordinary shares issued under the June 3, 2020 SPA, were issued to designees of the placement agent on the closing of the June 3, 2020 Offering. Upon closing, the warrants issued to such designees became exercisable immediately at an exercise price of $31.5465 per ordinary share, and will expire on June 3, 2025.

On June 30, 2020, we entered into the securities purchase agreement (June 30, 2020 SPA) with certain institutional investors pursuant to which we issued and sold in the June 30, 2020 Offering an aggregate of 224,845 ordinary shares, $0.01 nominal value per share, at a purchase price per share of $22.2375, for aggregate gross proceeds to us of $5.0 million and net proceeds of $4.2 million after deducting fees payable to the placement agent and other offering expenses payable by us. We offered the ordinary shares in the June 30, 2020 Offering pursuant to the 2019 Shelf Registration Statement. Pursuant to the June 30, 2020 SPA, in a concurrent private placement, we issued and sold to the June 30 Purchasers warrants to purchase up to 112,422 ordinary shares. Upon closing, the warrants were exercisable immediately at an exercise price of $21.30 per ordinary share, subject to adjustment in certain circumstances, and will expire on January 2, 2026. The June 30, 2020 Offering closed on July 2, 2020. Warrants to purchase 15,739 ordinary shares, amounting to 7% of the ordinary shares issued under the June 30, 2020 SPA, were issued to designees of the placement agent on closing of the June 30, 2020 Offering. Upon closing, the warrants issued to such designees became exercisable immediately at an exercise price of $27.7965 per ordinary share, and will expire on June 30, 2025.

On February 9, 2021, we entered into the securities purchase agreement (February SPA) with certain institutional investors pursuant to which we issued and sold in the February 2021 Registered Direct Offering an aggregate of 1,166,666 ordinary shares, $0.01 nominal value per share, at a purchase price of $30.00 per share, for aggregate net proceeds to us of $32.2 million after deducting placement agent fees and other offering expenses payable by us. We offered the ordinary shares in the February 2021 Registered Direct Offering pursuant to the 2019 Shelf Registration Statement. The February 2021 Registered Direct Offering closed on February 12, 2021. Warrants to purchase 81,666 ordinary shares, amounting to 7.0% of the aggregate number of ordinary shares issued under the February SPA, were issued to designees of the placement agent on closing of the February 2021 Registered Direct Offering. Upon closing, warrants issued to such designees became exercisable immediately at an exercise price of $37.50 per ordinary share and will expire on February 9, 2026.

October 2020 Offering

On October 27, 2020, we completed the October 2020 Offering in which we sold an aggregate of (i) 1,034,102 ordinary shares, $0.01 nominal value per share, (ii) pre-funded warrants exercisable for an aggregate of 760,769 ordinary shares and (iii) warrants exercisable for an aggregate of 1,346,153 ordinary shares. The pre-funded warrants were issued and sold to certain purchasers whose purchase of ordinary shares in the October 2020 Offering would have otherwise resulted in the purchaser, together with its affiliates and certain related parties, beneficially owning more than 4.99% (or, at the election of the purchaser, 9.99%) of our outstanding ordinary shares immediately following the consummation of the October 2020 Offering, if the purchaser so chose in lieu of ordinary shares that would have otherwise resulted in such excess ownership. The ordinary shares and pre-funded warrants were each offered together with the warrants, but the ordinary shares and pre-funded warrants were issued separately from the warrants. The combined offering price was $9.75 per ordinary share and warrant and $9.60 per pre-funded warrant and warrant. Our net proceeds from the October 2020 Offering, after deducting placement agent fees and other offering expenses payable by us, were approximately $15.5 million. The warrants are exercisable upon issuance at a price of $9.75 per ordinary share, subject to adjustment in certain circumstances, and expire on October 27, 2025. The pre-funded warrants are exercisable upon issuance at a price of $0.15 per ordinary share, subject to adjustment in certain circumstances, and expire when exercised in full, subject to certain conditions. All pre-funded warrants have been exercised for net proceeds of $0.11 million. In connection with the October 2020 Offering, we entered into a Purchase Agreement on October 22, 2020 with certain institutional investors. The Purchase Agreement contains customary representations and warranties of ours, termination rights of the parties, and certain indemnification obligations of ours. Warrants to purchase 125,641 ordinary shares, which represents a number of ordinary shares equal to 7.0% of the aggregate number of ordinary shares and pre-funded warrants sold in the October 2020 Offering, were issued to designees of the placement agent on closing of the October 2020 Offering. Upon closing, the warrants issued to such designees became exercisable immediately at an exercise price of $12.1875 per ordinary share and will expire on October 22, 2025.

February 2021 Underwritten Offering

On February 3, 2021, we entered into an underwriting agreement (the Underwriting Agreement) pursuant to which we issued and sold 2,318,840 ordinary shares, $0.01 nominal value per share, at a public offering price of $17.25 per share. We offered the ordinary shares in the February 2021 Underwritten Offering pursuant to the 2019 Shelf Registration Statement. The February 2021 Underwritten Offering closed on February 8, 2021. Pursuant to the Underwriting Agreement, we granted the underwriter an option for a period of 30 days to purchase up to an additional 347,826 ordinary shares on the same terms and conditions, which the underwriter exercised in full on February 10, 2021. This increased the total number of ordinary shares we sold in the February 2021 Underwritten Offering to 2,666,666 shares, which resulted in aggregate net proceeds of $42.1 million after deducting underwriting discounts and commissions and offering expenses. In addition, pursuant to the Underwriting Agreement, we agreed to issue to the underwriter's designees warrants to purchase 186,665 ordinary shares, which is equal to 7.0% of the aggregate number of ordinary shares sold in the February 2021 Underwritten Offering, including the underwriter's option to purchase an additional 347,826 ordinary shares. The warrants issued to such designees of the underwriter have an exercise price of $21.5625 per ordinary share, were exercisable upon issuance and will expire on February 3, 2026.

Payment Protection Program

In April 2020, we began deferring payment on our share of U.S. payroll taxes owed, as allowed by the Coronavirus Aid, Relief, and Economic Security Act (CARES Act) through December 31, 2020. We paid half of our share of the 2020 U.S. payroll taxes owed in December 2021, with the remaining half due in December 2022.

On April 3, 2020, the U.S. Small Business Administration (SBA) launched the Paycheck Protection Program, which was established following the signing of the CARES Act on March 27, 2020. On April 30, 2020, our wholly owned subsidiary, Iterum Therapeutics US Limited (Iterum US Limited), entered into the PPP loan with SVB under the Paycheck Protection Program, pursuant to Iterum US Limited receiving a loan of $0.7 million with a fixed 1% annual interest rate and a maturity of two years. Under the terms of the agreement, there were no payments due until the earlier of the SBA remitting the forgiveness amount to Iterum US Limited or the Deferral Period. Following the Deferral Period, equal monthly repayments of principal and interest were due to fully amortize the principal amount outstanding on the PPP loan by the maturity date. The SBA forgave $0.3 million of the loan in November 2020, and the remaining loan of $0.4 million began amortization in December 2020 with equal monthly repayments of $26 through March 2022. All outstanding amounts, including the final interest payment, were repaid on March 17, 2022, effectively terminating the PPP loan.

Cash Flows

The following table summarizes our cash flows for each of the periods presented (in thousands):

	Nine Months Ended September 30,	
	2022	2021
Net cash used in operating activities	(14,208)	(13,383)
Net cash (used in) / provided by investing activities	9,579	(50,129)
Net cash (used in) / provided by financing activities	(2,251)	84,756
Effect of exchange rates on cash and cash equivalents	(77)	(14)
Net (decrease) / increase in cash, cash equivalents and restricted cash	$ (6,957)	$ 21,230

Operating Activities

During the nine months ended September 30, 2022, operating activities used $14.2 million of cash, resulting from our net loss of $39.3 million and net cash used by changes in our operating assets and liabilities of $0.04 million, partially offset by net non-cash charges of $25.2 million.

During the nine months ended September 30, 2021, operating activities used $13.4 million of cash, resulting from our net loss of $87.4 million, and net cash used by changes in our operating assets and liabilities of $0.2 million, partially offset by net non-cash charges of $74.2 million.

Investing Activities

During the nine months ended September 30, 2022, net cash used in investing activities of $9.6 million was related to the proceeds from the sale of short-term investments of $45.6 million, partially offset by the purchase of short-term investments of $36.0 million.

During the nine months ended September 30, 2021, net cash used by investing activities of $50.1 million was related to the purchase of short-term investments of $60.1 million, partially offset by proceeds from the sale of short-term investments of $10.0 million.

Financing Activities

During the nine months ended September 30, 2022, net cash used in financing activities of $2.3 million was related to principal repayments made to SVB under the Loan and Security Agreement, including a final payment fee and the PPP loan. Both loans were repaid in full in March 2022.

During the nine months ended September 30, 2021, net cash provided by financing activities was $84.8 million and consisted of net cash proceeds of $42.1 million from the February 2021 Underwritten Offering, net cash proceeds of $32.2 million from the February 2021 Registered Direct Offering and $15.3 million from the exercise of warrants, partially offset by principal repayments of $4.8 million made to SVB under the Loan and Security Agreement and the PPP loan.

Funding Requirements

We expect to continue to incur significant expenses and increasing operating losses as we seek potential marketing approval for oral sulopenem, engage in any pre-commercialization activities and pursue the development of our sulopenem program in additional indications through preclinical and clinical development. Our expenses will also increase substantially if and as we:

•conduct additional clinical trials for oral sulopenem and/or sulopenem, which includes the ongoing Phase 3 clinical trial being conducted to support potential resubmission of our NDA for oral sulopenem;

•initiate other studies as part of our sulopenem program, some of which may be required for regulatory approval of our product candidates and/or may be conducted in response to the CRL;

•establish sales, marketing and distribution capabilities either directly or through a third-party, to commercialize oral sulopenem and/or sulopenem if we obtain marketing approval from the FDA;

•establish manufacturing and supply chain capacity sufficient to provide commercial quantities of oral sulopenem and/or sulopenem, if we obtain marketing approval and undertake commercialization activities;

•pursue the development of our sulopenem program in additional indications;

•maintain, expand, defend and protect our intellectual property portfolio;

•hire additional clinical, scientific and commercial personnel;

•add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts; and

•acquire or in-license other product candidates or technologies.

Because of the numerous risks and uncertainties associated with research, development and commercialization of pharmaceutical product candidates, we are unable to estimate the exact amount of our working capital requirements. Our future funding requirements, both short-term and long-term, will depend on many factors, including:

•the timing and costs of our clinical trials of oral sulopenem and sulopenem, including any clinical trials or non-clinical studies which may be required for regulatory approval of our product candidates, including the ongoing Phase 3 clinical trial and non-clinical development being conducted in response to the CRL and to support a potential resubmission of the NDA for approval of oral sulopenem;

•any other activities that may be required in connection with the potential resubmission of the NDA for oral sulopenem;

•the timing of regulatory filings including a potential resubmission of the NDA for oral sulopenem;

•the timing of regulatory review and potential approval of any product candidates, including oral sulopenem for the treatment of uUTI;

•the initiation, progress, timing, costs and results of preclinical studies and clinical trials of other potential product candidates and of our current product candidates in additional indications;

•the amount of funding that we receive under government awards that we may apply for in the future;

•the number and characteristics of product candidates that we pursue;

•the outcome, timing and costs of seeking regulatory approvals;

•the costs of commercialization activities for oral sulopenem and/or sulopenem and other product candidates if we receive marketing approval, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;

•the receipt of marketing approval and revenue received from any potential commercial sales of oral sulopenem and/or sulopenem;

•the terms and timing of any future collaborations, licensing or other arrangements that we may establish;

•the amount and timing of any payments we may be required to make, or that we may receive, in connection with the licensing, filing, prosecution, defense and enforcement of any patents or other intellectual property rights, including milestone and royalty payments and patent prosecution fees that we are obligated to pay pursuant to an exclusive license agreement with Pfizer Inc. (Pfizer) (the Pfizer License) or other future license agreements;

•the amount and timing of any payments we may be required to make in connection with the RLNs and the repaymemt of the Exchangeable Notes, if required;

•the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against any intellectual property related claims;

•the costs of operating as a public company;

•the extent to which we in-license or acquire other products and technologies;

•the impact of the COVID-19 pandemic on the economy and our business generally including the impact the pandemic may have on our ability to efficiently conduct and complete the ongoing Phase 3 clinical trial to support a potential resubmission of our NDA for oral sulopenem, timing of regulatory review, potential approval and commercialization of any future products, including oral sulopenem for the treatment of uUTI; and

•the outcome, impact, effects and results of our evaluation of corporate, strategic, financial and financing alternatives, including the terms, timing, structure, value, benefits and costs of any corporate, strategic, financial or financing alternative and our ability to complete one at all.

Until such time, if ever, that we can generate product revenue sufficient to achieve profitability, we expect to finance our cash needs through a combination of public or private equity offerings, debt financings, collaboration agreements, other third-party funding, strategic alliances, licensing arrangements, marketing and distribution arrangements or government funding. The disruption and volatility in the global and domestic capital markets resulting from the COVID-19 pandemic may increase the cost of capital and limit our ability to access capital. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our shareholders' ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our ordinary shareholders. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. The RLNs, the Exchangeable Notes and the investor rights agreement we entered into in connection with the Private Placement each impose operating and other restrictions on us. Such restrictions affect, and in many cases limit or prohibit, our ability to dispose of certain assets, pay dividends, incur additional indebtedness, undergo a change of control and enter into certain collaborations, strategic alliances or other similar partnerships, among other things. If we raise additional funds through other third-party funding, collaboration agreements, strategic alliances, licensing arrangements or marketing and distribution arrangements, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. 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 develop and market products or product candidates that we would otherwise prefer to develop and market ourselves. In addition, as described above, we are evaluating our corporate, strategic, financial and financing alternatives, with the goal of maximizing value for our stakeholders while prudently managing our existing resources.

Contractual Obligations and Commitments

Under the Pfizer License, we have agreed to make certain regulatory and sales milestone payments. We are also obligated to make a potential one-time payment related to sublicensing income that exceeds a certain threshold. We are obligated to pay Pfizer royalties ranging from a single-digit to mid-teens percentage based on marginal net sales of each licensed product.

Under the RLN Indenture, holders of RLNs will be entitled to payments based solely on a percentage of our net revenues from U.S. sales of specified sulopenem products (Specified Net Revenues). Payments will be due within 75 days of the end of each six-month payment measuring period (Payment Measuring Period), beginning with the Payment Measuring Period ending June 30, 2020 until (i) the "Maximum Return" (as described below) has been paid in respect of the RLNs, or (ii) the "End Date" occurs, which is December 31, 2045, or (iii) December 31, 2025, in the event that we have not yet received FDA approval with respect to one or more specified sulopenem products by such date. The aggregate amount of payments in respect of all RLNs during each Payment Measuring Period will be equal to the product of total Specified Net Revenues earned during such period and the applicable payment rate (the Payment Rate), determined based on which of the specified sulopenem products have received FDA approval. The Payment Rate will be based on the maximum aggregate principal amount of RLNs and will equal (i) up to 15% if we or one of our affiliates has received FDA approval for the use of specified sulopenem products for the treatment of uUTIs and (ii) up to 20% if we or one of our affiliates has received FDA approval for the use of specified sulopenem products for the treatment of cUTIs but has not received FDA approval for treatment of uUTIs. There was no payment due for the Payment Measuring Period ending June 30, 2020, December 31, 2020, June 30, 2021, December 31, 2021, June 30, 2022, and September 30, 2022. Prior to the End Date, we are obligated to make payments on the RLNs from Specified Net Revenues until each RLN has received payments equal to $160.00 (or 4,000 times the principal amount of such RLN) (Maximum Return).

Our operating lease obligations primarily consist of payments for office space and commercial property, which are described further in Note 8 of our condensed consolidated financial statements included in this Quarterly Report on Form 10-Q. Future contractual payments on operating lease obligations due within one year of September 30, 2022 are $0.6 million, and future contractual payments on operating lease obligations due greater than one year from September 30, 2022 are $1.4 million.

Emerging Growth Company Status

The Jumpstart Our Business Startups Act of 2012 permits an "emerging growth company" such as us to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have irrevocably elected to "opt out" of this provision and, as a result, we will comply with new or revised accounting standards when they are required to be adopted by public companies that are not emerging growth companies.

Item 3. Quantitative and Qualitative Disclosures About Market Risk.

As of September 30, 2022, we had cash, cash equivalents and short-term investments of $64.3 million, consisting of cash, money market funds, commercial paper and U.S. treasury and agency bills. The primary objectives of our investment activities are to preserve principal, provide liquidity and maximize income without significantly increasing risk. We are exposed to interest rate risk in connection with our investments in marketable securities. As interest rates change, the unrealized gains and losses associated with those securities will fluctuate accordingly. An immediate interest rate increase of 100 basis points would result in a decrease of $0.2 million in the fair market value of our portfolio as of September 30, 2022. Such losses would only be realized if we sold the investments prior to maturity.

We contract with CROs and CMOs globally. We may be subject to fluctuations in foreign currency rates in connection with certain of these agreements. Transactions denominated in currencies other than the functional currency are recorded based on exchange rates at the time such transactions arise. As of September 30, 2022 and December 31, 2021, substantially all of our liabilities were denominated in U.S. dollars. Realized net foreign currency gains and losses did not have a material effect on our results of operations for the nine months ended September 30, 2022 and 2021 or for the year ended December 31, 2021. We do not currently engage in any hedging activities against our foreign currency exchange rate risk.

Item 4. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer (our principal executive officer and principal financial officer, respectively), evaluated the effectiveness of our disclosure controls and procedures as of September 30, 2022. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate, to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of September 30, 2022, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Changes in Internal Control over Financial Reporting

No change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the three months ended September 30, 2022, that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

PART II—OTHER INFORMATION

Item 1. Legal Proceedings

On August 5, 2021, a putative class action lawsuit was filed against the Company, its Chief Executive Officer and Chief Financial Officer in the United States District Court for the Northern District of Illinois. The complaint purports to be brought on behalf of shareholders who purchased the Company's securities between November 30, 2020 and July 26, 2021. The complaint generally alleges that the defendants violated Section 10(b) and/or 20(a) of the Securities Exchange Act of 1934 and Rule 10b-5 promulgated thereunder by making purportedly material misstatements or omissions concerning the Company's submission of its NDA to the FDA for marketing approval of oral sulopenem for the treatment of uUTIs in patients with a quinolone non-susceptible pathogen and the likelihood of such approval. The complaint seeks, among other things, unspecified damages, attorneys' fees, expert fees and other costs. The court appointed a lead plaintiff and approved plaintiff's selection of lead counsel on November 3, 2021. On January 26, 2022, plaintiff filed an amended complaint which includes allegations similar to those made in the original complaint and seeks similar relief. On April 8, 2022, the Company filed a motion to dismiss with the court seeking dismissal of all claims asserted. Oral argument on the motion to dismiss occurred on August 17, 2022. The next status conference is scheduled for December 7, 2022.

The Company denies any and all allegations of wrongdoing and believes the defendants have valid defenses against these claims and, therefore, intends to vigorously defend against this lawsuit.

Item 1A. Risk Factors.

Careful consideration should be given to the following risk factors, in addition to the other information set forth in this Quarterly Report on Form 10-Q and in other documents that we file with the Securities and Exchange Commission, or SEC, in evaluating our company and our business. Investing in our ordinary shares involves a high degree of risk. If any of the events described in the following Risk Factors and the risks described elsewhere in this Quarterly Report on Form 10-Q actually occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected. In these circumstances, the market price of our ordinary shares could decline, and you may lose all or part of your investment.

Risks Related to Our Financial Position and Capital Requirements

We have incurred net losses in each year since our inception and anticipate that we will continue to incur significant losses unless we successfully commercialize our sulopenem program.

We are a clinical-stage pharmaceutical company with a limited operating history. We have not generated any product revenue and have incurred net losses in each year since our inception in 2015. As of September 30, 2022, we had an accumulated deficit of $417.8 million, cash and cash equivalents of $20.5 million and short-term investments of $43.8 million. Our product candidates, oral sulopenem and sulopenem (together, the sulopenem program), are in clinical development, and have not been approved for sale and we may never have our product candidates approved for commercialization. We submitted a New Drug Application (NDA) for oral sulopenem for the treatment of uncomplicated urinary tract infections (uUTIs) in patients with a quinolone non-susceptible pathogen in the fourth quarter of 2020 and the U.S. Food and Drug Administration (FDA) accepted the application for review in January 2021. We received a Complete Response Letter (CRL) from the FDA on July 23, 2021, in respect of our NDA. The CRL provided that the FDA had completed its review of the NDA and had determined that it could not approve the NDA in its present form. The CRL further provided that additional data are necessary to support approval of oral sulopenem for the treatment of adult women with uUTIs caused by designated susceptible microorganisms proven or strongly suspected to be non-susceptible to a quinolone and recommended that we conduct at least one additional adequate and well-controlled clinical trial, potentially using a different comparator drug. In July 2022 we reached an agreement with the FDA under the special protocol assessment (SPA) process on the design, endpoints and statistical analysis of a Phase 3 clinical trial for oral sulopenem for the treatment of uUTIs and we commenced enrollment in that clinical trial, known as REnewed ASsessment of Sulopenem in uUTI caused by Resistant Enterobacterales (REASSURE), in October 2022. The study is designed as a non-inferiority trial comparing oral sulopenem and Augmentin® (amoxicillin/clavulanate) in the Augmentin® susceptible population. Additionally, though not an approvability issue, the FDA recommended in its CRL that we conduct additional non-clinical Pharmacokinetics and Pharmacodynamics (PK/PD) studies to support dose selection for the proposed treatment indication(s). We have commenced additional non-clinical PK/PD investigations to support the dosing regimen selected for oral sulopenem, as recommended by the FDA.

We have financed our operations to date primarily with the issuance of ordinary shares and convertible preferred shares, pre-funded warrants and warrants, debt raised under a financing arrangement with Silicon Valley Bank (SVB), a sub-award from the Trustees of Boston University under the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X) program and the proceeds of a private placement which closed in January 2020 (the Private Placement) and a subsequent rights offering (the Rights Offering) pursuant to which our wholly owned subsidiary, Iterum Therapeutics Bermuda Limited (Iterum Bermuda), sold units (Units) consisting of (i) 6.500% Exchangeable Senior Subordinated Notes due 2025 (Exchangeable Notes); and (ii) Limited Recourse Royalty-Linked Subordinated Notes (RLNs and, together with the Exchangeable Notes, the Securities), to certain existing and new investors. In April 2018, we entered into a secured credit facility with SVB and made an initial drawdown of $15.0 million pursuant to a loan and security agreement. In April 2020, we entered into a note (PPP loan) with SVB of $0.7 million under the Paycheck Protection Program. In early June 2020, we issued and sold, in a registered direct offering (June 3, 2020 Offering), ordinary shares for aggregate gross proceeds to us of $5.0 million and net proceeds of $4.3 million after deducting fees payable to the placement agent and other offering expenses payable by us. In late June 2020, we issued and sold, in a registered direct offering (June 30, 2020 Offering), ordinary shares for aggregate gross proceeds to us of $5.0 million and net proceeds of $4.2 million after deducting fees payable to the placement agent and other offering expenses payable by us. In October 2020, we issued and sold, in a registered public offering (October 2020 Offering), ordinary shares and pre-funded warrants exercisable for ordinary shares, each offered together with warrants exercisable for ordinary shares, for aggregate gross proceeds to us of $17.4 million and net proceeds of $15.5 million after deducting fees payable to the placement agent and other offering expenses payable by us. On February 8 and February 10, 2021, we issued and sold, pursuant to an underwritten agreement and including the underwriter's exercise in full of its option to purchase additional ordinary shares (February 2021 Underwritten Offering), ordinary shares for aggregate gross proceeds to us of $46.0 million and net proceeds of $42.1 million after deducting fees payable to the underwriter and other offering expenses payable by us. On February 12, 2021, we issued and sold, in a registered public offering (February 2021 Registered Direct Offering), ordinary shares for aggregate gross proceeds to us of $35.0 million and net proceeds of $32.2 million after deducting fees payable to the placement agent and other offering expenses payable by us. At September 30, 2022, net proceeds of $16.2 million have been received from the exercise of certain warrants issued as part of the June 30, 2020 Offering, October 2020 Offering and February 2021 Underwritten Offering. We have devoted substantially all of our financial resources and efforts to research and development, including preclinical and clinical development, for our sulopenem program.

Following receipt of the CRL, in order to reduce operating expenses and conserve cash resources, we halted any remaining pre-commercial activities for oral sulopenem and plan to limit spending to essential costs required in connection with the potential resubmission of the NDA.

We expect to continue to incur significant expenses and increasing operating losses as we conduct clinical trials of oral sulopenem and sulopenem including the ongoing Phase 3 clinical trial being conducted in response to the CRL, seek marketing approval for oral sulopenem if clinical trials are successful, engage in pre-commercialization activities and pursue the development of our sulopenem program in additional indications, including through preclinical and clinical development. Our expenses will also increase substantially if and as we:

- conduct additional clinical trials for oral sulopenem and/or sulopenem, which includes the ongoing Phase 3 clinical trial being conducted to support potential resubmission of our NDA for oral sulopenem;
- initiate other studies as part of our sulopenem program, some of which may be required for regulatory approval of our product candidates and/or may be conducted in response to the CRL;
- establish sales, marketing and distribution capabilities either directly or through a third-party, to commercialize oral sulopenem and/or sulopenem in the United States if we obtain marketing approval from the FDA;
- establish manufacturing and supply chain capacity sufficient to provide commercial quantities of oral sulopenem and/or sulopenem, if we obtain marketing approval and undertake commercialization activities;
- pursue the development of our sulopenem program in additional indications;
- maintain, expand, defend and protect our intellectual property portfolio;
- hire additional clinical, scientific and commercial personnel;
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts; and
- acquire or in-license other product candidates or technologies.

We will require additional capital to fund our operations. If we fail to obtain financing when needed or on acceptable terms, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

Developing pharmaceutical products is a time-consuming, expensive and uncertain process that takes years to complete. We expect to continue to incur significant expenses and increasing operating losses as we conduct clinical trials of oral sulopenem and sulopenem, including the ongoing Phase 3 clinical trial and non-clinical development being conducted in response to the CRL, seek marketing approval for oral sulopenem if clinical trials are successful, engage in pre-commercialization activities, and pursue the development of our sulopenem program in additional indications, including through preclinical and clinical development. If we obtain marketing approval for oral sulopenem, sulopenem or any future product candidate and undertake commercialization activities, we expect to incur significant commercialization expenses related to product sales, marketing, distribution and manufacturing. Some of these expenses may be incurred in advance of marketing approval, and could be substantial.

Based on our current operating plan, we estimate that our cash, cash equivalents and short-term investments as of September 30, 2022 should be sufficient to fund our operating expenses into 2024. However, we have based this estimate on assumptions that may prove to be wrong, and our operating plans may change as a result of many factors and various risks and uncertainties.

We will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources. Adequate additional financing may not be available to us on acceptable terms, or at all. Although we have successfully raised capital in the past, there is no assurance that we will be successful in obtaining sufficient funding on terms acceptable to us to fund continuing operations, if at all. If we fail to obtain financing when needed or on acceptable terms, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts, which would have a negative effect on our financial condition and our ability to develop and commercialize our sulopenem program and otherwise pursue our business strategy.

Changing circumstances could cause us to consume capital significantly faster than we currently anticipate, and we may need to spend more than currently expected because of circumstances beyond our control. Our future funding requirements, both short-term and long-term, will depend on many factors, including:

- the timing and costs of our clinical trials of oral sulopenem and sulopenem, including any clinical trials or non-clinical studies which may be required for regulatory approval of our product candidates, including the ongoing Phase 3 clinical trial and non-clinical development being conducted in response to the CRL and to support a potential resubmission of the NDA for approval of oral sulopenem;
- any other activities that may be required in connection with the potential resubmission of the NDA for oral sulopenem;
- the timing of regulatory filings including a potential resubmission of the NDA for oral sulopenem;
- the timing of regulatory review and potential approval of any product candidates, including oral sulopenem for the treatment of uUTI;
- the initiation, progress, timing, costs and results of preclinical studies and clinical trials of other potential product candidates and of our current product candidates in additional indications;
- the amount of funding that we receive under government awards that we may apply for in the future;
- the number and characteristics of product candidates that we pursue;
- the outcome, timing and costs of seeking regulatory approvals;
- the costs of commercialization activities for oral sulopenem and/or sulopenem and other product candidates if we receive marketing approval, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;
- the receipt of marketing approval and revenue received from any potential commercial sales of oral sulopenem and/or sulopenem;
- the terms and timing of any future collaborations, licensing or other arrangements that we may establish;
- the amount and timing of any payments we may be required to make, or that we may receive, in connection with the licensing, filing, prosecution, defense and enforcement of any patents or other intellectual property rights, including milestone and royalty payments and patent prosecution fees that we are obligated to pay pursuant to an exclusive license agreement with Pfizer Inc. (Pfizer) (the Pfizer License) or other future license agreements;
- the amount and timing of any payments we may be required to make in connection with the RLNs and the repayment of the Exchangeable Notes, if required;

•the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against any intellectual property related claims;

•the costs of operating as a public company;

•the extent to which we in-license or acquire other products and technologies;

•the impact of the COVID-19 pandemic on the economy and our business generally including the impact the pandemic may have on our ability to efficiently conduct and complete the ongoing Phase 3 clinical trial to support a potential resubmission of our NDA for oral sulopenem, timing of regulatory review, potential approval and commercialization of any future products, including oral sulopenem for the treatment of uUTI; and

•the outcome, impact, effects and results of our evaluation of corporate, strategic, financial and financing alternatives, including the terms, timing, structure, value, benefits and costs of any corporate, strategic, financial or financing alternative and our ability to complete one at all.

Our financial statements include substantial non-operating gains or losses resulting from required quarterly revaluation under generally accepted accounting principles of our outstanding derivative instruments.

Generally accepted accounting principles in the United States require that we report the value of certain derivatives in instruments we have issued as liabilities on our balance sheet and report changes in the value of these derivatives as non-operating gains or losses on our statement of operations. The value of the derivatives is required to be recalculated (and resulting non-operating gains or losses reflected in our statement of operations and resulting adjustments to the associated liability amounts reflected on our balance sheet) on a quarterly basis. The valuations are based upon a number of factors and estimates, including estimates based upon management's judgment. Certain of the derivative values are directly correlated to the value of our ordinary shares. Due to the nature of the required calculations and the large number of ordinary shares involved in such calculations, changes in our share price and/or changes in management's assumptions may result in significant changes in the value of the derivatives and resulting gains and losses on our statement of operations.

In light of the FDA's CRL regarding our NDA for oral sulopenem, we halted any remaining pre-commercial activities while we work toward our goal of approval of oral sulopenem. Neither resubmission nor approval of our NDA for oral sulopenem is assured.

In July 2021, we received a CRL from the FDA regarding our NDA for oral sulopenem for the treatment of uUTIs in patients with a quinolone non-susceptible pathogen. In light of the CRL and in order to reduce operating expenses and conserve cash resources, we have halted all remaining pre-commercial activities for oral sulopenem.

In the CRL, the FDA determined that additional data are necessary to support approval for the treatment of adult women with uUTIs caused by designated susceptible microorganisms proven or strongly suspected to be non-susceptible to a quinolone. The FDA recommended that we conduct at least one additional adequate and well-controlled clinical trial, potentially using a different comparator drug. In July 2022 we reached an agreement with the FDA under the SPA process on the design, endpoints and statistical analysis of a Phase 3 clinical trial for oral sulopenem for the treatment of uUTIs and we commenced enrollment in that clinical trial, known as REASSURE, in October 2022. The study is designed as a non-inferiority trial comparing oral sulopenem and Augmentin® (amoxicillin/clavulanate) in the Augmentin® susceptible population. Additionally, though not an approvability issue, the FDA recommended in its CRL that we conduct additional non-clinical PK/PD studies to support dose selection for the proposed treatment indication(s). We have commenced additional non-clinical PK/PD investigations to support the dosing regimen selected for oral sulopenem, as recommended by the FDA. There can be no assurance that we will be in a position to resolve the matters set forth in the CRL, that we will be able to complete the ongoing Phase 3 clinical trial and complete the non-clinical studies intended to support a resubmission of our NDA or that any data generated by such clinical and non-clinical investigation will be adequate to support resubmission or approval of our NDA.

We and our Chief Executive Officer and Chief Financial Officer have been named as defendants in a lawsuit that could result in substantial costs and divert management's attention.

On August 5, 2021, a putative class action lawsuit was filed against us, our Chief Executive Officer and our Chief Financial Officer. The complaint generally alleges that the defendants violated Sections 10(b) and/or 20(a) of the Securities Exchange Act of 1934 and Rule 10b-5 promulgated thereunder by making purportedly material misstatements or omissions concerning our NDA to the FDA for marketing approval of oral sulopenem for the treatment of uUTIs in patients with a quinolone non-susceptible pathogen and the likelihood of such approval. The complaint seeks, among other things, unspecified damages, attorneys' fees, expert fees and other costs.

The defendants deny any and all allegations of wrongdoing and believe they have valid defenses against these claims and, therefore, intend to vigorously defend against this lawsuit. We are unable, however, to predict the outcome of this matter at this time. Moreover, any conclusion of this matter in a manner adverse to us and for which we incur substantial costs or damages not covered by our directors' and officers' liability insurance would have a material adverse effect on our financial condition and business. In addition, the litigation could adversely impact our reputation and divert management and our board of directors' attention and resources from other priorities, including the execution of our business plan and strategies that are important to our ability to grow our business, any of which could have a material adverse effect on our business. Additional lawsuits may be filed.

Provisions in the EN Indenture and RLN Indenture may deter or prevent us from raising additional capital to fund our operations.

Provisions in the agreements we entered into in connection with our financings may deter or prevent us from raising additional capital to fund our operations as and when needed. For example, the indenture governing the Exchangeable Notes (the EN Indenture) contains negative covenants prohibiting our wholly owned subsidiary, Iterum Therapeutics Bermuda Limited (Iterum Bermuda), as well as us and our wholly owned subsidiaries and their subsidiaries (the Guarantors), who guaranteed Iterum Bermuda's obligations under the Exchangeable Notes, from, among other things, incurring any indebtedness that is not permitted by the EN Indenture and entering into transactions with significant shareholders (as defined in the EN Indenture). In addition, the indenture governing the RLNs (the RLN Indenture) contains negative covenants prohibiting Iterum Bermuda and the Guarantors from, among other things, selling, transferring or assigning certain assets and taking other actions outside the ordinary course of business that would reasonably be expected to reduce the amount of payments under the RLNs.

These provisions could deter or prevent us from raising additional capital. Our failure to raise capital as and when needed would have a negative effect on our financial condition and our ability to develop and commercialize our sulopenem program and otherwise pursue our business strategy.

We are heavily dependent on the success of our sulopenem program, and our ability to develop, obtain marketing approval for and successfully commercialize oral sulopenem and sulopenem. If we are unable to achieve and sustain profitability, the market value of our ordinary shares will likely decline.

Our ability to become and remain profitable depends on our ability to generate revenue. To date, we have invested substantially all of our efforts and financial resources in the development of oral sulopenem and sulopenem, which are currently our two product candidates in development. Our prospects, including our ability to finance our operations and generate revenue from product sales, currently depend entirely on the development and commercialization of our sulopenem program.

We do not expect to generate significant revenue unless and until we obtain marketing approval for, and commercialize, oral sulopenem and/or sulopenem. Our ability to generate future revenue from product sales will require us to be successful in a range of challenging clinical and commercial activities, including:

- resolving the matters set out in the CRL received in July 2021 in connection with our NDA for oral sulopenem;
- enrolling and successfully completing any clinical trials that may be required for regulatory approval of our product candidates, including the ongoing Phase 3 clinical trial being conducted in response to the CRL;
- applying for and obtaining marketing approval for oral sulopenem and/or sulopenem;
- protecting and maintaining our rights to our intellectual property portfolio related to our sulopenem program;
- establishing and maintaining supply and manufacturing relationships with third parties that can support clinical development and can provide adequate commercial quantities of oral sulopenem and/or sulopenem, if approved;
- establishing sales, marketing and distribution capabilities either directly or through a third-party, to commercialize oral sulopenem and/or sulopenem or entering into collaboration arrangements for the commercialization of oral sulopenem and/or sulopenem where we choose not to commercialize directly ourselves; and
- obtaining market acceptance of oral sulopenem and/or sulopenem as viable treatment options.

Because of the numerous risks and uncertainties associated with developing pharmaceutical products, we are unable to predict the extent of any future losses or when, or if, we will become profitable. We may never succeed in any or all of these activities and, even if we do, we may never generate revenue that is significant or large enough to achieve profitability. Our expenses could increase if we are required by the FDA, the European Medicines Agency (EMA), or any comparable foreign regulatory authority, to perform different studies or studies in addition to those currently expected, including in response to the CRL received in July 2021, or if there are any delays in completing such studies or with the development of our sulopenem program or any future product candidates. Even if oral sulopenem or sulopenem are approved for commercial sale, we anticipate incurring significant costs associated with the commercial launch of oral sulopenem and/or sulopenem. Where we enter into collaboration arrangements with third-party collaborators for commercialization of product candidates, our product revenues or the profitability of these product revenues to us would likely be lower than if we were to directly market and sell products in those markets.

Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our company could cause our shareholders to lose all or part of their investment.

Our indebtedness imposes certain operating and other restrictions on us and could adversely affect our ability to raise additional capital.

The EN Indenture and the RLN Indenture each contain affirmative and negative covenants which impose operating and other restrictions on us, including, among other things, incurring any indebtedness that is not permitted by the EN Indenture or amending the terms of any subordinated indebtedness, entering into strategic transactions or transferring any material assets and undergoing a change of control transaction (subject to certain exceptions, including in the case of a change of control transaction, a transaction in which each holder of an outstanding Exchangeable Note receives cash consideration of at least 300% of the outstanding principal amount of such Exchangeable Notes). For example, pursuant to the EN Indenture, we are required to obtain the consent of a portion of the holders of the Exchangeable Notes prior to entering into collaboration agreements, exclusive selling arrangements or similar partnerships including a definitive agreement for commercialization services in the United States. Failure to comply with these terms could result in an event of default which could lead, among other things, to an acceleration of amounts due under the EN Indenture and the obligation to pay default interest. Moreover, obtaining a consent to a waiver of these terms is subject to a veto right of the holders of 30% of the outstanding Exchangeable Notes, in the case of the EN Indenture, and 30% of the outstanding RLNs, in the case of the RLN Indenture, and must include Sarissa Capital Offshore Master Fund LP, Sarissa Capital Catapult Fund LLC and Sarissa Capital Hawkeye Fund LP (collectively with their affiliates, Sarissa) so long as Sarissa and its affiliates own at least 10% of the outstanding RLNs. This veto right could make it more difficult for us to obtain a waiver than would otherwise be the case. In addition, the rate at which the Exchangeable Notes are exchangeable for our ordinary shares is subject to adjustment, including pursuant to anti-dilution protections. For example, following the October 2020 Offering, the exchange rate of the Exchangeable Notes increased and the exchange price of the Exchangeable Notes adjusted from the previous exchange price of $15.00 per ordinary share (at the exchange rate of 66.666 shares per $1000 of principal and interest on the Exchangeable Notes) to $11.6624 per ordinary share (at an adjusted exchange rate of 85.7456 shares per $1,000 of principal and interest on the Exchangeable Notes). As of September 30, 2022, approximately $12.6 million aggregate principal amount of Exchangeable Notes remained outstanding.

In addition, on October 7, 2022, we entered into a sales agreement (the Sales Agreement) with H.C. Wainwright & Co., LLC (HC Wainwright), as agent, pursuant to which we may offer and sell ordinary shares, nominal value $0.01 per share for aggregate gross sales proceeds of up to $16.0 million (not to exceed 4,478,180 ordinary shares as at the date of this filing), from time to time through HC Wainwright by any method permitted that is deemed to be an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended. As of the date of this filing, we have not issued or sold any ordinary shares pursuant to the Sales Agreement. Depending on the public offering prices, the number of shares that we sell pursuant to the Sales Agreement and any potential increase to the exchange rate of the Exchangeable Notes, we may not have sufficient authorized share capital or share issuance authorities to convert all of the Exchangeable Notes into ordinary shares following any sales of shares pursuant to the Sales Agreement and could be required to settle any exchanges with cash to the extent we do not have available authorized shares. If we elect to settle any exchanges in cash, or we do not have authorized and available ordinary shares needed to satisfy physical exchange of the Exchangeable Notes, our liquidity could be adversely affected and/or we may not have sufficient cash available at that time to satisfy such cash settlement. In addition, in the event we elect to settle exchanges of Exchangeable Notes with ordinary shares, we would be limited in our ability to issue equity for other purposes which could adversely affect our shareholders and our ability to raise additional capital.

In addition, the exercise price and the number of shares issuable under our outstanding warrants are subject to adjustment pursuant to the terms of the applicable warrant. This indebtedness could make it more difficult for us to raise additional capital to fund our operations.

Servicing our indebtedness will require a significant amount of cash, and we may not have sufficient cash flow from our business to pay our indebtedness.

Our ability to make payments of the principal of, to pay interest and special interest on the Exchangeable Notes, or to make cash payments, if we so elect, in connection with any exchange of Exchangeable Notes depends on our future performance, which is subject to economic, financial, competitive and other factors beyond our control. Our business may not generate cash flow sufficient to service the Exchangeable Notes or other indebtedness and make necessary capital expenditures. If we are unable to generate such cash flow, we may be required to adopt one or more alternatives, such as selling assets, restructuring indebtedness or obtaining additional equity capital on terms that may be onerous or highly dilutive. Our ability to refinance indebtedness will depend on the capital markets and our financial condition at such time. We may not be able to engage in any of these activities or engage in these activities on desirable terms, which could result in a default on our debt obligations.

We may incur substantially more debt or take other actions that would intensify the risks discussed above.

We and our subsidiaries may be able to incur substantial additional debt in the future, subject to the restrictions contained in our current and future debt instruments, some of which may be secured debt. While the EN Indenture restricts our ability to incur additional indebtedness, it allows for certain additional indebtedness and any such restrictions may be waived. If new debt is added to our current debt levels, the related risks that we now face could intensify.

We may not have the ability to raise the funds necessary to settle exchanges of the Exchangeable Notes in cash or to repurchase the Exchangeable Notes upon a fundamental change, and our future debt may limit our ability to pay cash upon exchange or repurchase of the Exchangeable Notes.

Holders of the Exchangeable Notes will have the right to require us to repurchase all or a portion of their Exchangeable Notes upon the occurrence of a fundamental change at specified repurchase prices. In addition, upon exchange of the Exchangeable Notes, unless we elect to deliver solely ordinary shares to settle such exchange (other than paying cash in lieu of delivering any fractional share), we would be required to make specified cash payments in respect of the Exchangeable Notes being exchanged. However, we may not have enough available cash or be able to obtain financing at the time we are required to make repurchases of Exchangeable Notes surrendered therefor or to pay cash with respect to Exchangeable Notes being exchanged. In addition, our ability to repurchase or to pay cash upon exchange of the Exchangeable Notes may be limited by law, regulatory authority, and future indebtedness.

Our failure to repurchase Exchangeable Notes at a time when the repurchase is required by the EN Indenture or to pay cash upon exchange of the Exchangeable Notes as required by the EN Indenture would constitute a default under the EN Indenture. A default under the EN Indenture or a fundamental change itself could also lead to a default under agreements governing our future indebtedness. If the payment of the related indebtedness were to be accelerated after any applicable notice or grace periods, we may not have sufficient funds to repay the indebtedness and any accrued and unpaid interest and repurchase the Exchangeable Notes or to pay cash upon exchange of the Exchangeable Notes. As of September 30, 2022, approximately $12.6 million aggregate principal amount of Exchangeable Notes remained outstanding.

The exchange feature of the Exchangeable Notes may adversely affect our financial condition and operating results.

Beginning January 21, 2021 and prior to the earlier of (i) the close of business on the scheduled trading day immediately preceding a mandatory exchange notice for the Exchangeable Notes, which would be triggered by the occurrence of any of certain mandatory exchange trigger events specified in the EN Indenture, and (ii) the close of business on the second scheduled trading day immediately preceding the interest record date, holders of Exchangeable Notes are entitled to exchange the Exchangeable Notes at any time at their option. If holders continue to elect to exchange their Exchangeable Notes, unless we elect to satisfy our exchange obligation by delivering solely ordinary shares (other than paying cash in lieu of delivering any fractional share), we would be required to settle a portion or all of our exchange obligation in cash, which could adversely affect our liquidity. The relevant accounting rules require that we recognize liabilities which appropriately reflect our obligations specified in the EN Indenture. Therefore, even if holders do not elect to exchange their Exchangeable Notes, our liabilities and statement of operations could be significantly impacted.

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

Unless and until we can generate a substantial amount of revenue from our sulopenem program or future product candidates, we expect to finance our future cash needs through equity offerings, debt financings, collaboration agreements, other third-party funding, strategic alliances, licensing arrangements, marketing and distribution arrangements or government funding.

We may seek additional capital due to favorable market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans.

We filed a universal shelf registration statement on Form S-3 with the SEC, which was declared effective on October 17, 2022 (File No. 333-267795), and pursuant to which we registered for sale up to $100.0 million of any combination of our debt securities, ordinary shares, preferred shares, subscription rights, purchase contracts, units and/or warrants from time to time and at prices and on terms that we may determine. The extent to which we are able to utilize a shelf registration statement as a source of funding will depend on a number of factors, including the prevailing market price of our ordinary shares, general market conditions and applicability of restrictions on our ability to utilize the shelf registration statement to sell more than one-third of the market value of our public float, meaning the aggregate market value of voting and non-voting ordinary shares held by non-affiliates, in any trailing 12-month period.

On October 7, 2022, we entered into the Sales Agreement with HC Wainwright, as agent, pursuant to which we may offer and sell ordinary shares, nominal value $0.01 per share for aggregate gross sales proceeds of up to $16.0 million (not to exceed 4,478,180), from time to time through HC Wainwright, by any method permitted that is deemed to be an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended.

Our issuance of additional securities, whether equity or debt, or the possibility of such issuance, may cause the market price of our ordinary shares to decline, and our shareholders may not agree with our financing plans or the terms of such financings. To the extent that we raise additional capital through the sale of ordinary shares, convertible securities or other equity securities, the ownership interests of our then existing shareholders may be materially diluted, and the terms of these securities could include liquidation or other preferences and antidilution protections that could adversely affect the rights of our then existing shareholders. Further debt financing, if available, would result in increased fixed payment obligations and may involve agreements that include restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends, which could adversely affect our ability to conduct our business. In addition, securing additional financing would require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect our management's ability to oversee the development of our product candidates.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial resources, we initially focused our sulopenem development program on the specific indications of uUTI, complicated urinary tract infections (cUTI) and complicated intra-abdominal infections (cIAI), all of which are focused on what we believe to be the most pressing near-term medical needs, in terms of both their potential for marketing approval and commercialization. As a result, we may forego or delay pursuit of opportunities with other potential product candidates or developing our sulopenem program in other indications that may prove to have greater commercial potential. For example, while we believe that sulopenem has the potential to treat cIAIs and cUTIs in humans based on the results of prior preclinical studies and clinical trials, sulopenem did not meet the primary endpoint of statistical non-inferiority compared to the control therapy in our Phase 3 cIAI and cUTI clinical trials. While we believe the secondary supporting analyses and safety data in all three prior Phase 3 clinical trials support the potential of sulopenem in the treatment of multi-drug resistant infections, we cannot guarantee that these supporting analyses are indicative of efficacy of sulopenem in treating cIAIs or cUTIs. Similarly, while we believe that sulopenem has the potential to treat uUTIs in humans based on the results of prior pre-clinical studies and clinical trials, oral sulopenem did not meet the primary endpoint of statistical non-inferiority compared to ciprofloxacin in the population of patients with baseline pathogens susceptible to ciprofloxacin in our prior Phase 3 uUTI clinical trial. However, in the uUTI clinical trial, in the population of patients with baseline pathogens resistant to quinolones, sulopenem achieved the related primary endpoint by demonstrating statistical significance in the overall response rate by treatment arm in the ciprofloxacin-resistant population, providing evidence of a treatment effect in patients with uUTI. Based on discussions with the FDA at a pre-NDA meeting in September 2020 and previous correspondence with the FDA, we submitted an NDA for oral sulopenem for the treatment of uUTIs in patients with a quinolone non-susceptible pathogen in the fourth quarter of 2020 and the FDA accepted the application for review in January 2021. We received a CRL from the FDA on July 23, 2021 for our NDA. The CRL provided that the FDA had completed its review of the NDA and had determined that it could not approve the NDA in its present form. The CRL further provided that additional data are necessary to support approval of oral sulopenem for the treatment of adult women with uUTIs caused by designated susceptible microorganisms proven or strongly suspected to be non-susceptible to a quinolone and recommended that we conduct at least one additional adequate and well-controlled clinical trial, potentially using a different comparator drug. In July 2022 we reached an agreement with the FDA under the SPA process on the design, endpoints and statistical analysis of a Phase 3 clinical trial for oral sulopenem for the treatment of uUTIs and we commenced enrollment in that clinical trial, known as REASSURE, in October 2022. The study is designed as a non-inferiority trial comparing oral sulopenem and Augmentin® (amoxicillin/clavulanate) in the Augmentin® susceptible population. Additionally, though not an approvability issue, the FDA recommended in its CRL that we conduct additional non-clinical PK/PD studies to support dose selection for the proposed treatment indication(s). We have commenced additional non-clinical PK/PD investigations to support the dosing regimen selected for oral sulopenem, as recommended by the FDA. There can be no assurance that we will be in a position to resolve the matters set forth in the CRL, that we will be able to complete the ongoing Phase 3 clinical trial and non-clinical studies intended to support a resubmission of our NDA or that any data generated by such clinical and non-clinical investigation will be adequate to support resubmission or approval of our NDA.

Further, due to a variety of factors, including those described in this "Risk Factors" section, we may nonetheless be delayed in obtaining or ultimately be unable to obtain FDA approval for oral sulopenem for uUTI or any other indication or for any other product or to successfully commercialize sulopenem.

Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable product candidates. 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 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 the product candidate.

We have broad discretion in the use of our funds and may not use them effectively.

We have broad discretion in the application of our available funds and could spend the funds in ways that do not improve our results of operations or enhance the value of our ordinary shares. Our failure to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our ordinary shares to decline and delay the development of our product candidates. Pending their use, we may invest funds in a manner that does not produce income or that loses value.

Risks Related to Clinical Development and Commercialization

We are heavily dependent on the success of our sulopenem program, and our ability to develop, obtain marketing approval for and successfully commercialize oral sulopenem and/or sulopenem. If we are unable to obtain marketing approvals for oral sulopenem or sulopenem, or if thereafter we fail to commercialize oral sulopenem or sulopenem or experience significant delays in doing so, our business will be materially harmed.

We currently have no products approved for sale and have invested substantially all of our efforts and financial resources in the development of our sulopenem program. Our near-term prospects are substantially dependent on our ability to develop, apply for and obtain marketing approval for and successfully commercialize oral sulopenem and/or sulopenem. The success of our sulopenem program will depend on several factors, including the following:

•resolving the issues set out in the CRL received in July 2021 in connection with our NDA for oral sulopenem;

•successful enrollment in, and completion of, clinical trials, including any clinical trials that may be required for regulatory approval of our product candidates, including the ongoing Phase 3 trial being conducted in response to the CRL;

•clinical trial results with safety, tolerability and efficacy profiles that are satisfactory to the FDA or any comparable foreign regulatory authority;

•timely completion of any additional clinical trials and non-clinical studies conducted to support the filing for regulatory approvals of our sulopenem program, if required by the FDA or any comparable foreign regulatory authority, including the ongoing Phase 3 clinical trial and non-clinical studies being conducted in response to the CRL;

•receipt of marketing approvals from applicable regulatory authorities;

•establishment and maintenance of arrangements with third-party manufacturers to obtain commercial supply at a scale sufficient to meet anticipated demand and at a cost appropriate for our commercialization;

•acquisition and maintenance of patent, trade secret and other intellectual property protection and regulatory exclusivity, both in the United States and internationally, including our ability to maintain the Pfizer License;

•protection of our rights in our intellectual property portfolio;

•launch of commercial sales of oral sulopenem and/or sulopenem, if approved, whether alone or in collaboration with others;

•the effectiveness of our own or any future collaborators' marketing, sales and distribution strategy and operations;

•acceptance of oral sulopenem and/or sulopenem, if approved, by patients, physicians and the medical community at large;

•our ability to obtain and sustain coverage and an adequate level of reimbursement by third-party payors;

•the prevalence, frequency and severity of adverse side effects of oral sulopenem and/or sulopenem;

•the availability, perceived advantages, relative cost and relative efficacy of alternative and competing therapies; and

•an acceptable safety profile of oral sulopenem and/or sulopenem following approval.

Many of these factors are beyond our control, including clinical development, the regulatory submission process, potential threats to our intellectual property rights, manufacturing and the impact of competition.

Based on discussions with the FDA at a pre-NDA meeting in September 2020 and previous correspondence with the FDA, we submitted an NDA for oral sulopenem for the treatment of uUTIs in patients with a quinolone non-susceptible pathogen in the fourth quarter of 2020 and the FDA accepted the application for review in January 2021. We received a CRL from the FDA on July 23, 2021 in respect of our NDA. The CRL provided that additional data are necessary to support approval of oral sulopenem for the treatment of adult women with uUTIs caused by designated susceptible microorganisms proven or strongly suspected to be non-susceptible to a quinolone and recommended that we conduct at least one additional adequate and well-controlled clinical trial, potentially using a different comparator drug. In July 2022 we reached an agreement with the FDA under the SPA process on the design, endpoints and statistical analysis of a Phase 3 clinical trial for oral sulopenem for the treatment of uUTIs and we commenced enrollment in that clinical trial, known as REASSURE, in October 2022. The study is designed as a non-inferiority trial comparing oral sulopenem and Augmentin® (amoxicillin/clavulanate) in the Augmentin® susceptible population. Additionally, though not an approvability issue, the FDA recommended in its CRL that we conduct additional non-clinical PK/PD studies to support dose selection for the proposed treatment indication(s). We have commenced additional non-clinical PK/PD investigations to support the dosing regimen selected for oral sulopenem, as recommended by the FDA. There can be no assurance that we will be in a position to resolve the matters set forth in the CRL, that we will be able to complete the ongoing Phase 3 clinical trial and non-clinical studies intended to support a resubmission of our NDA or that any data generated by such clinical and non-clinical investigation will be adequate to support resubmission or approval of our NDA. As we work with the FDA to resolve the issues set out in the CRL, we will be delayed in obtaining, and may ultimately be unable to obtain, FDA approval for sulopenem for this or any other indication or for any other product or to successfully commercialize sulopenem.

If we are unable to develop, receive marketing approval for, or successfully commercialize oral sulopenem and/or sulopenem, or if we experience delays as a result of any of these factors or otherwise, our business could be materially harmed.

Our company has no experience in obtaining regulatory approval for a drug.

Our company has never obtained regulatory approval for, or commercialized, a drug. We must complete extensive preclinical and clinical trials to demonstrate the safety and efficacy of our product candidates in humans before we will be able to obtain these approvals. To gain approval to market a product candidate, we must provide the FDA and foreign regulatory authorities with non-clinical, clinical and chemistry, manufacturing, and controls (CMC) data that adequately demonstrates the safety and efficacy of the product for the intended indication(s) applied for in the NDA(s) or other respective regulatory filing.

We may never succeed in achieving regulatory approval for any of our product candidates. For example, in the results of our cIAI clinical trial, sulopenem did not meet the primary endpoint of statistical non-inferiority compared to the control therapy for the cIAI trial. In the second quarter of 2020, we announced the results of our Phase 3 clinical trials of sulopenem for the treatment of cUTI and uUTI. In the cUTI trial, sulopenem did not meet the primary endpoint of statistical non-inferiority compared to the control therapies with the difference in response rates driven almost entirely by higher rates of asymptomatic bacteriuria on the sulopenem IV to oral sulopenem arm relative to the ertapenem IV to oral ciprofloxacin arm, only evident at the test of cure visit; the rates of patients receiving additional antibiotics or with residual cUTI symptoms were similar between therapies. Similarly, in the uUTI trial, sulopenem did not meet the primary endpoint of statistical non-inferiority compared to ciprofloxacin in the population of patients with baseline pathogens susceptible to ciprofloxacin driven to a large degree by a greater amount of asymptomatic bacteriuria in the sulopenem treated patients at the test of cure visit relative to those receiving ciprofloxacin. However, in the uUTI trial, in the population of patients with baseline pathogens resistant to quinolones, sulopenem achieved the related primary endpoint by demonstrating statistical significance in the overall response rate by treatment arm in the ciprofloxacin-resistant population, providing evidence of a treatment effect in patients with uUTI. Notwithstanding failure to meet the endpoints described above, in all three Phase 3 clinical trials, at all timepoints measured, the clinical response to sulopenem and/or oral sulopenem was similar to the comparator regimen (non-inferior), except in the instance of the quinolone non-susceptible population in the prior Phase 3 uUTI trial in which oral sulopenem was statistically superior. Based on discussions with the FDA at a pre-NDA meeting in September 2020 and previous correspondence with the FDA, we submitted an NDA for oral sulopenem for the treatment of uUTIs in patients with a quinolone non-susceptible pathogen in the fourth quarter of 2020 and the FDA accepted the application for review in January 2021. We received a CRL from the FDA on July 23, 2021 for our NDA. The CRL provided that additional data are necessary to support approval of oral sulopenem for the treatment of adult women with uUTIs caused by designated susceptible microorganisms proven or strongly suspected to be non-susceptible to a quinolone and recommended that we conduct at least one additional adequate and well-controlled clinical trial, potentially using a different comparator drug. In July 2022 we reached an agreement with the FDA under the SPA process on the design, endpoints and statistical analysis of a Phase 3 clinical trial for oral sulopenem for the treatment of uUTIs and we commenced enrollment in that clinical trial, known as REASSURE, in October 2022. The study is designed as a non-inferiority trial comparing oral sulopenem and Augmentin® (amoxicillin/clavulanate) in the Augmentin® susceptible population. Additionally, though not an approvability issue, the FDA recommended in its CRL that we conduct additional non-clinical PK/PD studies to support dose selection for the proposed treatment indication(s). We have commenced additional non-clinical PK/PD investigations to support the dosing regimen selected for oral sulopenem, as recommended by the FDA. Depending on the extent of these or any other FDA-required studies, approval of any NDA(s) or other application that we submit may be significantly delayed, possibly for several years, or may require us to expend more resources than we have available. There can be no assurance that we will be in a position to resolve the matters set forth in the CRL, that we will be able to complete the ongoing Phase 3 clinical trial and non-clinical studies intended to support a resubmission of our NDA or that any data generated by such clinical and non-clinical investigation will be adequate to support resubmission or approval of our NDA.

We may elect to discontinue, delay or modify clinical trials of some product candidates or focus on others. Any changes in the outcome of any of these variables with respect to the development of our product candidates in clinical development could mean a significant change in the costs and timing associated with the development of these product candidates.

Additionally, any failure or delay in obtaining regulatory approvals would prevent us from commercializing oral sulopenem and/or sulopenem, generating revenues and achieving and sustaining profitability. It is also possible that additional studies, if performed and completed, may not be considered sufficient by the FDA to approve any NDA(s) or other application that we submit. If any of these outcomes occur, we may be forced to abandon the development of our product candidates, which would materially adversely affect our business and could potentially cause us to cease operations. We face similar risks for our applications in other countries.

If clinical trials of oral sulopenem, sulopenem or any other product candidate that we may advance to clinical trials fail to demonstrate safety and efficacy to the satisfaction of the FDA or comparable foreign regulatory authorities, or do not otherwise produce favorable results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of oral sulopenem, sulopenem or any other product candidate.

We may not commercialize, market, promote, or sell any product candidate in the United States without obtaining marketing approval from the FDA or in other countries without obtaining approvals from comparable foreign regulatory authorities, such as the EMA, and we may never receive such approvals. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is inherently uncertain as to outcome. While we submitted an NDA for oral sulopenem for the treatment of uUTIs in patients with a quinolone non-susceptible pathogen in the fourth quarter of 2020, for which we received a CRL from the FDA on July 23, 2021, we had not previously submitted an NDA to the FDA or similar applications to comparable foreign regulatory authorities for any of our product candidates.

Our business currently heavily depends on the successful development, regulatory approval and commercialization of our sulopenem program. The clinical development of our sulopenem program, or any future product candidates, is susceptible to the risk of failure inherent at any stage of drug development, including failure to demonstrate efficacy in a clinical trial or across a broad population of patients, the occurrence of severe adverse events, failure to comply with protocols or applicable regulatory requirements, and determination by the FDA or any comparable foreign regulatory authority that a drug product is not approvable. A number of companies in the pharmaceutical industry, including biotechnology companies, have suffered significant setbacks in clinical trials, even after promising results in earlier non-clinical studies or clinical trials. The results of preclinical and other non-clinical studies and/or early clinical trials of our product candidates or future product candidates may not be predictive of the results of later-stage clinical trials and interim results of a clinical trial do not necessarily predict final results. Notwithstanding any promising results in early non-clinical studies or clinical trials, we cannot be certain that we will not face similar setbacks.

Preclinical and clinical data are often susceptible to varying interpretations and analyses. Although data from clinical trials of oral sulopenem and sulopenem provides support for the overall safety profile of the product candidates, many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for the product candidates. Even if we believe that the results of our clinical trials warrant marketing approval, the FDA or comparable foreign regulatory authorities may disagree and may not grant marketing approval of our product candidates. For example, we received a CRL from the FDA on July 23, 2021 for our NDA for oral sulopenem for the treatment of uUTIs in patients with a quinolone non-susceptible pathogen. The CRL provided that additional data are necessary to support approval of oral sulopenem for the treatment of adult women with uUTIs caused by designated susceptible microorganisms proven or strongly suspected to be non-susceptible to a quinolone and recommended that we conduct at least one additional adequate and well-controlled clinical trial, potentially using a different comparator drug. In July 2022 we reached an agreement with the FDA under the SPA process on the design, endpoints and statistical analysis of a Phase 3 clinical trial for oral sulopenem for the treatment of uUTIs and we commenced enrollment in that clinical trial, known as REASSURE, in October 2022. The study is designed as a non-inferiority trial comparing oral sulopenem and Augmentin® (amoxicillin/clavulanate) in the Augmentin® susceptible population. Additionally, though not an approvability issue, the FDA recommended in its CRL that we conduct additional non-clinical PK/PD studies to support dose selection for the proposed treatment indication(s). We have commenced additional non-clinical PK/PD investigations to support the dosing regimen selected for oral sulopenem, as recommended by the FDA. Notwithstanding our interactions with the FDA to date, there can be no assurance that we will be in a position to resolve the matters set forth in the CRL, that we will be able to complete the ongoing clinical trial and non-clinical studies intended to support a resubmission of our NDA or that any data generated by such clinical and non-clinical investigation will be adequate to support resubmission or approval of our NDA.

In some instances, there can be significant variability in safety and/or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, adherence to the dosing regimen and other trial protocols and the rate of dropout among clinical trial participants, among others. It is possible that even if one or more of our product candidates has a beneficial effect, that effect will not be detected during clinical evaluation as a result of one of the factors listed or otherwise. Conversely, as a result of the same factors, our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any. Similarly, in our clinical trials, we may fail to detect toxicity of or intolerability of our product candidates or may determine that our product candidates are toxic or not well tolerated when that is not in fact the case. In the case of our clinical trials, results may differ on the basis of the type of bacteria with which patients are infected. We cannot assure our shareholders that any clinical trials that we are conducting or other clinical trials that we may conduct will demonstrate consistent or adequate efficacy and safety to obtain regulatory approval to market our product candidates.

We may encounter unforeseen events prior to, during, or as a result of, clinical trials that could delay or prevent us from obtaining regulatory approval for oral sulopenem, sulopenem or any of our other product candidates, including:

- although we conducted our prior Phase 3 clinical trials pursuant to SPA agreements, the FDA or other comparable foreign regulatory authorities may ultimately disagree as to the design or implementation of such clinical trials or other clinical trials, or may request additional data to support approval, such as that requested in the CRL from July 2021;
- although we are conducting the additional Phase 3 clinical trial comparing oral sulopenem and Augmentin® (amoxicillin/clavulanate) pursuant to a SPA agreement, there is no guarantee that the FDA, or any other regulatory authorities, will approve any application that is supported by a clinical trial conducted in accordance with such agreement;
- we may not reach agreement on acceptable terms with all clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different trial sites;
- clinical trials of our product candidates, including the ongoing Phase 3 clinical trial being conducted in response to the CRL, may produce unfavorable or inconclusive results;
- we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- our third-party contractors, including those manufacturing our product candidates or conducting clinical trials on our behalf, may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- the FDA, the local National Health Authorities or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may have to suspend or terminate clinical trials of a product candidate for various reasons, including non-compliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we enter into agreement for clinical and commercial supplies; or
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate.

If we are required to conduct additional clinical trials or other testing of oral sulopenem, sulopenem or any other product candidate beyond the clinical trials and testing that we contemplate, if we are unable to successfully complete clinical trials or other testing of our product candidates, if the results of these clinical trials or tests are unfavorable or are only modestly favorable or if there are safety concerns associated with oral sulopenem, sulopenem or any other product candidate, we may:

- incur additional unplanned costs;
- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or significant safety warnings, including boxed warnings;
- be subject to additional post-marketing testing or other requirements; or
- be required to remove the product from the market after obtaining marketing approval.

Our failure to successfully initiate and complete clinical trials of our product candidates and to demonstrate the efficacy and safety necessary to obtain regulatory approval to market any of our product candidates would significantly harm our business. 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 and impair our ability to successfully commercialize our product candidates, which may harm our business and results of operations. In addition, many of the factors that cause, or lead to, delays of clinical trials may ultimately lead to the denial of regulatory approval of oral sulopenem, sulopenem or any other product candidate.

If we experience delays or difficulties in the enrollment of patients in clinical trials, clinical development activities could be delayed or otherwise adversely affected.

The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the study until its conclusion. While we successfully completed enrollment for all three of our prior Phase 3 clinical trials, we may not be able to initiate and/or continue or complete other clinical trials (including the ongoing Phase 3 clinical trial being conducted in response to the CRL) of oral sulopenem, sulopenem or any other product candidate that we develop if we are unable to locate and enroll a sufficient number of eligible patients to participate in clinical trials as required by the FDA or comparable foreign regulatory authorities, such as the EMA. Patient enrollment is a significant factor in the timing of clinical trials, and is affected by many factors, including:

- the size and nature of the patient population;
- the severity of the disease under investigation;
- the proximity of patients to clinical sites;
- the eligibility criteria for participation in the clinical trial;
- the number of sites at which we conduct the trial and the speed at which we are able to open such sites;
- the prevalence of antibiotic resistance to pathogens where we conduct the clinical trial;
- the accuracy of certain estimates and assumptions upon which the design of the protocols are predicated;
- our ability to recruit clinical trial investigators with appropriate experience;
- competing clinical trials and clinicians' and patients' perceptions as to the potential advantages and risks of the product candidate being studied in relation to other available therapies, including any new drugs that may be approved for the indications that we are investigating;
- our ability to obtain and maintain patient consents;
- the risk that patients enrolled in clinical trials will drop out of the clinical trials before completion; and
- the impact on access to hospitals and willingness of patients to participate in clinical trials including the ongoing Phase 3 clinical trial being conducted in response to the CRL, or any additional clinical trial(s) required for regulatory approval of our product candidates, as a result of pandemics, like COVID-19, and other health crises.

The inclusion and exclusion criteria for any clinical trials of oral sulopenem and sulopenem may adversely affect our enrollment rates for patients in those clinical trials. In addition, we may face competition in enrolling suitable patients as a result of other companies conducting clinical trials for antibiotic product candidates that are intended to treat similar infections, resulting in slower than anticipated enrollment in our clinical trials. Enrollment delays in our clinical trials may result in increased development costs for oral sulopenem and/or sulopenem, or slow down or halt our product development for oral sulopenem and/or sulopenem.

In response to the COVID-19 pandemic, the FDA issued guidance on March 18, 2020, and updated it in 2021 to address the conduct of clinical trials during the pandemic. The guidance sets out a number of considerations for sponsors of clinical trials impacted by the pandemic, including the requirement to include in the clinical study report (or as a separate document) contingency measures implemented to manage the study, and any disruption of the study as a result of COVID-19; a list of all study participants affected by COVID-19-related study disruptions by a unique subject identifier and by investigational site, and a description of how the individual's participation was altered; and analyses and corresponding discussions that address the impact of implemented contingency measures (e.g., participant discontinuation from investigational product and/or study, alternative procedures used to collect critical safety and/or efficacy data) on the safety and efficacy results reported for the study. In its most recent update to this guidance, the FDA addressed questions received during the past year from clinical practitioners who are adapting their operations in a pandemic environment. These questions focused on, among other things, when to suspend, continue or initiate a trial and how to submit changes to protocols for investigational new drugs and handle remote site monitoring visits. There can be no assurance that this guidance governing clinical studies during the pandemic will remain in effect or, even if it does, that it will help address the risks and challenges enumerated above.

Accordingly, our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or might require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials, such as the ongoing clinical trial being conducted in response to the CRL, may result in increased development costs for our product candidates, slow down or halt our product candidate development and approval process and jeopardize our ability to seek and obtain the marketing approval required to commence product sales and generate revenue, which would cause the value of our company to decline and limit our ability to obtain additional financing if needed. Furthermore, we rely on and expect to continue to rely on contract research organizations (CROs) and clinical trial sites to ensure the proper and timely conduct of our clinical trials, and we have limited influence over their performance or the impact of pandemics, like COVID-19, to their business.

Success in non-clinical testing and early clinical trials does not ensure that later clinical trials will be successful, and we cannot assure our shareholders that any clinical trials that we may conduct will demonstrate consistent or adequate efficacy and safety to obtain regulatory approval to market our sulopenem program in any indication.

Although we believe that oral sulopenem and sulopenem have the potential to treat uUTI, cUTI and cIAI in humans based on the results of prior preclinical studies and clinical trials, we cannot guarantee that oral sulopenem and/or sulopenem will demonstrate the expected efficacy in clinical trial patients to the satisfaction of the FDA and/or other regulators. We also cannot guarantee that the projections made from the pharmacokinetic and pharmacodynamic models that we developed from non-clinical and clinical oral sulopenem and sulopenem studies will be validated in these clinical trials. For example, while we believe that sulopenem has the potential to treat cIAIs and cUTIs in humans based on the results of prior preclinical studies and clinical trials, sulopenem did not meet the primary endpoint of statistical non-inferiority compared to the control therapy in our Phase 3 cIAI and cUTI clinical trials. While we believe the secondary supporting analyses and safety data in all three Phase 3 clinical trials support the potential of sulopenem in the treatment of multi-drug resistant infections, we cannot guarantee that these supporting analyses are indicative of efficacy of sulopenem in treating cIAI or cUTI. Similarly, while we believe that sulopenem has the potential to treat uUTI in humans based on the results of prior preclinical studies and clinical trials, and based on our prior Phase 3 uUTI clinical trial, in the population of patients with baseline pathogens resistant to quinolones, in which sulopenem met the related primary endpoint by demonstrating statistical significance in the overall response rate by treatment arm in the ciprofloxacin-resistant population, sulopenem did not meet the primary endpoint of statistical non-inferiority compared to ciprofloxacin in the population of patients with baseline pathogens susceptible to ciprofloxacin in our prior Phase 3 uUTI clinical trial. Based on discussions with the FDA at a pre-NDA meeting and previous correspondence with the FDA, we submitted an NDA for oral sulopenem for the treatment of uUTI in patients with a quinolone non-susceptible pathogen in the fourth quarter of 2020 and the FDA accepted the application for review in January 2021. On July 23, 2021, we received a CRL from the FDA in respect of the NDA. The CRL provided that additional data are necessary to support approval of oral sulopenem for the treatment of adult women with uUTIs caused by designated susceptible microorganisms proven or strongly suspected to be non-susceptible to a quinolone and recommended that we conduct at least one additional adequate and well-controlled clinical trial, potentially using a different comparator drug. In July 2022 we reached an agreement with the FDA under the SPA process on the design, endpoints and statistical analysis of a Phase 3 clinical trial for oral sulopenem for the treatment of uUTIs and we commenced enrollment in that clinical trial, known as REASSURE, in October 2022. The study is designed as a non-inferiority trial comparing oral sulopenem and Augmentin® (amoxicillin/clavulanate) in the Augmentin® susceptible population. Additionally, though not an approvability issue, the FDA recommended in its CRL that we conduct additional non-clinical PK/PD studies to support dose selection for the proposed treatment indication(s). We have commenced additional non-clinical PK/PD investigations to support the dosing regimen selected for oral sulopenem, as recommended by the FDA. There can be no assurance that we will be in a position to resolve the matters set forth in the CRL, that we will be able to complete the ongoing Phase 3 clinical trial and non-clinical studies intended to support a resubmission of our NDA or that any data generated by such clinical and non-clinical investigation will be adequate to support resubmission or approval of our NDA.

Other companies in the pharmaceutical industry have frequently suffered significant setbacks in later clinical trials, even after achieving promising results in earlier non-clinical studies or clinical trials.

Serious adverse events or undesirable side effects or other unexpected properties of oral sulopenem, sulopenem or any other product candidate may be identified during development or after approval that could delay, prevent or cause the withdrawal of regulatory approval, limit the commercial potential, or result in significant negative consequences following marketing approval.

Serious adverse events or undesirable side effects caused by, or other unexpected properties of, our product candidates could cause us, an institutional review board (IRB), or regulatory authorities to interrupt, delay or halt our clinical trials and could result in a more restrictive label, the imposition of distribution or use restrictions or the delay or denial of regulatory approval by the FDA or comparable foreign regulatory authorities. If oral sulopenem, sulopenem or any of our other product candidates is associated with serious or unexpected adverse events or undesirable side effects, the FDA or the IRBs at the institutions in which our studies are conducted, could suspend or terminate our clinical trials or the FDA or comparable foreign regulatory authorities could order us to cease clinical trials or deny approval of our product candidates for any or all targeted indications. Treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete the clinical trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

To date, sulopenem and sulopenem etzadroxil have generally been well tolerated in clinical trials conducted in healthy subjects and patients and there were no safety issues found in any patients treated with sulopenem in our prior Phase 3 clinical trials. During the development of oral sulopenem and sulopenem, patients have experienced drug-related side effects including diarrhea, temporary increases in hepatic enzymes, allergic reactions, and rash. In the Japanese program conducted by Pfizer in the early 1990s, one patient reported a serious adverse event related to sulopenem of a transient elevation in liver function tests. The patient died due to metastatic lung cancer. Other serious adverse events recorded in patients receiving sulopenem in the Japanese program, which were not considered by the investigator to be related to sulopenem, included myocardial infarction with respiratory failure and progression of underlying ovarian carcinoma, in both cases resulting in death. For each of these patients, sulopenem was not determined to be the cause of death.

While the active pharmaceutical ingredient in the bilayer tablet is sulopenem etzadroxil, the combination product with probenecid has not yet been tested extensively in patients. In the cIAI trial, patients received either sulopenem IV followed by sulopenem etzadroxil or ertapenem followed by ciprofloxacin/metronidazole or amoxicillin-clavulanate. Among 668 treated patients, treatment-related adverse events were observed in 6.0% and 5.1% of patients on sulopenem and ertapenem, respectively, with the most commonly reported drug-related adverse event being diarrhea, which was observed in 4.5% and 2.4% of patients on sulopenem and ertapenem, respectively. Discontinuations from treatment were uncommon for both regimens, occurring in 1.5% of patients on sulopenem and 2.1% of patients on ertapenem. Serious adverse events unrelated to study treatment were seen in 7.5% of patients on sulopenem and 3.6% of patients on ertapenem. In the cUTI trial, patients received either sulopenem IV followed by sulopenem etzadroxil, if eligible for oral therapy, or ertapenem IV followed by ciprofloxacin or amoxicillin-clavulanate, if eligible for oral therapy. Among 1,392 treated patients, treatment-related adverse events were observed in 6.0% and 9.2% of patients on sulopenem and ertapenem, respectively, with the most commonly reported adverse events being headache (3.0% and 2.2%), diarrhea (2.7% and 3.0%) and nausea (1.3% and 1.6%), on sulopenem and ertapenem, respectively. Discontinuations from treatment were uncommon for both regimens, occurring in 0.4% of patients on sulopenem and 0.6% of patients on ertapenem. Serious adverse events unrelated to study treatment were seen in 2.0% of patients on sulopenem and 0.9% of patients on ertapenem. In the uUTI trial, patients received either oral sulopenem or ciprofloxacin. Among 1,660 treated patients, treatment related adverse events were observed in 17.0% and 6.2% of patients on sulopenem and ciprofloxacin, respectively. The most commonly reported adverse events were diarrhea (12.4% and 2.5%), nausea (3.7% and 3.6%), and headache (2.2% and 2.2%), for sulopenem and ciprofloxacin patients, respectively. The difference in adverse events was driven by diarrhea which, in the majority of patients, was mild and self-limited. Overall discontinuations due to adverse events were uncommon on both regimens and were seen in 1.6% of patients on sulopenem and 1.0% of patients on ciprofloxacin. Serious adverse events were seen in 0.7% of patients on sulopenem with one drug-related serious adverse event due to transient angioedema and 0.2% of patients on ciprofloxacin with no drug-related serious adverse event.

While we believe these results support a positive safety and tolerability profile for sulopenem and there were no safety issues identified in the CRL received from the FDA in July 2021, in future trials there may be unforeseen serious adverse events or side effects that differ from those seen in our prior Phase 3 program, in Phase 1 normal healthy volunteers with oral sulopenem or the prior post-marketing experience with probenecid. There may also be unexpected adverse events associated with probenecid that have not been seen to date.

If unexpected adverse events occur in any of our clinical trials, we may need to abandon development of our product candidates, or limit development to lower doses or to certain uses or subpopulations in which the undesirable side effects or other unfavorable characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many compounds that initially showed promise in clinical or earlier stage testing are later found to cause undesirable or unexpected side effects that prevent further development of the compound.

Undesirable side effects or other unexpected adverse events or properties of oral sulopenem, sulopenem or any of our other future product candidates could arise or become known either during clinical development or, if approved, after the approved product has been marketed. If such an event occurs during development, our clinical trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of, or could deny approval of, oral sulopenem, sulopenem or other product candidates. If such an event occurs after such product candidates are approved, a number of potentially significant negative consequences may result, including:

- regulatory authorities may withdraw the approval of such product;
- we may be required to recall a product or change the way such product is administered to patients;
- regulatory authorities may require additional warnings on the label or impose distribution or use restrictions;
- regulatory authorities may require one or more post-marketing studies;
- regulatory authorities may require the addition of a “black box” warning;
- we may be required to implement a Risk Evaluation and Mitigation Strategy (REMS), including the creation of a medication guide outlining the risks of such side effects for distribution to patients;

•we could be sued and held liable for harm caused to patients;

•our product may become less competitive; and

•our reputation may suffer.

Additionally, if the safety warnings in our product labels are not followed, adverse medical situations in patients may arise, resulting in negative publicity and potential lawsuits, even if our products worked as we described. Any of these events could prevent us from achieving or maintaining market acceptance of the affected product candidate, if approved, or could substantially increase commercialization costs and expenses, which could delay or prevent us from generating revenue from the sale of our products and harm our business and results of operations.

Even if a product candidate does obtain regulatory approval, it may never achieve the market acceptance by physicians, patients, hospitals, third-party payors and others in the medical community that is necessary for commercial success, and the market opportunity may be smaller than we estimate.

Even if we obtain FDA or other regulatory approvals and are able to launch oral sulopenem, sulopenem or any other product candidate commercially, the product candidate may not achieve market acceptance among physicians, patients, hospitals (including pharmacy directors) and third-party payors and, ultimately, may not be commercially successful. For example, physicians are often reluctant to switch their patients from existing therapies even when new and potentially more effective or convenient treatments enter the market. Moreover, many antibiotics currently exist for the pathogens underlying uUTI, cUTI and cIAI. While many of those pathogens are resistant to certain drugs in the market, the selection is broad, and individual physicians' prescribing patterns vary widely and are affected by resistance rates in their geographies, whether their patients are at elevated risk, the ability of patients to afford branded drugs and concerns regarding generating resistance with specific classes of antibiotics.

Efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may not be successful. If oral sulopenem, sulopenem or any other product candidate that we develop does not achieve an adequate level of market acceptance, we may not generate significant product revenues and, therefore, we may not become profitable. Market acceptance of any product candidate for which we receive approval depends on a number of factors, including:

•the efficacy and safety of the product candidate as demonstrated in clinical trials as compared to alternative treatments;

•the potential and perceived advantages and disadvantages of the product candidates, including cost and clinical benefit relative to alternative treatments;

•relative convenience and ease of administration;

•the clinical indications for which the product candidate is approved;

•the willingness of physicians to prescribe the product;

•the willingness of hospital pharmacy directors to purchase the product for their formularies;

•acceptance by physicians, patients, operators of hospitals and treatment facilities and parties responsible for coverage and reimbursement of the product;

•the availability of coverage and adequate reimbursement by third-party payors and government authorities;

•the effectiveness of our sales and marketing efforts or those of collaborators, where we choose not to commercialize directly ourselves;

•the strength of marketing and distribution support;

•limitations or warnings, including distribution or use restrictions, contained in the product's approved labeling or an approved REMS;

•whether the product is designated under physician treatment guidelines as a first-line therapy or as a second- or third-line therapy for particular infections;

•the approval of other new products for the same indications;

•the timing of market introduction of the approved product as well as competitive products;

•adverse publicity about the product or favorable publicity about competitive products;

•the emergence of bacterial resistance to the product; and

•the rate at which resistance to other drugs in the target infections grows.

In addition, the potential market opportunity for oral sulopenem and sulopenem is difficult to estimate. Our estimates of the potential market opportunity are predicated on several key assumptions such as industry knowledge and publications, third-party research reports and other surveys. While we believe that our internal assumptions are reasonable, these assumptions involve the exercise of significant judgment on the part of our management, are inherently uncertain and the reasonableness of these assumptions has not been assessed by an independent source. If any of the assumptions prove to be inaccurate, then the actual market for oral sulopenem and/or sulopenem could be smaller than our estimates of the potential market opportunity. If the actual market for oral sulopenem and/or sulopenem is smaller than we expect, or if the product fails to achieve an adequate level of acceptance by physicians, health care payors, patients, hospitals and others in the medical community, our product revenue may be limited and it may be more difficult for us to achieve or maintain profitability.

We have a limited operating history and no history of commercializing pharmaceutical products, which may make it difficult to evaluate the prospects for our future viability.

We began operations in November 2015. Since our inception, we have devoted substantially all of our financial resources and efforts to organizing and staffing our company, business planning, raising capital, planning for potential commercialization, and research and development, including preclinical and clinical development, for our sulopenem program. While the members of our development team have successfully developed and registered other antibiotics in past roles at different companies, our company has limited experience and has not yet demonstrated an ability to successfully obtain marketing approval, manufacture a commercial scale product (or arrange for a third party to do so on our behalf), or conduct sales and marketing activities necessary for successful product commercialization. Consequently, predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing pharmaceutical products. Assuming we obtain marketing approval for oral sulopenem or sulopenem, we will need to transition from a company with a research and development focus to a company capable of supporting commercial activities whether we choose to commercialize product candidates directly ourselves or seek to commercialize them through third-party collaboration arrangements. We may encounter unforeseen expenses, difficulties, complications and delays, and may not be successful in such a transition.

We currently have no commercial organization. If we are unable to establish and maintain sales, marketing and distribution capabilities or enter into sales, marketing and distribution agreements with third parties, we may not be successful in commercializing oral sulopenem, sulopenem or any other product candidate if such product candidate is approved.

If we are unable to establish and maintain sales, marketing and distribution capabilities or enter into sales, marketing and distribution agreements with third parties, we may not be successful in commercializing oral sulopenem, sulopenem or any other product candidate if such product candidate is approved.

We are currently evaluating our commercialization strategy in the United States and other territories. We are focusing our initial commercial efforts on the United States market, which we believe represents the largest market opportunity for our sulopenem program. We currently do not have a sales, marketing or distribution infrastructure and we have no experience in the sales, marketing or distribution of pharmaceutical products. To achieve commercial success for any approved product, we must either build our marketing, sales, distribution, managerial and other non-technical capabilities, or make arrangements to outsource those functions to third parties. If oral sulopenem and/or sulopenem receive regulatory approval, we may build a commercial organization and recruit a targeted sales force with technical expertise, an internal marketing and health resource group, as well as a managed markets group focused on reimbursement activities with third-party payors and a specialty distribution team to ensure pharmacy-level stocking and, where we choose not to commercialize directly ourselves, we will seek to commercialize oral sulopenem and/or sulopenem through collaboration arrangements. We are not currently party to any such arrangements but engaged a potential commercial partner to provide pre-commercial activities and we commenced negotiations on a definitive agreement for commercialization services. Following receipt of the CRL in July 2021, in order to reduce operating expenses and conserve cash resources, we halted any remaining pre-commercial activities and paused negotiations on the definitive agreement for commercialization services. There is no assurance that we will seek or be able to reach a definitive agreement for commercialization services in the future.

The development of sales, marketing and distribution capabilities will require substantial resources, will be time-consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing and distribution capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization costs. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel. In addition, we may not be able to hire a sales force in the United States that is sufficient in size or has adequate expertise in the medical markets that we intend to target. If we are unable to establish a sales force and marketing and distribution capabilities, our operating results may be adversely affected. Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely impact the commercialization of our product candidates.

Other factors that may inhibit our efforts to commercialize our products directly include:

•challenges in developing a commercialization strategy or launching new drug products using a traditional marketing model during a global health crisis or pandemic, like COVID-19;

•our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;

•the inability of a health resources group to obtain access to educate physicians regarding the attributes of our future products;

•lack of adequate number of physicians to use or prescribe our products;

•the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines;

•costs and expenses associated with creating an independent sales and marketing organization; and

•our inability to reach a definitive agreement for commercialization services with respect to the potential commercialization of sulopenem in the United States or abroad, should we chose to outsource such services to a third party.

For those countries in which we choose not to commercialize directly ourselves, we intend to use collaborators that have direct sales forces and established distribution systems to assist with the commercialization of oral sulopenem, sulopenem and any other product candidate. As a result of entering into arrangements with third parties to perform sales, marketing and distribution services, our product revenues or the profitability of these product revenues to us would likely be lower than if we were to directly market and sell products in those markets.

Furthermore, we may be unsuccessful in entering into the necessary arrangements with third parties, or in obtaining all necessary approvals that may be required to enter into such arrangements, or may be unable to do so on terms that are favorable to us. In addition, we likely would have little control over such third parties, and any of them might fail to devote the necessary resources and attention to sell and market our products effectively.

If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

We face substantial competition from other pharmaceutical and biotechnology companies and our business may suffer if we fail to compete effectively.

The development and commercialization of new drug products is highly competitive. We face competition from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide with respect to oral sulopenem, sulopenem and other product candidates that we may seek to develop and commercialize in the future. There are a number of pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of product candidates for the treatment of multi-drug resistant infections. Potential competitors also include academic institutions, government agencies and other public and private research organizations. Our competitors may succeed in developing, acquiring or licensing technologies and drug products that are more effective or less costly than oral sulopenem, sulopenem or any other product candidates that we may develop, which could render our product candidates obsolete and noncompetitive.

There are a variety of available oral therapies marketed for the treatment of multi-drug resistant infections that we would expect would compete with oral sulopenem and sulopenem, such as levofloxacin, ciprofloxacin, nitrofurantoin, fosfomycin, amoxicillin-clavulanate, cephalexin and trimethoprim-sulfamethoxazole. Many of the available therapies are well established and widely accepted by physicians, patients and third-party payors. Insurers and other third-party payors may also encourage the use of generic products, for example in the fluoroquinolone class. If oral sulopenem or sulopenem is approved, the pricing may be at a significant premium over other competitive products that are generic. This may make it difficult for oral sulopenem or sulopenem to compete with these products.

There are also a few oral product candidates in clinical development by third parties that are intended to treat uUTIs. Late-stage product candidates include gepotidacin from GlaxoSmithKline and pivmecillinam from Utility Therapeutics Limited. If our competitors obtain marketing approval from the FDA or comparable foreign regulatory authorities for their product candidates more rapidly than us, it could result in our competitors establishing a strong market position before we are able to enter the market.

There are several IV-administered products marketed for the treatment of infections resistant to first-line therapy for gram-negative infections, including Avycaz from AbbVie Inc and Pfizer, Vabomere from Melinta Therapeutics, Inc., Zerbaxa from Merck & Co., Zemdri from Cipla, Xerava from La Jolla Pharmaceutical Company, Recarbrio from Merck & Co, and Fetroja from Shionogi & Co., Ltd. In addition, Nabriva Therapeutics plc's Contepo is an IV-administered product candidate in late-stage clinical development intended to treat resistant gram-negative infections.

Many of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific, management and sales and marketing personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

In July 2012, the Food and Drug Administration Safety and Innovation Act was passed, which included the Generating Antibiotics Incentives Now Act (the GAIN Act). The GAIN Act is intended to provide incentives for the development of new, qualified infectious disease products (QIDP). One such incentive is that, once a product receives QIDP designation and completes the necessary clinical trials and is approved by the FDA, it will be given an additional five years of regulatory exclusivity regardless of whether it is protected by a patent, provided that it is already eligible for another type of regulatory exclusivity. The FDA has designated sulopenem and oral sulopenem as QIDPs for the indications of uUTI, cUTI, cIAI, community-acquired bacterial pneumonia, acute bacterial prostatitis, gonococcal urethritis, and pelvic inflammatory disease. Fast track designation for these seven indications in both the oral and intravenous formulations has also been granted. In December 2016, the Cures Act was passed, providing additional support for the development of new infectious disease products. These incentives may result in more competition in the market for new antibiotics, and may cause pharmaceutical and biotechnology companies with more resources than we have to shift their efforts towards the development of product candidates that could be competitive with oral sulopenem, sulopenem and our other product candidates.

Even if we are able to commercialize oral sulopenem, sulopenem or any other product candidate, the product may become subject to unfavorable pricing regulations, or third-party payor coverage and reimbursement policies that could harm our business.

Marketing approvals, pricing, coverage and reimbursement for new drug products vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, which may negatively affect the revenues that we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

The commercial success of oral sulopenem and any future product candidates, if approved, will depend substantially, both in the United States and outside the United States, on the extent to which coverage and adequate reimbursement for the product and related treatments are available from government health programs, private health insurers and other third-party payors. If coverage is not available, or reimbursement is limited, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investments. Government authorities and third-party payors, such as health insurers and managed care organizations, publish formularies that identify the medications they will cover and the related payment levels. The healthcare industry is focused on cost containment, both in the United States and elsewhere. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications, which could affect our ability to sell our product candidates profitably.

In the United States, sales of our product candidates will depend, in part, on the availability and extent of coverage and reimbursement by third-party payors, such as government health programs, including Medicare and Medicaid, commercial insurance and managed healthcare organizations. There is no uniform coverage and reimbursement policy among third-party payors; however, private third-party payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Obtaining coverage and reimbursement approval for a product candidate from third-party payors is a time-consuming and costly process that may require the provision of supporting scientific, clinical and cost effectiveness data for the use of such product candidate to the third-party payor. There may be significant delays in obtaining such coverage and reimbursement for newly approved products, and coverage may be more limited than the purposes for which the product candidate is approved by the FDA. Moreover, eligibility for coverage and reimbursement does not imply that a product candidate will be paid for in all cases or at a rate that covers operating costs, including research, development, intellectual property, manufacture, sales and distribution expenses. Reimbursement rates may vary according to the use of the product candidate and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost products and may be incorporated into existing payments for other services. It is difficult to predict what third-party payors will decide with respect to coverage and reimbursement for our product candidates.

We currently expect that sulopenem IV, if approved, will be administered in a hospital setting, and oral sulopenem, if approved, will be used in a community setting and possibly be administered in a hospital inpatient setting as well. In the United States, third-party payors generally reimburse hospitals a single bundled payment established on a prospective basis intended to cover all items and services provided to the patient during a single hospitalization. Hospitals bill third-party payors for all or a portion of the fees associated with the patient's hospitalization and bill patients for any deductibles or co-payments. Because there is typically no separate reimbursement for drugs administered in a hospital inpatient setting, some of our target customers may be unwilling to adopt our product candidates in light of the additional associated cost. If we are forced to lower the price we charge for our product candidates, if approved, our gross margins may decrease, which would adversely affect our ability to invest in and grow our business. Centers for Medicare and Medicaid Services (CMS) recently revised its reimbursement system for certain antibiotics in order to address challenges associated with antimicrobial resistance. Based on the final rule published on August 2, 2019, CMS is finalizing an alternative new technology add-on payment pathway (NTAP) for certain breakthrough devices, and under this policy, a QIDP product will be considered new and will not need to demonstrate that it meets the substantial clinical improvement criterion. Instead it will only need to meet the cost criterion. CMS has also increased the NTAP percentage to 75 percent for an antimicrobial designated by the FDA as a QIDP. The potential impact of this rule on sulopenem has not yet been assessed.

On April 18, 2022, CMS released the Fiscal Year (FY) 2023 Inpatient Prospective Payment System (IPPS) proposed rule. Within each IPPS proposed rule, CMS assesses technologies that have been submitted for potential NTAP status and reconsiders the eligibility for technologies already so designated. In connection with this proposed rule, CMS assessed 13 technologies that were submitted for FY 2023 NTAP consideration through alternative application pathways. These pathways streamline the NTAP application process for (1) devices with FDA breakthrough designation, (2) drugs designated as qualified infectious disease products, and (3) technologies approved through the FDA's Limited Population Pathway for Antibacterial and Antifungal Drugs. CMS has once again proposed to approve these 13 technologies applying through the alternative pathway depending on FDA approval or clearance.

An inability to promptly obtain coverage and adequate payment rates from third-party payors for any approved product candidates that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

We cannot predict whether bacteria may develop resistance to oral sulopenem or sulopenem, which could affect their revenue potential.

We are developing oral sulopenem and sulopenem to treat drug-resistant bacterial infections. The bacteria responsible for these infections evolve quickly and readily transfer their resistance mechanisms within and between species. We cannot predict whether or when bacterial resistance to oral sulopenem and sulopenem may develop.

As with some commercially available carbapenems, oral sulopenem and sulopenem are not active against organisms expressing a resistance mechanism mediated by enzymes known as carbapenemases. Although occurrence of this resistance mechanism is currently uncommon, we cannot predict whether carbapenemase-mediated resistance will become widespread in regions where we intend to market sulopenem if it is approved. The use of carbapenems or penems in areas with drug-resistant infections or in countries with poor public health infrastructures, or the potentially extensive use of oral sulopenem or sulopenem outside of controlled hospital settings or in the community, could contribute to the rise of resistance. In addition, prescribers may be less likely to prescribe oral sulopenem and sulopenem if they are concerned about contributing to the rise of antibiotic resistance. If resistance to oral sulopenem or sulopenem becomes prevalent, or concerns about such resistance are strong, our ability to generate revenue from oral sulopenem and sulopenem could suffer.

We may be subject to costly product liability claims related to our clinical trials and product candidates and, if we are unable to obtain adequate insurance or are required to pay for liabilities resulting from a claim excluded from, or beyond the limits of our insurance coverage, a material liability claim could adversely affect our financial condition.

Because we conduct clinical trials with human patients, we face the risk that the use of our product candidates may result in adverse side effects to patients in our clinical trials. We face even greater risks upon any commercialization of our product candidates. Although we have product liability insurance, which covers our clinical trials for up to $10.0 million, our insurance may be insufficient to reimburse us for any expenses or losses we may suffer. We will need to increase our insurance coverage if and when we receive marketing approval for and begin selling oral sulopenem, sulopenem or any other product candidate. We do not know whether we will be able to continue to obtain product liability coverage and obtain expanded coverage if we require it, on acceptable terms, if at all.

We may not have sufficient resources to pay for any liabilities resulting from a claim excluded from, or beyond the limits of, our insurance coverage. Where we have provided indemnities in favor of third parties under our agreements with them, there is also a risk that these third parties could incur a liability and bring a claim under such indemnities. An individual may bring a product liability claim against us alleging that one of our product candidates or products causes, or is claimed to have caused, an injury or is found to be unsuitable for consumer use. Any product liability claim brought against us, with or without merit, could result in:

- withdrawal of clinical trial volunteers, investigators, patients or trial sites;
- the inability to commercialize our product candidates;
- decreased demand for our product candidates;
- regulatory investigations that could require costly recalls or product modifications;
- loss of revenue;
- substantial costs of litigation;
- liabilities that substantially exceed our product liability insurance, which we would then be required to pay ourselves;
- an increase in our product liability insurance rates or the inability to maintain insurance coverage in the future on acceptable terms, if at all;
- the diversion of management's attention from our business; and
- damage to our reputation and the reputation of our products.

Our operations, including our use of hazardous materials, chemicals, bacteria and viruses, require us to comply with regulatory requirements and expose us to significant potential liabilities.

Our operations involve the use of hazardous materials, including chemicals, and may produce dangerous waste products. Accordingly, we, along with the third parties that conduct clinical trials and manufacture our products and product candidates on our behalf, are subject to federal, state, local and foreign laws and regulations that govern the use, manufacture, distribution, storage, handling, exposure, disposal and recordkeeping with respect to these materials. We are also subject to a variety of environmental and occupational health and safety laws. Compliance with current or future laws and regulations can require significant costs and we could be subject to substantial fines and penalties in the event of non-compliance. In addition, the risk of contamination or injury from these materials cannot be completely eliminated. In such event, we could be held liable for substantial civil damages or costs associated with the cleanup of hazardous materials.

If we experience a significant disruption in our information technology systems or breaches of data security, our business could be adversely affected.

We rely on information technology systems to keep financial records, capture laboratory data, maintain clinical trial data and corporate records, communicate with staff and external parties and operate other critical functions. Our information technology systems are potentially vulnerable to disruption due to breakdown, malicious intrusion and computer viruses or other disruptive events including, but not limited to, natural disaster. If we were to experience a prolonged system disruption in our information technology systems or those of certain of our vendors, it could delay or negatively impact the development and commercialization of our sulopenem program and any future product candidates or technology, which could adversely impact our business. Although we maintain offsite back-ups of our data, if operations at our facilities were disrupted, it may cause a material disruption in our business if we are not capable of restoring function on an acceptable timeframe. In addition, our information technology systems are potentially vulnerable to data security breaches, whether by employees or others, which may expose sensitive data to unauthorized persons. Such data security breaches could lead to the loss of trade secrets or other intellectual property, or could lead to the public exposure of personal information (including sensitive personal information) of our employees and others, any of which could have a material adverse effect on our business, financial condition and results of operations. Moreover, a security breach or privacy violation that leads to disclosure or modification of, personally identifiable information, could harm our reputation, compel us to comply with applicable European, and United States federal and/or state, breach notification laws, subject us to mandatory corrective action, require us to verify the correctness of database contents and otherwise subject us to litigation and liability under laws and regulations that protect personal data, resulting in increased costs or loss of revenue. In addition, a data security breach could result in loss of clinical trial data or damage to the integrity of that data. If we are unable to prevent such security breaches or privacy violations or implement satisfactory remedial measures, our operations could be disrupted, and we may suffer reputational damage, financial loss and other negative consequences because of lost or misappropriated information. In addition, these breaches and other inappropriate access can be difficult to detect, and any delay in identifying them may lead to increased harm of the type described above.

Risks Related to Our Dependence on Third Parties

If we fail to comply with our obligations in our agreement with Pfizer, we could lose such rights that are important to our business.

We rely heavily on the Pfizer License pursuant to which we exclusively in-license certain patent rights and know-how related to sulopenem etzadroxil and certain know-how related to the IV formulation of sulopenem. The Pfizer License imposes diligence, development and commercialization timelines, milestone payments, royalties, insurance and other obligations on us, and we may enter into additional agreements, including license agreements, with other parties in the future which impose similar obligations.

The Pfizer License gives us exclusive worldwide rights to develop, manufacture, and commercialize sulopenem etzadroxil and sulopenem, or any other prodrug of sulopenem previously identified by Pfizer as well as the right to use relevant information and regulatory documentation developed by Pfizer to support any regulatory filing worldwide. In exchange for those rights, we are obligated to satisfy diligence requirements, including using commercially reasonable efforts to develop, obtain regulatory approval for and commercialize sulopenem etzadroxil and sulopenem by implementing a specified development plan and providing an update on progress on an annual basis. Under the Pfizer License, we paid Pfizer a one-time non-refundable upfront fee of $5.0 million, clinical milestone payments totaling $15.0 million, upon first patient dosing of oral sulopenem and sulopenem in a Phase 3 clinical trial, and are obligated to pay Pfizer milestone payments upon the achievement of other specified regulatory and sales milestones, as well as royalties ranging from a single-digit to mid-teens percentage based on the amount of marginal net sales of each licensed product. Pfizer also received 381,922 of our Series A preferred shares (which converted to ordinary shares in connection with our initial public offering (IPO)) as additional payment for the licensed rights.

If we fail to comply with our obligations to Pfizer under the Pfizer License, Pfizer may have the right to terminate the Pfizer License, in which event we would not be able to develop, obtain regulatory approval for, manufacture or market any product candidate that is covered by the Pfizer License, including sulopenem etzadroxil and sulopenem, which would materially harm our business, financial condition, results of operations and growth prospects. Any termination of the Pfizer License or reduction or elimination of our rights thereunder may result in our having to negotiate new or reinstated agreements with less favorable terms. Any termination of the Pfizer License would cause us to lose our rights to important intellectual property or technology.

We expect to depend on collaborations with third parties for the development and commercialization of oral sulopenem and/or sulopenem in certain territories. Our prospects with respect to those product candidates will depend in part on the success of those collaborations.

Although we are focusing our initial commercial efforts on the United States market, which we believe represents the largest market opportunity for our sulopenem program, we are also evaluating our commercialization strategy both within and outside the United States. We currently do not have a sales, marketing or distribution infrastructure and we have no experience in the sales, marketing or distribution of pharmaceutical products. To achieve commercial success for any approved product, we must either build our marketing, sales, distribution, managerial and other non-technical capabilities, or make arrangements to outsource those functions to third parties. For those countries in which we choose not to commercialize directly ourselves, we intend to seek to commercialize oral sulopenem and/or sulopenem through collaboration arrangements. In addition, we may seek third-party collaborators for development and commercialization of other product candidates in the United States and other territories. Our likely collaborators for any marketing, distribution, development, licensing or broader collaboration arrangements include service providers to the pharmaceutical industry, large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. We are not currently party to any such arrangements but engaged a potential commercial partner to provide pre-commercial activities and we commenced negotiations on a definitive agreement for commercialization services. Following receipt of the CRL in July 2021, in order to reduce operating expenses and conserve cash resources, we halted any remaining pre-commercial activities and paused negotiations on a definitive agreement for commercialization services. There is no assurance that we will seek or be able to reach a definitive agreement for commercialization services in the future.

We may derive revenue from research and development fees, license fees, milestone payments and royalties under any collaborative arrangement into which we enter. Our ability to generate revenue from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. In addition, our collaborators may have the right to abandon research or development projects and terminate applicable agreements, including funding obligations, prior to or upon the expiration of the agreed upon terms. As a result, we can expect to relinquish some or all of the control over the future success of a product candidate that we license to a third party.

We face significant competition in seeking and obtaining appropriate collaborators. Collaborations involving our product candidates may pose a number of risks, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;

•collaborators may not perform their obligations as expected;

•collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;

•collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;

•product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;

•a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;

•disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time consuming and expensive;

•collaborators may not properly maintain, defend or enforce our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;

•collaborators may infringe, misappropriate or otherwise violate the intellectual property rights of third parties, which may expose us to litigation and potential liability; and

•collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.

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Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a collaborator of ours is involved in a business combination, it could decide to delay, diminish or terminate the development or commercialization of any product candidate licensed to it by us.

If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund and undertake development or commercialization activities on our own, we will need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates or bring them to market or continue to develop our product platform.

We may rely on third parties to perform many essential services for any products that we commercialize, including services related to warehousing and inventory control, distribution, government price reporting, customer service, accounts receivable management, cash collection, and pharmacovigilance and adverse event reporting. If these third parties fail to perform as expected or to comply with legal and regulatory requirements, our ability to commercialize our product candidates will be significantly impacted and we may be subject to regulatory sanctions.

We may retain third-party service providers to perform a variety of functions related to the sale and distribution of our product candidates, key aspects of which will be out of our direct control. These service providers may provide key services related to warehousing and inventory control, distribution, customer service, accounts receivable management, and cash collection. If we retain a service provider, we would substantially rely on it as well as other third-party providers that perform services for us, including entrusting our inventories of products to their care and handling. If these third-party service providers fail to comply with applicable laws and regulations, fail to meet expected deadlines, or otherwise do not carry out their contractual duties to us, or encounter physical or natural damage at their facilities, our ability to deliver product to meet commercial demand would be significantly impaired and we may be subject to regulatory enforcement action. In addition, we may engage third parties to perform various other services for us relating to pharmacovigilance and adverse event reporting, safety database management, fulfillment of requests for medical information regarding our product candidates and related services. If the quality or accuracy of the data maintained by these service providers is insufficient, or these third parties otherwise fail to comply with regulatory requirements, we could be subject to regulatory sanctions. Additionally, we may contract with a third party to calculate and report pricing information mandated by various government programs. If a third party fails to timely report or adjust prices as required, or errors in calculating government pricing information from transactional data in our financial records, it could impact our discount and rebate liability, and potentially subject us to regulatory sanctions or False Claims Act lawsuits.

We rely on third parties to conduct our preclinical studies and our clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may be unable to obtain regulatory approval for or commercialize any of our product candidates. If they do not perform satisfactorily, our business may be materially harmed.

We do not independently conduct non-clinical studies that comply with good laboratory practice (GLP) requirements. We also do not have the ability to independently conduct clinical trials of any of our product candidates. We rely on third parties, such as CROs, clinical data management organizations, medical institutions, and clinical investigators to conduct our clinical trials of oral sulopenem and sulopenem and expect to rely on these third parties to conduct clinical trials of any potential product candidates. 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 clinical development activities limits our control over these activities but we remain responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards. For example, notwithstanding the obligations of a CRO for a clinical trial of one of our product candidates, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the clinical trial. While we will have agreements governing their activities, we control only certain aspects of their activities and have limited influence over their actual performance. The third parties with whom we contract for execution of our GLP studies and our clinical trials play a significant role in the conduct of these studies and clinical trials and the subsequent collection and analysis of data.

Although we rely on these third parties to conduct our GLP-compliant non-clinical studies and clinical trials, we remain responsible for ensuring that each of our non-clinical studies and clinical trials are conducted in accordance with applicable laws and regulations, and our reliance on the CROs does not relieve us of our regulatory responsibilities. The FDA and regulatory authorities in other jurisdictions also require us to comply with standards, commonly referred to as good clinical practices (GCPs), for conducting, monitoring, recording and reporting the results of clinical trials to assure that data and reported results are accurate and that the trial subjects are adequately informed of the potential risks of participating in clinical trials. The FDA enforces these GCPs through periodic inspections of trial sponsors, principal investigators, clinical trial sites and institutional review boards. If we or our third-party contractors fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving our product candidates, which would delay the regulatory approval process. We cannot assure our shareholders that, upon inspection, the FDA will determine that any of our clinical trials comply with GCPs. We are also required to register clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Furthermore, the third parties conducting clinical trials on our behalf are not our employees, and except for remedies available to us under our agreements with such contractors, we cannot control whether or not they devote sufficient time and resources to our development programs. These contractors may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities, which could impede their ability to devote appropriate time to our clinical programs. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we may not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates. If that occurs, we may not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates. In such an event, our financial results and the commercial prospects for oral sulopenem, sulopenem or other product candidates could be harmed, our costs could increase and our ability to generate revenue could be delayed, impaired or foreclosed.

We also rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of any resulting products, producing additional losses and depriving us of potential product revenue.

We contract with third parties for the manufacture of preclinical and clinical supplies of oral sulopenem and sulopenem and expect to continue to do so in connection with any future clinical trials and future commercialization of our product candidates and potential product candidates. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not have the internal infrastructure or capability to manufacture oral sulopenem and sulopenem for use in the conduct of our preclinical research or clinical trials or for commercialization. We rely on third-party contract manufacturers to manufacture supplies of oral sulopenem and sulopenem, and we expect to rely on third-party contract manufacturers to manufacture commercial quantities of any product candidate that we commercialize following approval for marketing by applicable regulatory authorities, if any. Reliance on third-party manufacturers entails risks, including:

- manufacturing delays if our third-party manufacturers give greater priority to the supply of other products over our product candidates or otherwise do not satisfactorily perform according to the terms of their agreement with us;
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us;
- the possible breach of the manufacturing agreement by the third party;
- the failure of the third-party manufacturer to comply with applicable regulatory requirements; and
- the possible misappropriation of our proprietary information, including our trade secrets and know-how.

We currently rely on a small number of third-party contract manufacturers for all of our required raw materials, drug substance and finished product for our preclinical research and clinical trials. We do not have long-term agreements with any of these third parties. We also do not have any current contractual relationships for the manufacture of commercial supplies of any of our product candidates. If any of our existing manufacturers should become unavailable to us for any reason, we may incur delays in identifying or qualifying replacements.

We will enter into agreements with third-party contract manufacturers for the commercial production of oral sulopenem and/or sulopenem. This process is difficult and time consuming and we may face competition for access to manufacturing facilities as there are a limited number of contract manufacturers operating under current Good Manufacturing Practices, or cGMPs, that are capable of manufacturing our product candidates. Consequently, we may not be able to reach agreement with third-party manufacturers on satisfactory terms, which could delay our commercialization.

Third-party manufacturers are required to comply with cGMPs and similar regulatory requirements outside the United States. Facilities used by our third-party manufacturers must be approved by the FDA after we submit an NDA(s) and before potential approval of the product candidate. Similar regulations apply to manufacturers of our product candidates for use or sale in countries outside of the United States. We have no direct control over the ability of our third-party manufacturers to maintain adequate quality control, quality assurance and qualified personnel, and are completely dependent on our third-party manufacturers for compliance with the applicable regulatory requirements for the manufacture of our product candidates. If our manufacturers cannot successfully manufacture material that conforms to the strict regulatory requirements of the FDA and any applicable regulatory authority, they will not be able to secure the applicable approval for their manufacturing facilities. If these facilities are not approved for commercial manufacture, we may need to find alternative manufacturing facilities, which could result in delays in obtaining approval for the applicable product candidate. In addition, our manufacturers are subject to ongoing periodic unannounced inspections by the FDA and corresponding state and foreign agencies for compliance with cGMPs and similar regulatory requirements. Failure by any of our manufacturers to comply with applicable cGMPs or other regulatory requirements could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspensions or withdrawals of approvals, operating restrictions, interruptions in supply and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates and have a material adverse effect on our business, financial condition and results of operations.

We and our third-party suppliers also continue to refine and improve the manufacturing process, certain aspects of which are complex and unique, and we may encounter difficulties with new or existing processes, particularly as we seek to significantly increase our capacity to commercialize oral sulopenem and/or sulopenem. Our reliance on contract manufacturers also exposes us to the possibility that they, or third parties with access to their facilities, will have access to and may appropriate our trade secrets or other proprietary information.

As drug candidates are developed through non-clinical studies to late-stage clinical trials towards approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods, methods of making drug formulations, and drug formulations, are altered along the way in an effort to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could cause our drug candidates to perform differently and affect the results of clinical trials or other future clinical trials conducted with the altered materials. Such changes may also require additional testing, FDA notification or FDA approval. This could delay completion of clinical trials, require us to conduct bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our drug candidates and jeopardize our ability to commence sales and generate revenue.

While no issues with regard to third-party manufacturers or the manufacturing process were identified in the CRL received from the FDA in July 2021, there can be no assurance that issues will not be identified in the future or that our third-party manufacturers will continue to maintain adequate quality control, quality assurance and qualified personnel and/or will continue to comply with the applicable regulatory requirements for the manufacture of our product candidates.

Our current and anticipated future dependence upon others for the manufacture of oral sulopenem and sulopenem and any future product candidates may adversely affect our future profit margins and our ability to commercialize any products for which we receive marketing approval on a timely and competitive basis.

Risks Related to Our Intellectual Property

We rely heavily on the Pfizer License for the patent rights and know-how required to develop and commercialize oral sulopenem and the know-how required to develop the IV formulation of sulopenem.

We rely heavily on the Pfizer License for intellectual property rights that are important or necessary for the development of oral sulopenem and sulopenem. We do not own or license any patent rights that cover the IV formulation of sulopenem. In addition, all patents directed to the compound sulopenem expired prior to us entering into the Pfizer License. Licenses to additional third-party intellectual property, technology and materials that may be required for the development and commercialization of our sulopenem program or any other product candidates or technology may not be available at all or on commercially reasonable terms. In that event, we may be required to expend significant time and resources to redesign our sulopenem program and any other product candidates or technology we may obtain in the future or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize oral sulopenem or sulopenem or other future product candidates or technologies, which could materially harm our business, financial condition, results of operations and growth prospects.

Under the Pfizer License, and we expect under certain of our future license agreements, we are responsible for prosecution and maintenance of the licensed patents and for bringing any actions against any third party for infringing on such patents. In addition, the Pfizer License requires, and we expect certain of our future license agreements would also require, us to meet certain development thresholds to maintain the license, including establishing a set timeline for developing and commercializing products. In addition, such license agreements are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations and growth prospects. Disputes may arise regarding intellectual property subject to the Pfizer License or any of our future license agreements, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe, misappropriate or otherwise violate any intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights under the license agreement;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and
- the priority of invention of patented technology.

In spite of our best efforts, Pfizer and any potential future licensors might conclude that we have materially breached our license agreements and might therefore terminate the relevant license agreements, thereby removing our ability to develop and commercialize products and technology covered by such license agreements. If any of our inbound license agreements are terminated, or if the underlying patents fail to provide the intended exclusivity, competitors would have the freedom to seek regulatory approval of, and to market, products identical to ours. This could have a material adverse effect on our competitive position, business, financial condition, results of operations and growth prospects.

If we are unable to obtain and maintain patent protection or other intellectual property rights for oral sulopenem or our other technology and product candidates, or if the scope of the patent protection or intellectual property rights we obtain is not sufficiently broad, we may not be able to successfully develop or commercialize oral sulopenem or any other product candidates or technology or otherwise compete effectively in our markets.

We rely upon a combination of patents, trademarks, trade secret protection, confidentiality agreements and other proprietary rights to protect the intellectual property related to our development programs and product candidates. Our success depends, in part, on obtaining and maintaining patent protection and successfully enforcing these patents and defending them against third-party challenges in the United States and other countries. If we or our licensors are unable to obtain or maintain patent protection with respect to oral sulopenem or any other product candidates or technology we develop, our business, financial condition, results of operations and growth prospects could be materially harmed.

We have sought to protect our proprietary position by in-licensing patents in the United States and abroad related to oral sulopenem. Our patent portfolio contains two nationalized patent families, one addressing the effect of probenecid on the plasma concentrations of sulopenem after multi-day dosing and the second related to a method of preparing a bilayer tablet composed of sulopenem etzadroxil and probenecid. The patent portfolio also contains a patent family related to a combination of valproic acid, a β-lactam compound, and probenecid, as well as its method of use. The patent prosecution process is expensive and time-consuming, and we and our licensors may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner or in all jurisdictions. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, although we control prosecution of the patents we have licensed from Pfizer related to our sulopenem program, we may not always have the right to control the preparation, filing and prosecution of patent applications, or to maintain, enforce or defend the patents, covering technology that we may license from third parties. Therefore, these patents and patent applications may not be prosecuted, maintained, enforced or defended in a manner consistent with the best interests of our business.

If any patent applications we may own or in-license in the future with respect to our development programs or product candidates fail to issue, if their breadth or strength of protection is threatened or if they fail to provide meaningful exclusivity for our current and future product candidates, it could dissuade companies from collaborating with us to develop product candidates and threaten our ability to commercialize products. Any such outcome could materially harm our competitive position, business, financial condition, results of operations and growth prospects.

The patent position of pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. In addition, the laws of countries outside the United States may not protect our rights to the same extent as the laws of the United States. For example, European Union (EU) patent law restricts the patentability of methods of treatment of the human body more than U.S. law does. In addition, publications of discoveries in scientific literature often lag behind the actual discoveries, patent applications in the United States and other jurisdictions remain confidential for a period after filing, and some remain so until issued. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in the patents or pending patent applications we currently own, license or may own or license in the future, or that we were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. There is no assurance that all potentially relevant prior art relating to our patent rights has been found, and such prior art could potentially invalidate one or more of the patents we currently license or may own or license in the future or prevent a patent from issuing from one or more pending patent applications we own or may own or license in the future. There is also no assurance that prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim in our patent rights, may, nonetheless, ultimately be found to affect the validity or enforceability of a claim. Even if patents do successfully issue and even if such patents cover our current and future product candidates, third parties may challenge their ownership, validity, enforceability or scope, which may result in such patents being narrowed, invalidated or held unenforceable, which could allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. Any successful opposition to these patents or any other patents owned by us in the future or licensed to us could deprive us of rights necessary for the successful commercialization of any product candidates that we may develop. Furthermore, even if they are unchallenged, our patents rights may not adequately protect our product candidates and technology, provide exclusivity for our product candidates, prevent others from designing around our claims or provide us with a competitive advantage. Any of these outcomes could impair our ability to prevent competition from third parties. Changes in either the patent laws or interpretation of the patent laws in the United States or other countries may diminish the value of our patent rights or narrow the scope of our patent protection.

We cannot offer any assurances about whether any issued patents will be found invalid and unenforceable or will be challenged by third parties. Any successful challenge or opposition to patents owned by or licensed to us could deprive us of rights necessary for the successful commercialization of any product candidates that we may develop. 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.

Furthermore, our patent rights may be subject to a reservation of rights by one or more third parties. For example, certain research we conducted was funded in part by the U.S. government. As a result, the U.S. government may have certain march-in rights to patents and technology arising out of such research, if any. When new technologies are developed with government funding, the government generally obtains certain rights in any resulting patents, including a non-exclusive license authorizing the government to use the invention. These rights may permit the government to disclose our confidential information to third parties and to exercise march-in rights to use or allow third parties to use our licensed technology. The government can exercise its march-in rights if it determines that action is necessary because we fail to achieve practical application of the government-funded technology, to alleviate health or safety needs, to meet requirements of federal regulations or to give preference to U.S. industry. In addition, our rights in such inventions may be subject to certain requirements to manufacture products embodying such inventions in the United States. Any exercise by the government of such rights could harm our competitive position, business, financial condition, results of operations and growth prospects.

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

We cannot guarantee that any of our or our licensors' patent searches or analyses, including but not limited to the identification of relevant patents, the scope of patent claims or the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third-party patent and pending application in the United States and abroad that is relevant to or necessary for the commercialization of our product candidates in any jurisdiction. For example, U.S. applications filed before November 29, 2000 and certain U.S. applications filed after that date that will not be filed outside the United States remain confidential until patents issue. Patent applications in the United States and elsewhere are published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Therefore, patent applications covering our product candidates could have been filed by others without our knowledge. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our product candidates or the use of our product candidates. The scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect, which may negatively impact our ability to market our product candidates. We may incorrectly determine that our product candidates are not covered by a third-party patent or may incorrectly predict whether a third party's pending application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States or abroad that we consider relevant may be incorrect, which may negatively impact our ability to develop and market our product candidates. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our product candidates.

The patent protection for our product candidates may expire before we are able to maximize their commercial value which may subject us to increased competition and reduce or eliminate our opportunity to generate product revenue.

Patents have a limited lifespan. In the United States, if all maintenance fees are paid timely, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. The patents for our product candidates have varying expiration dates and, if these patents expire, we may be subject to increased competition and we may not be able to recover our development costs. For example, our licensed U.S. patent claim for a composition of matter patent for oral sulopenem is due to expire in 2029, subject to potential extension to 2034 under the Drug Price Competition and Patent Term Restoration Act of 1984 (referred to as the Hatch-Waxman Act) and our newly granted patent directed to the composition of the bilayer tablet of sulopenem etzadroxil and probenecid is due to expire no earlier than 2039, absent any extensions. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such product candidates are commercialized. As a result, our patent rights may not provide us with sufficient rights to exclude others from commercializing product candidates similar or identical to ours.

The FDA designated sulopenem and oral sulopenem as QIDPs for the indications of uUTI, cUTI, cIAI, community-acquired bacterial pneumonia, acute bacterial prostatitis, gonococcal urethritis, and pelvic inflammatory disease. Fast track designation for these seven indications in both the oral and intravenous formulations has also been granted. QIDP status provides the potential for a more rapid review cycle for an NDA and could add five years to any regulatory exclusivity period that we may be granted. However, that does not guarantee that we will receive any regulatory exclusivity or that any such exclusivity will be for a period sufficient to provide us with any commercial advantage. Moreover, we do not own or license any patent directed to the compound sulopenem.

Depending upon the timing, duration and conditions of FDA marketing approval of our product candidates, one or more of the U.S. patents we currently license and/or own may be eligible for limited patent term extension under the Hatch-Waxman Act, and similar legislation in the European Union. The Hatch-Waxman Act permits a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended. We may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of the relevant patents or otherwise fail to satisfy applicable requirements and the length of the extension could be less than we request. To the extent we wish to pursue patent term extension based on a patent that we in-license from Pfizer or another third party, we would need the cooperation of Pfizer or the third party. Moreover, similar extensions may be available in some of the larger economic territories but may not be available in all of our markets of interest.

If we are unable to obtain patent term extension/restoration or some other exclusivity, or the term of any such extension is less than we request, the period during which we can enforce our exclusive rights for that product will be shortened and our competitors may obtain approval to market competing products sooner. As a result, we could be subject to increased competition and our opportunity to establish or maintain product revenue could be substantially reduced or eliminated. Furthermore, we may not have sufficient time to recover our development costs prior to the expiration of our U.S. and non-U.S. patent rights. If this occurs, our competitors may take advantage of our investment in development and trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case. Any of the foregoing would materially harm our business, financial condition, results of operations and growth prospects.

Intellectual property rights do not necessarily address all potential threats to our business.

Once granted, patents may remain open to opposition, interference, re-examination, post-grant review,*inter partes* review, nullification or derivation action in court or before patent offices or similar proceedings for a given period after allowance or grant, during which time third parties can raise objections against such grant. In the course of such proceedings, which may continue for a protracted period of time, the patent owner may be compelled to limit the scope of the allowed or granted claims thus attacked, or may lose the allowed or granted claims altogether. In addition, the degree of future protection afforded by our intellectual property rights is uncertain because even granted intellectual property rights have limitations, and may not adequately protect our business. The following examples are illustrative:

- others may be able to make compounds or formulations that are similar to oral sulopenem and sulopenem compounds or formulations but that are not covered by the claims of our patent rights;
- the patents of third parties may have an adverse effect on our business;
- we or our licensors or any future strategic partners might not have been the first to conceive or reduce to practice the inventions covered by the issued patents that we own or have exclusively licensed;
- we or our licensors or any future strategic partners might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible our pending patent applications, and any future patent applications, will not lead to issued patents or afford meaningful protection for our product candidates;
- issued patents that we may own in the future or have exclusively licensed may not provide us with any competitive advantage, or may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- third parties performing manufacturing or testing for us using our product candidates or technologies could use the intellectual property of others without obtaining a proper license; and
- we may not develop additional proprietary technologies that are patentable.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

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

As is the case with other pharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the pharmaceutical industry involves both technological complexity and legal complexity. Therefore, obtaining and enforcing pharmaceutical patents is costly, time-consuming and inherently uncertain. In addition, the America Invents Act (the AIA) was signed into law on September 16, 2011, and many of its substantive changes became effective on March 16, 2013.

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

Among some of the other changes introduced by the AIA are changes that limit where a patentee may file a patent infringement suit and providing opportunities for third parties to challenge any issued patent in the USPTO, including through post-issuance patent review procedures such as *inter partes* review, post-grant review and covered business methods. This applies to all U.S. patents, including those issued before March 16, 2013. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. The AIA and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

In the last few years, the USPTO has developed regulations and procedures to govern administration of the AIA, and many of the substantive changes to patent law associated with the AIA, in particular, the first to file provisions only became effective on March 16, 2013. Accordingly, it is not clear what, if any, impact the AIA will have on the operation of our business and this may not be known until such time as we, or our licensors or collaboration partners, are filing patent applications for an invention or seeking to defend issued patents. However, the AIA and its implementation could increase the uncertainties and costs surrounding the prosecution of our or our licensors' or collaboration partners' patent applications and the enforcement or defense of our or our licensors' or collaboration partners' issued patents, all of which could have an adverse effect on our business and financial condition.

Moreover, the standards that the USPTO and foreign patent office's use to grant patents are not always applied predictably or uniformly and can change. Consequently, any patents we currently license or may own or license in the future may have a shorter patent term than expected or may not contain claims that will permit us to stop competitors from using our technology or similar technology or from copying our products. Similarly, the standards that courts use to interpret patents are not always applied predictably or uniformly and may evolve, particularly as new technologies develop. In addition, changes to patent laws in the United States or other countries may be applied retroactively to affect the ownership, validity, enforceability or term of patents we currently license or may own or license in the future.

For example, the U.S. Supreme Court's rulings on several patent cases in recent years, such as *Association for Molecular Pathology v. Myriad Genetics, Inc.*, *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, and *Alice Corporation Pty. Ltd. v. CLS Bank International*, either narrow the scope of patent protection available in certain circumstances or weaken the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. Similarly, the complexity and uncertainty of European patent laws has also increased in recent years. In addition, the European patent system is relatively stringent in the type of amendments that are allowed during prosecution. These changes could limit our ability to obtain new patents in the future that may be important for our business.

We may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time consuming and unsuccessful.

Competitors may infringe, misappropriate or otherwise violate our patents, trademarks, copyrights or other intellectual property or those of our licensors. To counter infringement, misappropriation, unauthorized use or other violations, we may be required to file legal claims, which can be expensive and time consuming and divert the time and attention of our management and scientific personnel. We may not be able to prevent, alone or with our licensors, infringement, misappropriation or other violations of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents. In addition, in a patent infringement proceeding, there is a risk that a court will decide that a patent of ours is invalid or unenforceable, in whole or in part, and that we do not have the right to stop the other party from using the invention at issue. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent's claims narrowly or decide that we do not have the right to stop the other party from using the invention at issue on the grounds that our patents do not cover the invention. An adverse outcome in a litigation or proceeding involving our patents could limit our ability to assert our patents against those parties or other competitors, and may curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. Any of these occurrences could adversely affect our competitive business position, business prospects and financial condition. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

In any infringement, misappropriation or other intellectual property litigation, any award of monetary damages we receive may not be commercially valuable. 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 litigation. Moreover, there can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings.

Third parties may initiate legal proceedings alleging that we are infringing, misappropriating or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could have a negative impact on the success of our business.

Our commercial success depends, in part, upon our ability, and the ability of our future collaborators, to develop, manufacture, market and sell oral sulopenem, sulopenem and any future product candidates, if approved, and use our proprietary technologies without alleged or actual infringement, misappropriation or other violation of the patents and other intellectual property rights of third parties. There have been many lawsuits and other proceedings involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions and reexamination proceedings before the USPTO and corresponding foreign patent offices. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing product candidates. Some claimants may have substantially greater resources than we do and may be able to sustain the costs of complex intellectual property litigation to a greater degree and for longer periods of time than we could. In addition, patent holding companies that focus solely on extracting royalties and settlements by enforcing patent rights may target us. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the intellectual property rights of third parties.

We may in the future become party to, or be threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to oral sulopenem, sulopenem or any future product candidates and technology, including interference or derivation proceedings, post grant review and *inter partes* review before the USPTO or similar adversarial proceedings or litigation in other jurisdictions. Similarly, we or our licensors or collaborators may initiate such proceedings or litigation against third parties, e.g., to challenge the validity or scope of intellectual property rights controlled by third parties. In order to successfully challenge the validity of any U.S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court would invalidate the claims of any such U.S. patent. Moreover, third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit. There is a risk that third parties may choose to engage in litigation with us to enforce or to otherwise assert their patent rights against us. Even if we believe such claims are without merit, a court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, and the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable patents, or until such patents expire or are finally determined to be invalid or unenforceable. Similarly, if any third-party patents were held by a court of competent jurisdiction to cover aspects of our compositions, formulations, or methods of treatment, prevention or use, the holders of any such patents may be able to block our ability to develop and commercialize the applicable product candidate unless we obtained a license or until such patent expires or is finally determined to be invalid or unenforceable. In either case, such a license may not be available on commercially reasonable terms, or at all. Even if we were able to obtain a license, it could be nonexclusive, thereby giving our competitors access to the same technologies licensed to us. Furthermore, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In such an event, we would be unable to further practice our technologies or develop and commercialize any of our product candidates at issue, which could harm our business significantly.

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, if approved. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of management and employee time and resources from our business. Third parties making such claims may have the ability to dedicate substantially greater resources to these legal actions than we or our licensors or collaborators can. In the event of a successful claim of infringement, misappropriation or other violation 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.

There has been substantial litigation and other proceedings regarding patent and other intellectual property rights in the pharmaceutical and biotechnology industries. In addition to infringement claims against us, we may become a party to other patent litigation and other adversarial proceedings such as proceedings before the Patent Trial and Appeal Board and opposition proceedings in the European Patent Office regarding intellectual property rights with respect to our products and technology.

Patent litigation and other proceedings may also absorb significant management time. The cost to us of any patent litigation or other proceeding, even if resolved in our favor, could be substantial. During the course of any patent or other intellectual property litigation or other proceeding, there could be public announcements of the results of hearings, rulings on motions, and other interim proceedings or developments and if securities analysts or investors regard these announcements as negative, the perceived value of our product candidates or intellectual property could be diminished. Accordingly, the market price of our ordinary shares may decline. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our business, ability to compete in the marketplace, financial condition, results of operations and growth prospects.

We may not be able to protect our intellectual property rights globally, which could negatively impact our business.

Filing, prosecuting and defending patents covering oral sulopenem, sulopenem and any future product candidates globally would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Further, licensing partners may not prosecute patents in certain jurisdictions in which we may obtain commercial rights, thereby precluding the possibility of later obtaining patent protection in these countries. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and may also export infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our product candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and any current or future patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. Furthermore, while we intend to protect our intellectual property rights in our expected significant markets, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our product candidates. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate, which may have an adverse effect on our ability to successfully commercialize our product candidates in all of our expected significant foreign markets.

Additionally, the requirements for patentability may differ in certain countries, particularly developing countries. For example, unlike other countries, China has a heightened requirement for patentability, and specifically requires a detailed description of medical uses of a claimed drug. In India, unlike the United States, there is no link between regulatory approval of a drug and its patent status. Furthermore, generic or biosimilar drug manufacturers or other competitors may challenge the scope, validity or enforceability of our or our licensors' patents, requiring us or our licensors to engage in complex, lengthy and costly litigation or other proceedings. Generic or biosimilar drug manufacturers may develop, seek approval for, and launch biosimilar versions of our products. In addition, certain countries in Europe and developing countries, including China and India, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In those countries, we and our licensors may have limited remedies if patents are infringed or if we or our licensors are compelled to grant a license to a third party, which could materially diminish the value of those patents. This could limit our potential revenue opportunities. Accordingly, our and our licensors' efforts to enforce intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we own or license.

We may be subject to claims that we or our employees, consultants, contractors or advisors have infringed, misappropriated or otherwise violated the intellectual property of a third party, or claiming ownership of what we regard as our own intellectual property.

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees do not use the intellectual property and other proprietary information, know-how or trade secrets of others in their work for us, we may be subject to claims that we or these employees have used or disclosed such intellectual property or other proprietary information. Litigation may be necessary to defend against these claims.

In addition, we may in the future be subject to claims that former employees, collaborators or other third parties have an interest in our patents or other intellectual property as an inventor or co-inventor. While we typically require our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. To the extent that we fail to obtain such assignments, such assignments do not contain a self-executing assignment of intellectual property rights or such assignments are breached, we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products. Such a license may not be available on commercially reasonable terms or at all. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our management and scientific personnel.

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

Periodic maintenance and annuity fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or a patent application include failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we or our licensors fail to maintain the patents covering our products, our competitors might be able to enter the market, which would have a material adverse effect on our business, financial condition, results of operations and growth prospects.

If we are unable to protect the confidentiality of our trade secrets, the value of our technology could be materially adversely affected and our business would be harmed.

In addition to seeking patents for some of our technology and products, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, in seeking to develop and maintain a competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, consultants, independent contractors, advisors, corporate collaborators, outside scientific collaborators, contract manufacturers, suppliers and other third parties. We, as well as our licensors, also enter into confidentiality and invention or patent assignment agreements with employees and certain consultants. We also seek to preserve the integrity and confidentiality of our data, trade secrets and know-how by maintaining physical security of our premises and physical and electronic security of our information technology systems. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. We cannot guarantee that our trade secrets and other proprietary and confidential information will not be disclosed or that competitors will not otherwise gain access to our trade secrets. Any party with whom we have executed such an agreement may breach that agreement and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time consuming and the outcome is unpredictable. In addition, some courts both within and outside the United States may be less willing or unwilling to protect trade secrets. Further, if any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such third party, or those to whom they communicate such technology or information, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our business and competitive position could be harmed.

Trade secrets and know-how can be difficult to protect as trade secrets and know-how will over time be disseminated within the industry through independent development, the publication of journal articles, and the movement of personnel skilled in the art from company to company or academic to industry scientific positions. If we fail to prevent material disclosure of the know-how, trade secrets and other intellectual property related to our technologies to third parties, we will 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. Even if we are able to adequately protect our trade secrets and proprietary information, our trade secrets could otherwise become known or could be independently discovered by our competitors. For example, competitors could purchase our products and attempt to replicate some or all of the competitive advantages we derive from our development efforts, design around our protected technology or develop their own competitive technologies that fall outside of our intellectual property rights. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, in the absence of patent protection, we would have no right to prevent them, or those to whom they communicate, from using that technology or information to compete with us.

We may not be able to prevent misappropriation of our intellectual property, trade secrets or confidential information, 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.

We have not yet registered our trademarks in certain jurisdictions. Failure to secure those registrations could adversely affect our business.

We have registered trademarks for "Iterum" in the United States, European Union, Japan, Switzerland and Canada. If we are unable to secure registrations for our trademarks in other countries, we may encounter more difficulty in enforcing them against third parties than we otherwise would, which could adversely affect our business. We are in the process of registering trademarks for our product candidates in the United States, Europe and Canada. Any trademark applications we have filed for our product candidates or may file in the future are not guaranteed to be allowed for registration, and even if they are, we may fail to maintain or enforce such registered trademarks. During trademark registration proceedings in the United States, Europe, Canada and other jurisdictions, we may receive rejections. We are given an opportunity to respond to those rejections, but we may not be able to overcome such rejections. In addition, in the USPTO and in comparable agencies in many other jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings.

In addition, any proprietary name we propose to use with oral sulopenem, sulopenem or any other product candidate in the United States must be approved by the FDA, and in Europe by the EMA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA and the EMA each typically conduct a review of proposed product names, including an evaluation of potential for confusion with other product names. We had submitted our proposed proprietary name for oral sulopenem in connection with our NDA for oral sulopenem and we received conditional acceptance from the FDA at that time. However, as provided in the CRL received in July 2021, we will be required to resubmit the proposed proprietary name if and when we respond to the application deficiencies and resubmit the NDA for oral sulopenem and as such, there is no guarantee that the FDA will conclude that the proprietary name continues to be acceptable when resubmitted. If the FDA objects to our proposed proprietary product name, we may be required to expend significant additional resources in an effort to identify a suitable proprietary product name that would qualify under applicable trademark laws, not infringe, misappropriate or otherwise violate the existing rights of third parties and be acceptable to the FDA.

Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely impact our business, financial condition, results of operations and growth prospects.

Risks Related to Regulatory Approval and Other Legal Compliance Matters

If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize oral sulopenem, sulopenem or other future product candidates, and our ability to generate revenue will be materially impaired.

Our product candidates, oral sulopenem and sulopenem, and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by comparable foreign regulatory authorities, with regulations differing from country to country. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. We currently do not have any products approved for sale in any jurisdiction. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party CROs to assist us in this process.

Although we have QIDP status and fast track designation for sulopenem and oral sulopenem for the indications of uUTI, cUTI and cIAI (and for the indications of community-acquired bacterial pneumonia, acute bacterial prostatitis, gonococcal urethritis, and pelvic inflammatory disease) which may provide for a more rapid NDA review cycle, the time required to obtain approval, if any, by the FDA and comparable foreign authorities is unpredictable and typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, the COVID-19 pandemic could impact the FDA's regulatory review process, including delays in meetings related to planned or completed clinical trials and ultimately the review and approval of our product candidates. Approval policies, regulations, or the type and amount of clinical data necessary to gain approval may also change during the course of a product candidate's clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any product candidate and it is possible that we will not be able to obtain regulatory approval for sulopenem or any product candidates or other indications that we may seek to develop in the future will ever obtain regulatory approval. Neither we nor any future collaborator is permitted to market any of our product candidates in the United States until we or they receive regulatory approval of an NDA(s) from the FDA.

In order to obtain approval to commercialize a product candidate in the United States or abroad, we or our collaborators must demonstrate to the satisfaction of the FDA or foreign regulatory agencies, that such product candidates are safe and effective for their intended uses. Results from non-clinical studies and clinical trials can be interpreted in different ways. Even if we believe that the non-clinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA and other regulatory authorities. Although we conducted our prior Phase 3 clinical trials pursuant to SPA agreements, met with the FDA at a pre-NDA meeting and had our NDA application accepted for review by the FDA in January 2021, we received a CRL from the FDA on July 23, 2021 in respect of our NDA. The CRL provided that the FDA had completed its review of the NDA and had determined that it could not approve the NDA in its present form. The CRL further provided that additional data are necessary to support approval of oral sulopenem for the treatment of adult women with uUTIs caused by designated susceptible microorganisms proven or strongly suspected to be non-susceptible to a quinolone and recommended that we conduct at least one additional adequate and well-controlled clinical trial, potentially using a different comparator drug. In July 2022 we reached an agreement with the FDA under the SPA process on the design, endpoints and statistical analysis of a Phase 3 clinical trial for oral sulopenem for the treatment of uUTIs and we commenced enrollment in that clinical trial, known as REASSURE, in October 2022. The study is designed as a non-inferiority trial comparing oral sulopenem and Augmentin® (amoxicillin/clavulanate) in the Augmentin® susceptible population. Additionally, though not an approvability issue, the FDA recommended in its CRL that we conduct additional non-clinical PK/PD studies to support dose selection for the proposed treatment indication(s). We have commenced additional non-clinical PK/PD investigations to support the dosing regimen selected for oral sulopenem, as recommended by the FDA. There can be no assurance that we will be in a position to resolve the matters set forth in the CRL, that we will be able to complete the ongoing Phase 3 clinical trial and non-clinical studies intended to support a resubmission of our NDA or that any data generated by such clinical and non-clinical investigation will be adequate to support resubmission or approval of our NDA.

An NDA must include extensive preclinical and clinical data and supporting information to establish the product candidate's safety and efficacy for each desired indication. The NDA must also include significant information regarding the CMC for the product candidate. Obtaining approval of an NDA is a lengthy, expensive and uncertain process. The FDA has substantial discretion in the review and approval process and may refuse to accept for filing any application or may decide that our data is insufficient for approval and require additional non-clinical, clinical or other studies. Foreign regulatory authorities have differing requirements for approval of drugs with which we must comply prior to marketing. Obtaining marketing approval for marketing of a product candidate in one country does not ensure that we will be able to obtain marketing approval in other countries, but the failure to obtain marketing approval in one jurisdiction could negatively affect our ability to obtain marketing approval in other jurisdictions. The FDA or any foreign regulatory body can delay, limit or deny approval of our product candidates or require us to conduct additional non-clinical or clinical testing or abandon a program for many reasons, including:

- the FDA or the applicable foreign regulatory agency's disagreement with the design or implementation of our clinical trials, such as the FDA stating in the CRL received in July 2021 that additional data are necessary to support approval of oral sulopenem;
- negative or ambiguous results from our clinical trials or results that may not meet the level of statistical significance required by the FDA or comparable foreign regulatory agencies for approval;
- serious and unexpected drug-related side effects experienced by participants in our clinical trials or by individuals using drugs similar to our product candidates;
- our inability to demonstrate to the satisfaction of the FDA or the applicable foreign regulatory body that our product candidates are safe and effective for the proposed indication(s);
- the FDA's or the applicable foreign regulatory agency's disagreement with the interpretation of data from non-clinical studies or clinical trials;
- our inability to demonstrate the clinical and other benefits of our product candidates outweigh any safety or other perceived risks;
- the FDA's or the applicable foreign regulatory agency's requirement for additional non-clinical studies or clinical trials, such as the FDA's request for additional clinical trial work in the CRL received in July 2021;
- the FDA's or the applicable foreign regulatory agency's disagreement regarding the formulation, labeling and/or the specifications for our product candidates; or
- the potential for approval policies or regulations of the FDA or the applicable foreign regulatory agencies to significantly change in a manner rendering our clinical data insufficient for approval.

Of the large number of drugs in development, only a small percentage complete the FDA or foreign regulatory approval processes and are successfully commercialized. The lengthy review process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval, which would significantly harm our business, financial condition, results of operations and growth prospects.

Even if we eventually receive approval of an NDA or foreign marketing application for our product candidates, the FDA or the applicable foreign regulatory agency may grant approval contingent on the performance of costly additional clinical trials, often referred to as Phase 4 clinical trials, and the FDA may require the implementation of a REMS, which may be required to ensure safe use of the drug after approval. The FDA or the applicable regulatory agency also may approve a product candidate for a more limited indication or patient population than we originally requested, and the FDA or applicable foreign regulatory agency may not approve the labeling that we believe is necessary or desirable for the successful commercialization of a product candidate. Any delay in obtaining, or inability to obtain, applicable regulatory approval would delay or prevent commercialization of that product candidate and would materially adversely impact our business and prospects.

Although we are conducting the ongoing Phase 3 clinical trial comparing oral sulopenem and Augmentin® (amoxicillin/clavulanate) under a SPA agreement with the FDA, a SPA agreement does not guarantee marketing approval of, or any other particular outcome from, regulatory review.

We are conducting the ongoing Phase 3 clinical trial comparing oral sulopenem and Augmentin® (amoxicillin/clavulanate) under a SPA agreement with the FDA. Under the SPA process, the FDA provides a clinical trial sponsor with an official evaluation and written guidance on the design of a proposed protocol intended to form the basis for an NDA. A SPA agreement indicates concurrence by the FDA with the adequacy and acceptability of specific critical elements of the overall protocol design for a clinical trial intended to support a future marketing application, but it does not indicate FDA concurrence on every protocol detail. A SPA agreement also does not ensure the receipt of marketing approval or that the approval process will be faster than conventional procedures. A determination regarding marketing approval is addressed during the review of a submitted NDA and depends on efficacy and safety results and an evaluation of the overall benefits and risks of treatment after review of the data from the development program in its totality.

Even after the FDA agrees to the design, execution, and analysis proposed in a protocol reviewed under the SPA process, the FDA may revoke or alter its agreement if a substantial scientific issue essential to determining the safety or effectiveness of the drug has been identified after the testing has begun. A SPA agreement may also be changed through written agreement between the sponsor and the FDA. A revocation or alteration in an existing SPA agreement could delay or prevent approval an NDA. In addition, any significant change to the protocol for a clinical trial subject to a SPA agreement would require prior FDA approval, which could delay implementation of such a change and the conduct of the related clinical trial. The FDA retains significant discretion in interpreting the terms of the SPA agreement and the data and results from any study that is the subject of the SPA agreement.

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

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including for 35 days beginning on December 22, 2018, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Separately, in response to the COVID-19 pandemic, a number of companies announced in 2021 receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. Following a period of false starts and temporary suspensions due to the omicron variant, the FDA resumed domestic inspections in February 2022 and indicated that it would conduct foreign inspections beginning in April 2022 on a prioritized basis. However, the FDA may not be able to continue its current pace and review timelines could be extended, including where a pre-approval inspection or an inspection of clinical sites is required and due to the ongoing COVID-19 pandemic and travel restrictions, the FDA is unable to complete such required inspections during the review period. Regulatory authorities outside the U.S. may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities. If a prolonged government shutdown or other disruption occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Future shutdowns or other disruptions could also affect other government agencies such as the SEC, which may also impact our business by delaying review of our public filings, to the extent such review is necessary, and our ability to access the public markets.

If we are unable to obtain marketing approval in jurisdictions outside the United States, we will not be able to market our product candidates outside of the United States.

In order to market and sell oral sulopenem, sulopenem or our other future product candidates in the European Union and many other jurisdictions, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. The approval procedure varies among countries and can involve additional testing. In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. For example, although we have obtained agreement on an SPA with the FDA for the additional Phase 3 clinical trial for oral sulopenem, the EMA or other regulatory authorities may not agree with the overall protocol design for this additional clinical trial. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We may not obtain approvals from regulatory authorities outside the United States on a timely basis or at all.

For example, we obtained scientific advice from the EMA for each of the prior Phase 3 clinical trials in the uUTI, cUTI and cIAI indications, as well as to gain alignment on non-clinical supportive information required for EMA submission. We are not in alignment with regard to the comparator agent selected for the cUTI clinical trial and would need to consider other options to accommodate a European filing for this indication. The EMA may request that we conduct one or more additional clinical trials or non-clinical studies to support potential approval for oral sulopenem and sulopenem for the cUTI indication. We cannot predict how the EMA will interpret the data and results from our Phase 3 clinical trial and other elements of our development program, or whether oral sulopenem or sulopenem will receive any regulatory approvals in the European Union.

We are currently evaluating our commercialization strategy in the United States and other territories. We believe that in addition to the United States, Europe represents a significant market opportunity because of rising rates of extended spectrum ß-lactamases (ESBL) resistance.

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. Following protracted negotiations, the United Kingdom left the European Union on January 31, 2020 and a transition period to December 31, 2020, was established to allow the United Kingdom and the European Union to negotiate the United Kingdom's withdrawal. As a result, effective January 1, 2021, the United Kingdom is no longer part of the European Single Market and European Union Customs Union.

Since the regulatory framework for pharmaceutical products in the United Kingdom covering the quality, safety, and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales, and distribution of pharmaceutical products is derived from European Union directives and regulations, the consequences of Brexit and the impact the future regulatory regime that applies to products and the approval of product candidates in the United Kingdom remains unclear. As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or the MHRA, became responsible for supervising medicines and medical devices in Great Britain, comprising England, Scotland and Wales under domestic law, whereas Northern Ireland will continue to be subject to European Union rules under the Northern Ireland Protocol. The MHRA will rely on the Human Medicines Regulations 2012 (SI 2012/1916) (as amended), or the HMR, as the basis for regulating medicines. The HMR has incorporated into the domestic law of the body of European Union law instruments governing medicinal products that pre-existed prior to the United Kingdom's withdrawal from the European Union. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, may force us to restrict or delay efforts to seek regulatory approval in the United Kingdom for our product candidates, which could significantly and materially harm our business.

If we receive regulatory approval for any product candidate, we will be subject to ongoing obligations and continuing regulatory review, which may result in significant additional expense. Our product candidates, including oral sulopenem and sulopenem, if approved, could be subject to restrictions or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our product candidates, when and if approved.

Any product candidate, including oral sulopenem and sulopenem, for which we obtain marketing approval will also be subject to ongoing regulatory requirements for labeling, packaging, storage, distribution, advertising, promotion, record-keeping and submission of safety and other post marketing information. For example, approved products, manufacturers and manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs. As such, we and our contract manufacturers will be subject to continual review and periodic inspections to assess compliance with cGMPs. Accordingly, we and others with whom we work must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production and quality control. We will also be required to report certain adverse reactions and production problems, if any, to the FDA and to comply with requirements concerning advertising and promotion for our products.

In addition, even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed, may be subject to significant conditions of approval or may impose requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product. The FDA may also require a REMS as a condition of approval of our product candidates, which could include requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA closely regulates the post-approval marketing and promotion of drugs to ensure that drugs are marketed only for the approved indications and in accordance with the provisions of the approved labelling and regulatory requirements. The FDA also imposes stringent restrictions on manufacturers' communications regarding off-label use and if we do not restrict the marketing of our products only to their approved indications, we may be subject to enforcement action for off-label marketing. In September 2021, the FDA published final regulations which describe the types of evidence that the agency will consider in determining the intended use of a drug product.

If a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, or disagrees with the promotion, marketing or labeling of a product, it may impose restrictions on that product or us. In addition, if any product fails to comply with applicable regulatory requirements, a regulatory agency may:

- issue fines, warning letters, untitled letters or impose holds on clinical trials if any are still ongoing;
- mandate modifications to promotional materials or require provision of corrective information to healthcare practitioners;
- impose restrictions on the product or its manufacturers or manufacturing processes;
- impose restrictions on the labeling or marketing of the product;
- impose restrictions on product distribution or use;
- require post-marketing clinical trials;
- require withdrawal of the product from the market;
- refuse to approve pending applications or supplements to approved applications that we submit;
- require recall of the product;
- require entry into a consent decree, which can include imposition of various fines (including restitution or disgorgement of profits or revenue), reimbursements for inspection costs, required due dates for specific actions and penalties for non-compliance;
- suspend or withdraw marketing approvals;
- refuse to permit the import or export of the product;
- seize or detain supplies of the product; or
- issue injunctions or impose civil or criminal penalties.

Similar restrictions apply to the approval of our products in the European Union. The holder of a marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include compliance with the European Union's stringent pharmacovigilance or safety reporting rules, which can impose post-authorization studies and additional monitoring obligations; the manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory; and the marketing and promotion of authorized drugs, which are strictly regulated in the European Union and are also subject to EU Member State laws.

Accordingly, in connection with our currently approved products and assuming we, or our collaborators, receive marketing approval for one or more of our product candidates, we, and our collaborators, and our and their contract manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control. If we, and our collaborators, are not able to comply with post-approval regulatory requirements, our or our collaborators' ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

Any relationships we may have with customers, healthcare providers and professionals and third-party payors, among others, will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to penalties, including criminal sanctions, civil penalties, contractual damages, reputational harm, fines, disgorgement, exclusion from participation in government healthcare programs, curtailment or restricting of our operations and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any products for which we are able to obtain marketing approval. Any arrangements we have with healthcare providers, third-party payors and customers will subject us to broadly applicable fraud and abuse and other healthcare laws and regulations. The laws and regulations may constrain the business or financial arrangements and relationships through which we conduct clinical research, market, sell and distribute any products for which we obtain marketing approval. These include the following:

Anti-Kickback Statute. The federal Anti-Kickback Statute prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration (including any kickback, bribe or rebate), directly or indirectly, in cash or in kind, to induce or reward or in return for, either the referral of an individual for or the purchase, lease or order of a good, facility, item or service for which payment may be made under a federal healthcare program such as Medicare and Medicaid.

False Claims Laws. The federal false claims and civil monetary penalties laws, including the federal civil False Claims Act, impose criminal and civil penalties, including through civil whistleblower or *qui tam* actions against individuals or entities for, among other things, knowingly presenting or causing to be presented false or fraudulent claims for payment by a federal healthcare program or making a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties.

Health Insurance Portability and Accountability Act of 1996 (HIPAA). HIPAA imposes criminal and civil liability for, among other things, executing a scheme or making materially false statements in connection with the delivery of or payment for health care benefits, items or services. Additionally, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations on covered entities and their business associates that perform certain functions or activities that involve the use or disclosure of protected health information on their behalf, including mandatory contractual terms and technical safeguards, with respect to maintaining the privacy, security and transmission of individually identifiable health information.

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

Analogous State and Foreign Laws. Analogous state and foreign fraud and abuse laws and regulations, such as state anti-kickback and false claims laws, can apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors and are generally broad and are enforced by many different federal and state agencies as well as through private actions. Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not pre-empted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that any business arrangements we have with third parties and our business generally, will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, individual imprisonment, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, disgorgement, contractual damages, reputational harm and the curtailment or restructuring of our operations. Defending against any such actions can be costly, time-consuming and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. Further, if any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the European Union. The provision of benefits or advantages to physicians is governed by the national anti-bribery laws of EU Member States. In addition, payments made to physicians in certain EU Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual EU Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the EU Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

Healthcare legislative reform measures may have a material adverse effect on our business and results of operations.

In the United States, there have been and continue to be a number of legislative and regulatory changes, and proposed changes, that could affect the future results of our business and operations. In particular, there have been and continue to be a number of initiatives at the federal and state levels that seek to reduce healthcare costs. For example, in March 2010 the Patient Protection and Affordable Care Act (as amended by the Health Care and Education Reconciliation Act) (ACA) was enacted, which has substantially changed the way health care is financed by both governmental and private insurers, and significantly impacted the U.S. pharmaceutical industry.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013. The Coronavirus Aid, Relief, and Economic Security (CARES) Act suspended the 2% Medicare sequester from May 1, 2020 through December 31, 2020, and extended the sequester by one year, through 2031.These Medicare sequester reductions were suspended through the end of June 2022 but the full 2% cut resumed thereafter on July 1, 2022. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Since enactment of the ACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, or the TCJA, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. Further, on December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA, and therefore because the mandate was repealed as part of the TCJA, the remaining provisions of the ACA are invalid as well. The U.S. Supreme Court heard this case on November 10, 2020 and, on June 17, 2021, dismissed this action after finding that the plaintiffs do not have standing to challenge the constitutionality of the ACA. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The Trump Administration also took executive actions to undermine or delay implementation of the ACA, including directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On January 28, 2021, however, President Biden issued a new executive order which directs federal agencies to reconsider rules and other policies that limit Americans' access to health care, and consider actions that will protect and strengthen that access. Under this executive order, federal agencies are directed to re-examine: policies that undermine protections for people with pre-existing conditions, including complications related to COVID-19; demonstrations and waivers under Medicaid and the ACA that may reduce coverage or undermine the programs, including work requirements; policies that undermine the Health Insurance Marketplace or other markets for health insurance; policies that make it more difficult to enroll in Medicaid and the ACA; and policies that reduce affordability of coverage or financial assistance, including for dependents.

In addition, the CMS has proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. On November 30, 2018, CMS announced a proposed rule that would amend the Medicare Advantage and Medicare Part D prescription drug benefit regulations to reduce out of pocket costs for plan enrollees and allow Medicare plans to negotiate lower rates for certain drugs. Among other things, the proposed rule changes would allow Medicare Advantage plans to use pre authorization (PA) and step therapy (ST) for six protected classes of drugs, with certain exceptions, permit plans to implement PA and ST in Medicare Part B drugs; and change the definition of "negotiated prices" while adding a definition of "price concession" in the regulations. It is unclear whether these proposed changes will be accepted, and if so, what effect such changes will have on our business.

We expect that these healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product and/or the level of reimbursement physicians receive for administering any approved product we might bring to market. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. Accordingly, such reforms, if enacted, could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain marketing approval and may affect our overall financial condition and ability to develop or commercialize product candidates.

The prices of prescription pharmaceuticals in the United States and foreign jurisdictions are subject to considerable legislative and executive actions and could impact the prices we obtain for our products, if and when approved.

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. There have been several recent U.S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, and reduce the costs of pharmaceuticals under Medicare and Medicaid.

In October 2020, the Department of Health and Human Services (HHS) and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program (SIP), to import certain prescription drugs from Canada into the United States. The final rule is currently the subject of ongoing litigation, but at least six states (Vermont, Colorado, Florida, Maine, New Mexico, and New Hampshire) have passed laws allowing for the importation of drugs from Canada with the intent of developing SIPs for review and approval by the FDA. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed until January 1, 2026 by the Infrastructure Investment and Jobs Act.

On July 9, 2021, President Biden signed Executive Order 14063, which focuses on, among other things, the price of pharmaceuticals. To address these costs, the executive order directs HHS to create a plan within 45 days to combat "excessive pricing of prescription drugs and enhance domestic pharmaceutical supply chains, to reduce the prices paid by the federal government for such drugs, and to address the recurrent problem of price gouging." Thereafter, on September 9, 2021, HHS released its plan to reduce drug prices. The key features of that plan are to: (a) make drug prices more affordable and equitable for all consumers and throughout the health care system by supporting drug price negotiations with manufacturers; (b) improve and promote competition throughout the prescription drug industry by supporting market changes that strengthen supply chains, promote biosimilars and generic drugs, and increase transparency; and (c) foster scientific innovation to promote better healthcare and improve health by supporting public and private research and making sure that market incentives promote discovery of valuable and accessible new treatments.

More recently, with passage of the Inflation Reduction Act in August 2022, Congress authorized Medicare beginning in 2026 to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars. This provision is limited in terms of the number of pharmaceuticals whose prices can be negotiated in any given year and it only applies to drug products that have been approved for at least nine years and biologics that have been licensed for 13 years. Drugs and biologics that have been approved for a single rare disease or condition are categorically excluded from price negotiation. Further, the new legislation provides that if pharmaceutical companies raise prices in Medicare faster than the rate of inflation, they must pay rebates back to the government for the difference. The new law also caps Medicare out-of-pocket drug costs at an estimated $4,000 a year in 2024 and, thereafter beginning in 2025, at $2,000 a year.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care organizations and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

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

In markets outside of the United States and the European Union, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action in the United States, the European Union or any other jurisdiction. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, our product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.

Reporting and payment obligations under the Medicaid Drug Rebate Program and other governmental drug pricing programs are complex and may involve subjective decisions. Any failure to comply with those obligations could subject us to penalties and sanctions.

As a condition of reimbursement by various federal and state health insurance programs, pharmaceutical companies are required to calculate and report certain pricing information to federal and state agencies. The regulations governing the calculations, price reporting and payment obligations are complex and subject to interpretation by various government and regulatory agencies, as well as the courts. Reasonable assumptions have been made where there is lack of regulations or clear guidance and such assumptions involve subjective decisions and estimates. Pharmaceutical companies are required to report any revisions to our calculation, price reporting and payment obligations previously reported or paid. Such revisions could affect liability to federal and state payers and also adversely impact reported financial results of operations in the period of such restatement.

Uncertainty exists as new laws, regulations, judicial decisions, or new interpretations of existing laws, or regulations related to our calculations, price reporting or payments obligations increases the chances of a legal challenge, restatement or investigation. If a company becomes subject to investigations, restatements, or other inquiries concerning compliance with price reporting laws and regulations, it could be required to pay or be subject to additional reimbursements, penalties, sanctions or fines, which could have a material adverse effect on the business, financial condition and results of operations. In addition, it is possible that future healthcare reform measures could be adopted, which could result in increased pressure on pricing and reimbursement of products and thus have an adverse impact on financial position or business operations.

Further, state Medicaid programs may be slow to invoice pharmaceutical companies for calculated rebates resulting in a lag between the time a sale is recorded and the time the rebate is paid. This results in a company having to carry a liability on its consolidated balance sheets for the estimate of rebate claims expected for Medicaid patients. If actual claims are higher than current estimates, the company's financial position and results of operations could be adversely affected.

In addition to retroactive rebates and the potential for 340B Program refunds, if a pharmaceutical firm is found to have knowingly submitted any false price information related to the Medicaid Drug Rebate Program to CMS, it may be liable for civil monetary penalties. Such failure could also be grounds for CMS to terminate the Medicaid drug rebate agreement, pursuant to which companies participate in the Medicaid program. In the event that CMS terminates a rebate agreement, federal payments may not be available under government programs, including Medicaid or Medicare Part B, for covered outpatient drugs.

Additionally, if a pharmaceutical company overcharges the government in connection with the Family Self-Sufficiency Program or Tricare Retail Pharmacy Program, whether due to a misstated Federal Ceiling Price or otherwise, it is required to refund the difference to the government. Failure to make necessary disclosures and/or to identify contract overcharges can result in allegations against a company under the False Claims Act and other laws and regulations. Unexpected refunds to the government, and responding to a government investigation or enforcement action, would be expensive and time-consuming, and could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

We are subject to anti-corruption laws, as well as export control laws, customs laws, sanctions laws and other laws governing our operations. If we fail to comply with these laws, we could be subject to civil or criminal penalties, other remedial measures and legal expenses, which could adversely affect our business, results of operations and financial condition.

Our operations are subject to anti-corruption laws, including the U.S. Foreign Corrupt Practices Act (FCPA), the Irish Criminal Justice (Corruption Offenses) Act 2018, and other anti-corruption laws that apply in countries where we do business and may do business in the future. The FCPA and these other laws generally prohibit us, our officers, and our employees and intermediaries from bribing, being bribed or making other prohibited payments to government officials or other persons to obtain or retain business or gain some other business advantage. We may in the future operate in jurisdictions that pose a high risk of potential FCPA violations, and we may participate in collaborations and relationships with third parties whose actions could potentially subject us to liability under the FCPA or local anti-corruption laws. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in that existing laws might be administered or interpreted.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

We are also subject to other laws and regulations governing our international operations, including regulations administered by the governments of the United States, and authorities in the European Union, including applicable export control regulations, economic sanctions on countries and persons, customs requirements and currency exchange regulations, collectively referred to as the trade control laws. Further, the provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order, or use of medicinal products is prohibited in the European Union. The provision of benefits or advantages to physicians is also governed by the national anti-bribery laws of European Union member states, such as the UK Bribery Act 2010. Infringement of these laws could result in substantial fines and imprisonment. Payments made to physicians in certain European Union member states must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization, and/or the regulatory authorities of the individual European Union member states. These requirements are provided in the national laws, industry codes, or professional codes of conduct applicable in the European Union member states. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines, or imprisonment.

There is no assurance that we will be effective in ensuring our compliance with all applicable anti-corruption laws, including the FCPA or other legal requirements, including trade control laws. If we are not in compliance with the FCPA and other anti-corruption laws or trade control laws, we may be subject to criminal and civil penalties, disgorgement and other sanctions and remedial measures, and legal expenses, which could have an adverse impact on our business, financial condition, results of operations and liquidity. Likewise, any investigation of any potential violations of the FCPA, other anti-corruption laws or trade control laws by U.S. or other authorities could also have an adverse impact on our reputation, our business, results of operations and financial condition.

We are subject to various laws protecting the confidentiality of certain patient health information, and our failure to comply could result in penalties and reputational damage. Compliance with global privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the failure to comply with such requirements could subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations.

The regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate has established its own data security and privacy frameworks with which we must comply. For example, the collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the European Union, including personal health data, is subject to the EU General Data Protection Regulation (GDPR), which took effect across all member states of the European Economic Area (EEA), in May 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data (including health and other sensitive data), including the following: to provide information to individuals regarding data processing activities; to implement safeguards to protect the security and confidentiality of personal data; to make a mandatory breach notification in certain circumstances; and to take certain measures when engaging third-party processors. The GDPR increases our obligations with respect to clinical trials conducted in the EEA by expanding the definition of personal data to include coded data and requiring changes to informed consent practices and more detailed notices for clinical trial subjects and investigators. In addition, the GDPR also imposes strict rules on the transfer of personal data to countries outside the European Union, including the United States and, as a result, increases the scrutiny that clinical trial sites located in the EEA should apply to transfers of personal data from such sites to countries that are considered to lack an adequate level of data protection, such as the United States. The GDPR also permits data protection authorities to require destruction of improperly gathered or used personal information and/or impose substantial fines for violations of the GDPR, which can be up to four percent of global revenues or 20 million Euros, whichever is greater. The GDPR also confers a private right of action on data subjects to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR provides that EU member states may make their own further laws and regulations limiting the processing of personal data, including genetic, biometric or health data adding to the complexity of processing personal data in the European Union.

Similar actions are either in place or under way in the United States. There are a broad variety of data protection laws that are applicable to our activities, and a wide range of enforcement agencies at both the state and federal levels that can review companies for privacy and data security concerns based on general consumer protection laws. The Federal Trade Commission and state Attorneys General all are aggressive in reviewing privacy and data security protections for consumers. New laws also are being considered at both the state and federal levels. For example, the California Consumer Privacy Act—which went into effect on January 1, 2020—is creating similar risks and obligations as those created by GDPR, though the Act does exempt certain information collected as part of a clinical trial subject to the Federal Policy for the Protection of Human Subjects (the Common Rule). Many other states are considering similar legislation. A broad range of legislative measures also have been introduced at the federal level. Accordingly, failure to comply with federal and state laws (both those currently in effect and future legislation) regarding privacy and security of personal information could expose us to fines and penalties under such laws. There also is the threat of consumer class actions related to these laws and the overall protection of personal data. 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 reputation and our business.

Given the breadth and depth of changes in data protection obligations, complying with the GDPR's requirements is rigorous and time intensive and requires significant resources and a review of our technologies, systems and practices, as well as those of any third-party collaborators, service providers, contractors or consultants that process or transfer personal data collected in the European Union. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could require us to change our business practices and put in place additional compliance mechanisms, may interrupt or delay our development, regulatory and commercialization activities, and could lead to government enforcement actions, private litigation and significant fines and penalties against us, all of which could increase our cost of doing business and have a material adverse effect on our business, financial condition or results of operations. Similarly, failure to comply with federal and state laws regarding privacy and security of personal information could expose us to fines and penalties under such 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 reputation and our business.

Further, we cannot assure you that our third-party service providers with access to our or our customers', suppliers', trial patients' and employees' personally identifiable and other sensitive or confidential information in relation to which we are responsible will not breach contractual obligations imposed by us, or that they will not experience data security breaches or attempts thereof, which could have a corresponding effect on our business, including putting us in breach of our obligations under privacy laws and regulations and/or which could in turn adversely affect our business, results of operations and financial condition. We cannot assure you that our contractual measures and our own privacy and security-related safeguards will protect us from the risks associated with the third-party processing, storage and transmission of such information.

Our employees, independent contractors, principal investigators, CROs, consultants or vendors may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements.

We are exposed to the risk that our employees, independent contractors, principal investigators, CROs, consultants or vendors may engage in fraudulent or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violates FDA regulations, including those laws requiring the reporting of true, complete and accurate information to the FDA; manufacturing standards; federal and state healthcare fraud and abuse laws and regulations; or laws that require the true, complete and accurate reporting of financial information or data. Specifically, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Activities subject to these laws also involve the improper use or misrepresentation of information obtained in the course of clinical trials or creating fraudulent data in our preclinical studies or clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter misconduct by our employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. Additionally, we are subject to the risk that a person could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, disgorgement, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, individual imprisonment, additional reporting obligations and oversight if subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, curtailment of our operations, contractual damages, reputational harm, and diminished potential profits and future earnings, any of which could adversely affect our business, financial condition, results of operations or growth prospects.

Risks Related to Employee Matters and Managing Growth

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

Our industry has experienced a high rate of turnover of management personnel in recent years. We are highly dependent on the development, regulatory, commercialization and business development expertise of Corey N. Fishman, our Chief Executive Officer, as well as the other principal members of our management team. Although we have formal employment agreements with our executive officers, these agreements do not prevent them from terminating their employment with us at any time. We do not maintain "key man" insurance with respect to any of our executive officers or key employees.

If we lose one or more of our executive officers or key employees, our ability to implement our business strategy successfully could be seriously harmed. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain regulatory approval of and commercialize product candidates successfully. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these additional key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we have in the past, and may continue to do so in the future, relied on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be engaged by entities other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to develop and commercialize product candidates will be limited.

We may encounter difficulties in managing growth, which could disrupt our operations.

We could experience growth in the number of our employees and the scope of our operations, if we need to conduct additional clinical trials or non-clinical investigation to support the potential resubmission of our NDA or in the event we are successful in obtaining regulatory approval particularly in the areas of manufacturing, regulatory affairs, sales, marketing and health resources. Our management may need to divert a disproportionate amount of its attention away from our day-to-day activities to devote time to managing these growth activities. To manage these growth activities, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. Our inability to effectively manage any expansion of our operations 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. Any growth experienced could require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If our management is unable to effectively manage such growth, our expenses may increase more than expected, our potential ability to generate revenue could be reduced and we may not be able to implement our business strategy.

In addition, we have and may continue to need to adjust the size of our workforce as a result of changes to our expectations for our business, which can result in diversion of management attention, disruptions to our business, and related expenses.

If approvals are obtained outside of the United States, we will be subject to additional risks in conducting business in those markets.

Even if we are able to obtain approval for commercialization of a product candidate in a country outside of the United States, we will be subject to additional risks related to international business operations, including:

- potentially reduced protection for intellectual property rights;
- the potential for so-called parallel importing, which is what happens when a local seller, faced with high or higher local prices, opts to import goods from a market outside of the United States (with low or lower prices) rather than buying them locally;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular economies and markets;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting a product candidate and/or finished drug product supply or manufacturing capabilities abroad;

•business interruptions resulting from geo-political actions, including war and terrorism, or natural disasters, including earthquakes, hurricanes, typhoons, floods and fires, public health crises, or pandemics, like COVID-19; and

•failure to comply with Office of Foreign Asset Control rules and regulations and the FCPA.

These and other risks may materially adversely affect our ability to attain or sustain revenue from markets outside of the United States.

Our business, results of operations, financial condition, cash flows and share price can be adversely affected by pandemics, epidemics or other public health emergencies, such as the COVID-19 pandemic, which could delay our ability to complete our clinical trials including our ongoing Phase 3 clinical trial, delay the initiation of future clinical trials, disrupt regulatory activities or have other adverse effects on our business and operations. In addition, the COVID-19 pandemic has caused substantial disruption in the financial markets and may adversely impact economies worldwide, both of which could result in adverse effects on our business and operations.

Our business, results of operations, financial condition, cash flows and share price may be adversely affected by pandemics, epidemics or other public health emergencies, such as the outbreak of COVID-19 which has spread worldwide, including to the United States and Ireland. In March 2020, the World Health Organization characterized COVID-19 as a pandemic, and the President of the United States declared the COVID-19 outbreak a national emergency. The pandemic has resulted in governments around the world implementing stringent measures to help control the spread of the virus, including quarantines, "shelter in place" and "stay at home" orders, travel restrictions, business curtailments, school closures, and other measures. These responsive measures have had a significant impact, both direct and indirect, on business and commerce worldwide, as worker shortages have occurred, supply chains have been disrupted, and facilities and production have been suspended.

The COVID-19 pandemic may negatively affect our business and operations in a number of ways, and its long-term effects are uncertain. The spread of COVID-19 and the responsive measures taken to date have limited our access to our facilities and caused the majority of our employees to work from home. Responsive measures to COVID-19 have resulted in restrictions on operations at clinical trial sites which could impact patient enrollment in the ongoing Phase 3 clinical trial being conducted in response to the CRL to support a potential resubmission of our NDA. In addition, the COVID-19 pandemic could impact the FDA's regulatory review process, including delays in meetings related to planned or completed clinical trials and ultimately the review and approval of our product candidates. The FDA's review of any resubmitted NDA for oral sulopenem for the treatment of uUTI may be delayed due to COVID-19, including an inability to schedule, or delays in scheduling, meetings and inspections. Additionally, the COVID-19 pandemic may negatively impact our ability to initiate or complete future clinical trials, including the ongoing Phase 3 clinical trial being conducted in response to the CRL, disrupt our regulatory and commercialization activities, and result in other adverse effects on our business and operations. For example, current and future restrictions on in-person interactions may impact how we commercialize our product candidates, if approved, and we may need to apply non-traditional marketing methods, which may ultimately not be efficient or successful.

In addition, our suppliers and manufacturers located in countries that have been affected by COVID-19 may also be disrupted, which may affect our ability to procure items that are essential for our research and development activities or commercialization in the event any of our product candidates is approved, and may cause disruptions in our current or future trials or commercialization activities. The response to the COVID-19 pandemic may redirect resources with respect to regulatory matters in a way that would adversely impact our ability to progress regulatory approval. We may also face impediments to regulatory meetings and approvals due to measures intended to limit in-person interactions. Additionally, we may also choose to redirect our own resources in a way that may adversely impact or delay certain of our programs.

We cannot foresee if and when the COVID-19 pandemic will be effectively contained, nor can we predict the severity and duration of its impact. If the COVID-19 pandemic is not effectively and timely controlled, we may experience prolonged disruption of our clinical trials, suppliers or contract manufacturers, extended closures of facilities, such as clinical trial sites, suppliers, manufacturers and distributors, including single source suppliers, and delays with respect to regulatory approvals or the commercialization of any of our product candidates, if approved. Such events may materially and adversely affect our business operations and financial condition. Additionally, the COVID-19 pandemic has already caused significant disruptions in the financial markets, and may continue to cause such disruptions, which could impact our ability to raise additional funds and has also impacted, and may continue to impact, the volatility of our stock price and trading in our stock. Moreover, it is possible the COVID-19 pandemic will significantly impact economies worldwide, which could result in adverse effects on our business and operations. We cannot be certain what the overall impact of the COVID-19 pandemic will be on our business, our operations or the global and political environment as a whole but it has the potential to materially adversely affect our business, financial condition, results of operations, and prospects.

We may engage in acquisitions that could disrupt our business, cause dilution to our shareholders or reduce our financial resources.

In the future, we may enter into transactions to acquire other businesses, products or technologies. Any such proposed acquisitions may be subject to the consent of certain holders of the Securities in accordance with the terms and conditions of the EN Indenture and RLN Indenture. If we do identify suitable candidates for acquisition, we may not be able to make such acquisitions on favorable terms, or at all, and we may not be able to obtain approval of or consent to such acquisitions from holders of the Securities. Any acquisitions we make may not strengthen our competitive position, and these transactions may be viewed negatively by customers or investors. We may decide to incur debt in connection with an acquisition or issue our ordinary shares or other equity securities to the shareholders of the acquired company, which would reduce the percentage ownership of our then current shareholders. We could incur losses resulting from undiscovered liabilities of the acquired business that are not covered by the indemnification we may obtain from the seller. In addition, we may not be able to successfully integrate the acquired personnel, technologies and operations into our existing business in an effective, timely and non-disruptive manner. Acquisitions may also divert management attention from day-to-day responsibilities, increase our expenses and reduce our cash available for operations and other uses. We cannot predict the number, timing or size of future acquisitions or the effect that any such transactions might have on our operating results.

Risks Related to Taxation

As used in this section, Risks Related to Taxation, the term "U.S. Holder" means a beneficial owner of our ordinary shares that is, for U.S. federal income tax purposes, (1) an individual who is a citizen or resident of the United States, (2) a corporation (or entity treated as a corporation) created or organized in or under the laws of the United States, any state thereof, or the District of Columbia or otherwise treated as a "domestic corporation" for such purposes, (3) an estate the income of which is subject to U.S. federal income tax regardless of its source or (4) a trust (x) with respect to which a court within the United States is able to exercise primary supervision over its administration and one or more United States persons have the authority to control all of its substantial decisions or (y) that has elected under applicable U.S. Treasury regulations to be treated as a domestic trust. If a partnership or other pass-through entity holds our ordinary shares, the U.S. federal income tax treatment of a partner in that partnership or entity generally will depend upon the status of that partner and the activities of that partnership or entity.

We have been a passive foreign investment company for U.S. federal income tax purposes in the past and we could be a passive foreign investment company in the future, which could subject U.S. Holders to adverse U.S. federal income tax consequences.

We were a passive foreign investment company (PFIC) for U.S. federal income tax purposes for our taxable year ended December 31, 2017. Based on our gross income and average value of our gross assets, we do not believe we (or our wholly owned non-U.S. subsidiaries) were a PFIC for the taxable year ended December 31, 2018 or for any subsequent completed taxable year. We do not expect to be a PFIC for the taxable year ending December 31, 2022; however, our status, and the status of our non-U.S. subsidiaries, in any taxable year will depend on our assets and activities as determined at various times throughout that taxable year. As our PFIC status is a factual determination made annually after the end of each taxable year, there can be no assurances as to that status for the current taxable year or any future taxable year.

We will be a PFIC in any taxable year if at least (i) 75% of our gross income is "passive income" or (ii) 50% of the average gross value of our assets, determined on a quarterly basis, is attributable to assets that produce, or are held for the production of, passive income. We refer to the passive income test as the "PFIC Income Test" and the asset test as the "PFIC Asset Test".

If we are a PFIC in any taxable year in which a U.S. Holder holds the shares of our stock, subject to the next sentence, we always will be a PFIC with respect to those shares, regardless of the results of the PFIC Income Test or the PFIC Asset Test as applied to us in subsequent taxable years. However, under applicable Treasury regulations, if the preceding sentence applies to a U.S. Holder we will cease to be treated as a PFIC with respect to that U.S. Holder if, in the manner and at the time required by those regulations, the U.S. Holder elects to recognize (and pay tax on, in the manner described in the next paragraph) any unrealized gain in the shares of our stock owned by that U.S. Holder.

If we are a PFIC and a U.S. Holder does not make a mark-to-market election (discussed below) with respect to our ordinary shares, under the so-called "excess distribution" regime that U.S. Holder may be subject to adverse tax consequences, including deferred tax and interest charges, with respect to certain distributions on our ordinary shares, any gain realized on a disposition of our ordinary shares and certain other events. The effect of these tax consequences could be materially adverse to the shareholder. If, in any taxable year during which a U.S. Holder holds our ordinary shares and any of our non-U.S. subsidiaries is a PFIC (i.e., a lower-tier PFIC), such U.S. Holder would be treated as owning a proportionate amount (by value) of the shares of the lower-tier PFIC and would be taxed under the excess distribution regime on distributions by the lower-tier PFIC and on gain from the disposition of shares of the lower-tier PFIC even though such U.S. Holder would not receive the proceeds of those distributions or dispositions.

If a U.S. Holder makes a valid and timely mark-to-market election with respect to our ordinary shares, that U.S. Holder will recognize as ordinary income or loss in each taxable year that we meet the PFIC Income Test or PFIC Asset Test an amount equal to the difference between that U.S. Holder's adjusted basis in our ordinary shares and the fair market value of the ordinary shares, thus also possibly giving rise to phantom income and a potential out-of-pocket tax liability. Ordinary loss generally is recognized only to the extent of net mark-to-market gains previously included in income. The mark-to-market election generally will not be available with respect to any of our subsidiaries that is a PFIC and gain recognized on the sale of our ordinary shares that is attributable to a subsidiary that is a PFIC may result in such gain being subject to deferred tax and interest charges.

In certain circumstances a U.S. Holder may make a qualified electing fund, or "QEF election," under the U.S. federal income tax laws with respect to that holder's interest in a PFIC. Such an election may mitigate some of the adverse U.S. federal income tax consequences that could otherwise apply to a U.S. Holder under the excess distribution regime. However, we do not expect to provide U.S. Holders with the information necessary to make a valid QEF election, and U.S. Holders should therefore assume that a QEF election will not be available.

If the IRS determines that we are not a PFIC, and a U.S. Holder previously paid taxes pursuant to a mark-to-market election, that holder may have paid more taxes than the holder legally owed.

If the U.S. Internal Revenue Service (IRS) makes a determination that we were not a PFIC in a prior taxable year and a U.S. Holder previously paid taxes pursuant to a mark-to-market election, that U.S. Holder may have paid more taxes than were legally owed due to such election. If such U.S. Holder does not, or is not able to, file a refund claim before the expiration of the applicable statute of limitations, that U.S. Holder will not be able to claim a refund for those taxes.

Changes to U.S. federal income tax laws could have material consequences for us and U.S. Holders of our ordinary shares.

Future U.S. legislation, U.S. Treasury regulations, judicial decisions and IRS rulings could affect the U.S. federal income tax treatment of us and U.S. Holders of our ordinary shares, possibly with retroactive effect.

A future transfer of a shareholder's ordinary shares, other than one effected by means of the transfer of book entry interests in DTC, may be subject to Irish stamp duty.

Transfers of our ordinary shares effected by means of the transfer of book entry interests in the Depository Trust Company (DTC) should not be subject to Irish stamp duty. Where the ordinary shares are traded through DTC through brokers who hold such ordinary shares on behalf of customers an exemption should be available because our ordinary shares are traded on a recognized stock exchange in the U.S. However, if a shareholder holds their ordinary shares directly rather than beneficially through DTC through a broker, any transfer of their ordinary shares could be subject to Irish stamp duty (currently at the rate of 1% of the higher of the price paid or the market value of the shares acquired). Payment of Irish stamp duty is generally a legal obligation of the transferee. The potential for stamp duty to arise could adversely affect the price of our ordinary shares.

Dividends paid by us may be subject to Irish dividend withholding tax.

We have never declared or paid cash dividends on our ordinary shares and we do not expect to pay dividends for the foreseeable future. To the extent that we do make dividend payments (or other returns to shareholders that are treated as "distributions" for Irish tax purposes), it should be noted that, in certain limited circumstances, dividend withholding tax (currently at a rate of 25%) may arise in respect of dividends paid on our ordinary shares. A number of exemptions from dividend withholding tax exist, such that shareholders resident in EU member states (other than Ireland) or other countries with which Ireland has signed a double tax treaty, which includes the United States, should generally be entitled to exemptions from dividend withholding tax provided that the appropriate documentation is in place. The ability of a U.S. Holder to credit any Irish dividend withholding tax against that U.S. Holder's tentative U.S. federal tax liability may be subject to limitations.

Dividends received by Irish residents and certain other shareholders may be subject to Irish income tax.

We have never declared or paid cash dividends on our ordinary shares and we do not expect to pay dividends for the foreseeable future. To the extent that we do make dividend payments (or other returns to shareholders that are treated as "distributions" for Irish tax purposes), it should be noted that shareholders who are entitled to an exemption from Irish dividend withholding tax on dividends received from us will not be subject to Irish income tax in respect of those dividends, unless they have some connection with Ireland other than their shareholding in Iterum Therapeutics plc (for example, they are resident in Ireland) or they hold their ordinary shares through a branch or agency in Ireland which carries out a trade of their behalf. Shareholders who are not resident nor ordinarily resident in Ireland, but who are not entitled to an exemption from Irish dividend withholding tax, will generally have no further liability to Irish income tax on those dividends which suffer dividend withholding tax.

Our ordinary shares received by means of a gift or inheritance could be subject to Irish capital acquisitions tax.

Irish capital acquisitions tax (CAT) could apply to a gift or inheritance of our ordinary shares irrespective of the place of residence, ordinary residence or domicile of the parties. This is because our ordinary shares will be regarded as property situated in Ireland. The person who receives the gift or inheritance has primary liability for CAT.

Risks Related to Our Ordinary Shares

An active trading market for our ordinary shares may not be sustained.

Our ordinary shares began trading on the Nasdaq Global Market on May 25, 2018 and on December 23, 2020, we transferred the listing of our ordinary shares to The Nasdaq Capital Market. Given the relatively limited trading history of our ordinary shares and the intermittent volume of trading of our ordinary shares during that time, there is a risk that an active trading market for our shares may not be sustained, which could put downward pressure on the market price of our ordinary shares and thereby affect the ability of shareholders to sell their shares. An inactive trading market for our ordinary shares may also impair our ability to raise capital to continue to fund our operations by issuing shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

The price of our ordinary shares has been volatile and could be subject to volatility related or unrelated to our operations and our shareholders' investment in us could suffer a decline in value.

Our share price has been and may continue to be volatile. The daily closing market price for our ordinary shares has varied between a high price of $9.13 on November 11, 2021, and a low price of $1.55 on November 8, 2022, in the twelve-month period ending on November 8, 2022. During this time, the price per ordinary share has ranged from an intra-day low of $1.55 per share to an intra-day high of $9.15 per share. 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 ordinary shares at or above the price paid for the shares.

We may continue to incur rapid and substantial increases or decreases in our stock price in the foreseeable future that may not coincide in timing with the disclosure of news or developments by or affecting us. Accordingly, the market price of our ordinary shares may fluctuate dramatically, and may decline rapidly, regardless of any developments in our business.

The trading price of our ordinary shares could be subject to wide fluctuations in response to various factors, some of which are beyond our control. The market price for our ordinary shares may be influenced by those factors discussed elsewhere in this "Risk Factors" section of this document and others, such as:

- results from, and any delays in, clinical trials;
- announcements of regulatory approval, failure to obtain regulatory approvals or receipt of a "complete response letter" from the FDA with respect to any of our product candidates;
- announcements with respect to the outcome, impact, effects or results of our evaluation of corporate, strategic, financial and financing alternatives, including the terms, timing, structure, value, benefits and costs of any corporate, strategic, financial or financing alternative and our ability to complete one at all;
- our need to raise additional funds;
- announcements relating to changes to our capital structure including a reorganization, recapitalization, share split or reverse share split, exchange of shares, or any similar equity restructuring transaction;
- the sentiment of retail investors including the perception of our clinical trial results by such retail investors, which investors may be subject to the influence of information provided by social media, third party investor websites and independent authors distributing information on the internet;
- delays in the commercialization of oral sulopenem, sulopenem or any future product candidates;
- manufacturing and supply issues related to our development programs and commercialization of oral sulopenem, sulopenem or any of our future product candidates;
- quarterly variations in our results of operations or those of our competitors;
- changes in our earnings estimates or recommendations, or withdrawal of coverage, by securities analysts;
- announcements by us or our competitors of new product candidates, significant contracts, commercial relationships, acquisitions or capital commitments;

•announcements relating to future development or license agreements including termination of such agreements;

•adverse developments with respect to our intellectual property rights or those of our principal collaborators;

•commencement of litigation involving us or our competitors;

•changes in our board of directors, management, or key scientific personnel;

•new legislation in the United States relating to the prescription, sale, distribution or pricing of drugs;

•product liability claims, other litigation or public concern about the safety of oral sulopenem, sulopenem or future products;

•failure to comply with the Nasdaq Capital Market continued listing requirements;

•market conditions in the healthcare market in general, or in the antibiotics segment in particular, including performance of our competitors;

•publication of research reports about us or our industry, or antibiotics in particular;

•changes in the market valuations of similar companies;

•sales of large blocks of our ordinary shares by our existing shareholders; and

•general economic conditions in the United States and abroad, including resulting from geo-political actions, including war and terrorism, natural disasters, including earthquakes, hurricanes, typhoons, floods and fires, public health crises, or pandemics, like COVID-19.

In addition, the stock market in general, or the market for equity securities in our industry, may experience extreme volatility unrelated to our operating performance. In recent years, the market for pharmaceutical and biotechnology companies in particular has experienced significant price and volume fluctuations that have often been unrelated or disproportionate to changes in the operating performance of the companies whose shares are experiencing those price and volume fluctuations. These broad market fluctuations may adversely affect the trading price or liquidity of our ordinary shares regardless of our actual operating performance. Any sudden decline in the market price of our ordinary shares could trigger securities class-action lawsuits against us. If any of our shareholders were to bring such a lawsuit against us, we could incur substantial costs defending the lawsuit and the time and attention of our management would be diverted from our business and operations. For example, we and our Chief Executive Officer and Chief Financial Officer have been named as defendants in a putative class action lawsuit following our announcement in July 2021 that the FDA issued a CRL in connection with our NDA for oral sulopenem for the treatment of uUTIs, stating that the FDA was unable to approve the application in its present form. See "Risks Related to our Financial Position and Capital Requirements—We and our Chief Executive Officer and Chief Financial Officer have been named as defendants in a lawsuit that could result in substantial costs and divert management's attention." We also could be subject to damages claims if we are found to be at fault in connection with a decline in our share price.

The volatility of our shares and shareholder base may hinder or prevent us from engaging in beneficial corporate initiatives.

Our shareholder base is comprised of a large number of retail (or non-institutional) investors, which creates more volatility since shares change hands frequently. In accordance with our governing documents and applicable laws, there are a number of initiatives that require the approval of shareholders at an annual or extraordinary general meeting of shareholders. To hold a valid meeting, a quorum comprised of one or more Members (as defined in our Amended and Restated Constitution) whose name is entered in our register of members as a registered holder of our ordinary shares, present in person or by proxy (whether or not such Member actually exercises his voting rights in whole, in part or at all), holding not less than a majority of our issued and outstanding ordinary shares entitled to vote at a meeting of shareholders, is required. A record date is established to determine which shareholders are eligible to vote at the meeting, which record date must not be more than 60 days prior to the date of the meeting. Since our shares change hands frequently, there can be a significant turnover of shareholders between the record date and the meeting date which makes it harder to get shareholders to vote. While we make every effort to engage retail investors, such efforts can be expensive and the frequent turnover creates logistical issues for obtaining shareholder approval. Further, retail investors tend to be less likely to vote in comparison to institutional investors. Failure to secure sufficient votes or to achieve the minimum quorum needed for a meeting to happen may impede our ability to move forward with initiatives that are intended to grow the business and create shareholder value or prevent us from engaging in such initiatives at all. If we find it necessary to delay or adjourn meetings or to seek approval again, it will be time consuming and we will incur additional costs.

If we fail to comply with the listing requirements of the Nasdaq Capital Market, we may be delisted and the price of our ordinary shares, our ability to access the capital markets and our financial condition could be negatively impacted and the delisting of our ordinary shares would result in an event of default and/or fundamental change under our debt instruments.

Our ordinary shares are currently listed for quotation on the Nasdaq Capital Market. To maintain the listing of our ordinary shares on the Nasdaq Capital Market, we are required to meet certain listing requirements, including, among others:

- a minimum closing bid price of $1.00 per share, and
- a market value of publicly held shares (excluding shares held by our officers, directors and 10% or more shareholders) of at least $1.0 million.

In addition to the above requirements, we must meet at least one of the following requirements:

- shareholders' equity of at least $2.5 million; or
- a market value of listed securities of at least $35 million; or
- net income from continuing operations of $500,000.

On September 7, 2021, we received a letter from the Listing Qualifications Department of The Nasdaq Stock Market, LLC (Nasdaq), indicating that, based on the closing bid price for the previous 30 consecutive business days, the listing of our ordinary shares was not in compliance with Nasdaq Listing Rule 5550(a)(2) to maintain a minimum bid price of $1.00 per share (the Bid Price Rule). Under Nasdaq Listing Rule 5810(c)(3)(A), we were given a period of 180 calendar days, or until March 7, 2022, to regain compliance with the Bid Price Rule. Subsequently, on March 9, 2022 we were granted an additional 180-day compliance period, or until September 5, 2022, in which to regain compliance with the Bid Price Rule after meeting the continued listing requirement for market value of publicly held shares and all other initial listing standards for The Nasdaq Capital Market, with the exception of the Bid Price Rule, and providing written notice to Nasdaq of our intention to cure the deficiency during the second compliance period, by effecting a reverse share split, if necessary. At the annual general meeting of shareholders on June 15, 2022 our shareholders approved, subject to and conditional upon the board of directors determining, in its sole discretion, that a reverse share split is necessary for the Company to comply with the Bid Price Rule, a proposal to effect a reverse share split (i.e., a consolidation of share capital under Irish law), whereby every 15 ordinary shares of $0.01 (nominal value) each in the authorized and unissued and authorized and issued share capital of the Company be consolidated into 1 ordinary share of $0.15 (nominal value) each, and the subsequent (i) reduction in the nominal value of the ordinary shares in the authorized and unissued and authorized and issued share capital of the Company from $0.15 each to $0.01 each and (ii) increase in the authorized ordinary share capital of the Company in order to round up the authorized share capital to an even number following the reverse share split, with our board of directors able to elect to abandon such amendments and not effect the reverse share split authorized by the shareholders, in its sole discretion. On August 17, 2022, we filed an Amended and Restated Memorandum and Articles of Association with the Irish Companies Registration Office and effected, as of 5:00 p.m. Eastern Standard Time on August 17, 2022, a one-for-fifteen reverse share split of our ordinary shares. Trading of the ordinary shares on a reverse share split-adjusted basis began at the opening of trading on August 18, 2022.

On September 1, 2022, we received notification from Nasdaq that, for 10 consecutive business days from August 18, 2022 to August 31, 2022, the closing bid price of our ordinary shares was above $1.00, confirming that we had regained compliance with the Bid Price Rule.

Although we have been able to regain compliance with the listing requirements within the manner and time periods prescribed by Nasdaq in the past, there can be no assurance that we will be able to maintain compliance with the Nasdaq Capital Market continued listing requirements in the future or regain compliance with respect to any future deficiencies. This could impair the liquidity and market price of our ordinary shares. In addition, the delisting of our ordinary shares from a national exchange could have a material adverse effect on our access to capital markets, and any limitation on market liquidity or reduction in the price of our ordinary shares as a result of that delisting could adversely affect our ability to raise capital on terms acceptable to us, or at all. The delisting of our ordinary shares from The Nasdaq Stock Market could also negatively impact our financial condition as it would constitute a fundamental change under the EN Indenture, which could trigger an obligation for us to repurchase the Exchangeable Notes at a repurchase price of 300% of the principal amount of the outstanding Exchangeable Notes.

Through the RLNs, we transferred to the holders thereof rights to receive certain payments in connection with commercial sales of sulopenem, which may reduce our ability to realize potential future revenue from such sales.

As part of a private placement which closed in January 2020 (the Private Placement) and subsequent rights offering (the Rights Offering), Iterum Bermuda issued RLNs which entitle the holders thereof to certain payments in connection with commercial sales of sulopenem. Holders of RLNs are entitled to payments based solely on a percentage of our net revenues from U.S. sales of specified sulopenem products (Specified Net Revenues). Payments will be due within 75 days of the end of each six-month payment measuring period (each, a Payment Measuring Period), beginning with the Payment Measuring Period ending June 30, 2020 until (i) the "Maximum Return" (as defined below) has been paid in respect of the RLNs, or (ii) December 31, 2045 (the End Date), or (iii) December 31, 2025, in the event that we have not yet received FDA approval with respect to one or more specified sulopenem products by such date. The aggregate amount of payments in respect of all RLNs during each Payment Measuring Period will be equal to the product of total Specified Net Revenues earned during such period and the applicable payment rate (Payment Rate), determined based on which of the specified sulopenem products have received FDA approval. The Payment Rate will be based on the maximum aggregate principal amount of RLNs and will equal (i) up to 15% if we or one of our affiliates has received FDA approval for the use of specified sulopenem products for the treatment of uUTIs and (ii) up to 20% if we or one of our affiliates has received FDA approval for the use of specified sulopenem products for the treatment of cUTIs but has not received FDA approval for treatment of uUTIs.

Prior to the End Date, Iterum Bermuda will be obligated to make payments on the RLNs from Specified Net Revenues until each RLN has received payments equal to $160.00 (or 4,000 times the principal amount of such RLN) (the Maximum Return). The principal amount of the RLNs, equal to $0.04 per RLN, is the last portion of the Maximum Return amount to which payments from Specified Net Revenue are applied. If any portion of the principal amount of the outstanding RLNs has not been paid as of the End Date, Iterum Bermuda must pay the unpaid portion of the principal amount. If Iterum Bermuda fails to pay any amounts on the RLNs that are due and payable, such defaulted amounts will accrue default interest at a rate per annum equal to the prime rate plus three percent (3.00%). Default interest will also accrue on the Principal Amount Multiple (as defined in the RLN Indenture) as a result of certain other defaults under the RLN Indenture at a rate per annum equal to four percent (4.00%).

Iterum Bermuda may at any time redeem for cash all, but not less than all, of the RLNs, at its option. The redemption price per RLN will be equal to the Maximum Return for each RLN, less payments made through and including the redemption date, plus certain accrued but unpaid default interest (if any). Upon a change of control of our company, we will require the ultimate beneficial owner or owners controlling the acquiring person or persons to guarantee the obligations of Iterum Bermuda under the RLN Indenture. In the event that a change of control occurs before we receive FDA approval with respect to one or more specified sulopenem products, the redemption price per RLN will be reduced to 50% of the Maximum Return for each RLN, less payments made through and including the redemption date, plus certain accrued but unpaid default interest (if any).

The payment obligations under the RLNs may reduce the revenue we are able to derive from commercial sales of sulopenem and a redemption of the RLNs would require us to use our cash resources, which could adversely affect the value of our company and the prices that investors are willing to pay for our ordinary shares and could adversely affect our business, financial condition and results of operations.

If securities or industry analysts do not publish research or reports about our company, or if they issue adverse or misleading opinions regarding us or our ordinary shares, our share price and trading volume could decline.

The trading market for our ordinary shares relies, in part, on the research and reports that industry or financial analysts publish about our company. If no, or only a few, analysts publish research or reports about our company, the market price for our ordinary shares may be adversely affected. Our share price also may decline if any analyst who covers us issues an adverse or misleading opinion regarding us, our business model, our intellectual property or our share performance, or if our pivotal safety and efficacy studies and operating results fail to meet analysts' expectations. If one or more analysts cease coverage of us or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our share price or trading volume to decline and possibly adversely affect our ability to engage in future financings.

The issuance of additional ordinary shares may dilute our existing shareholders' level of ownership in our Company or require us to relinquish rights.

Any issuance of securities we may undertake, whether in the future to raise additional capital or upon exchange or exercise of outstanding convertible securities, could cause the price of our ordinary shares to decline, or require us to issue shares at a price that is lower than that paid by holders of our ordinary shares in the past, which would result in those newly issued shares being dilutive.

In addition, the Exchangeable Notes are exchangeable for ordinary shares, cash or a combination of ordinary shares and cash, at our election, upon the terms and conditions specified therein. If we elect for physical settlement, the issuance of ordinary shares for the Exchangeable Notes may dilute the ownership percentage or voting power of our shareholders. As of September 30, 2022, approximately $12.6 million aggregate principal amount of Exchangeable Notes remained outstanding. The outstanding warrants that we issued the purchasers and/or the designees of the placement agent and underwriter, as applicable, in connection with the June 3, 2020 Offering, the June 30, 2020 Offering, the October 2020 Offering, the February 2021 Underwritten Offering and the February 2021 Registered Direct Offering are exercisable at any time until a specified expiration date, and any exercise of outstanding warrants will increase the number of shares outstanding, which may dilute the ownership percentage or voting power of our shareholders. Similarly, the outstanding warrants that we issued SVB and Life Sciences Fund II LLC in connection with the secured credit facility with SVB are exercisable at any time until April 27, 2028, and any exercise of such warrants will increase the number of shares outstanding, which may dilute the ownership percentage or voting power of our shareholders. Additionally, the exercise of outstanding options and vesting of restricted share units under our equity incentive plans or equity inducement incentive plan or exercise of other outstanding warrants for ordinary shares may also dilute the ownership percentage or voting power of our shareholders.

Further, if we obtain funds through the sale of equity or a debt financing or through the issuance of convertible debt or preference securities, these securities would likely have rights senior to the rights of our ordinary shareholder, which could impair the value of our ordinary shares. Any debt financing we enter into may include covenants that limit our flexibility in conducting our business. We also could be required to seek funds through arrangements with collaborators or others, which might require us to relinquish valuable rights to our intellectual property or product candidates that we would have otherwise retained.

Sales of a substantial number of our ordinary shares in the public market, or the perception that these sales could occur, could cause our share price to fall.

A substantial portion of our outstanding ordinary shares can be traded without restriction at any time. If our current shareholders sell, or indicate an intention to sell, substantial amounts of our ordinary shares in the public market, the trading price of our ordinary shares could decline.

A portion of our outstanding ordinary shares is currently restricted as a result of federal securities laws but can be sold at any time subject to applicable volume limitations.

In addition, the Exchangeable Notes are exchangeable for our ordinary shares upon the terms and conditions specified therein and a substantial portion have been exchanged for our ordinary shares. Pursuant to the investor rights agreement we entered into in connection with the Private Placement, we have filed a registration statement covering the resale of the ordinary shares issuable in connection with the exchange of the Exchangeable Notes issued as part of the Private Placement, among other securities, and the resale of the ordinary shares issuable in connection with the exchange of the Exchangeable Notes issued in connection with the Rights Offering are also covered by a registration statement. Also, in connection with our June 3, 2020 Offering and June 30, 2020 Offering, we filed a registration statement providing for the resale by the purchasers in such offerings of ordinary shares issued and issuable upon exercise of the warrants purchased in such offerings and a substantial portion of the warrants have been exercised. As a result, the shares issuable upon exchange of such notes and upon exercise of such warrants are able to be sold by the holders thereof without restrictions, subject to compliance with securities laws.

In addition, on October 7, 2022, we entered into the Sales Agreement with HC Wainwright as agent, pursuant to which we may offer and sell ordinary shares, nominal value $0.01 per share for aggregate gross sales proceeds of up to $16.0 million, from time to time through HC Wainwright by any method permitted that is deemed to be an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended. We cannot predict if and when shares sold pursuant to the Sales Agreement, if any, will be resold in the public markets. Any of our outstanding shares that are not restricted as a result of securities laws may be resold in the public market without restriction unless purchased by our affiliates.

Furthermore, ordinary shares that are issuable upon exercise of outstanding options or reserved for future issuance under our equity incentive plans and equity inducement plan or are issuable upon exercise of our other outstanding warrants will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules or performance criteria, and applicable securities laws. If any of these additional ordinary shares are sold, or if it is perceived that they will be sold, in the public market, the trading price of our ordinary shares could decline.

We are currently limited in our authorized share capital and an increase in authorized shares will be required for future financings or other strategic transactions.

We will need to seek the additional capital necessary to fund our operations through public or private equity offerings, debt financings, and collaborative and licensing arrangements, including through sales under the Sales Agreement with HC Wainwright. We have limited ordinary shares currently available and authorized for issuance. Investors in prior transactions have purchased our ordinary shares or our convertible securities, such as warrants and the Exchangeable Notes, for which we must reserve unissued ordinary shares. Furthermore, the warrants and Exchangeable Notes are subject to certain anti-dilution protections, including, for the outstanding Exchangeable Notes, upon the issuance of shares at a price per share less than the exchange price of the outstanding Exchangeable Notes. We therefore will likely need to increase the number of authorized ordinary shares, which requires shareholder approval, in order to issue ordinary shares or securities convertible, exercisable or exchangeable into ordinary shares to investors and other strategic partners, to utilize the full availability under the Sales Agreement and/or in other capital raising transactions. If we are unable to increase our authorized shares, we will be limited in our efforts to raise additional capital and/or could be required to settle any exchanges of our outstanding Exchangeable Notes with cash. As a result, our operations and financial condition may be materially and adversely affected.

Irish law differs from the laws in effect in the United States and may afford less protection to holders of our securities.

Shareholders may have difficulties enforcing, in actions brought in courts in jurisdictions located outside the United States, judgments obtained in the U.S. courts under the U.S. securities laws. In particular, if a shareholder sought to bring proceedings in Ireland based on U.S. securities laws, the Irish court might consider:

- that it did not have jurisdiction;
- that it was not the appropriate forum for such proceedings;
- that, applying Irish conflict of law rules, U.S. law (including U.S. securities laws) did not apply to the relationship between the shareholder and us or our directors and officers; or
- that the U.S. securities laws were of a penal nature and violated Irish public policy and should not be enforced by the Irish court.

It may not be possible to enforce court judgments obtained in the United States against us in Ireland based on the civil liability provisions of the U.S. federal or state securities laws. In addition, there is some uncertainty as to whether the courts of Ireland would recognize or enforce judgments of U.S. courts obtained against us or our directors or officers based on the civil liabilities provisions of the U.S. federal or state securities laws. We have been advised that the United States currently does not have a treaty with Ireland providing for the reciprocal recognition and enforcement of judgments in civil and commercial matters. Therefore, a final judgment for the payment of money rendered by any U.S. federal or state court based on civil liability, whether or not based solely on U.S. federal or state securities laws, would not automatically be enforceable in Ireland.

A judgment obtained against us will be enforced by the courts of Ireland only if the following general requirements are met:

- U.S. courts must have had jurisdiction in relation to the particular defendant according to Irish conflict of law rules (the submission to jurisdiction by the defendant would satisfy this rule); and
- the judgment must be final and conclusive and the decree must be final and unalterable in the court which pronounces it.

A judgment can be final and conclusive even if it is subject to appeal or even if an appeal is pending. But where the effect of lodging an appeal under the applicable law is to stay execution of the judgment, it is possible that in the meantime the judgment may not be actionable in Ireland. It remains to be determined whether final judgment given in default of appearance is final and conclusive. Irish courts may also refuse to enforce a judgment of the U.S. courts which meets the above requirements for one of the following reasons:

- the judgment is not for a definite sum of money;
- the judgment was obtained by fraud;
- the enforcement of the judgment in Ireland would be contrary to natural or constitutional justice;
- the judgment is contrary to Irish public policy or involves certain U.S. laws which will not be enforced in Ireland; or
- jurisdiction cannot be obtained by the Irish courts over the judgment debtors in the enforcement proceedings by personal service in Ireland or outside Ireland under Order 11 of the Irish Superior Courts Rules.

As an Irish company, we are governed by the Irish Companies Act 2014 (the Irish Companies Act), which differs in some material respects from laws generally applicable to U.S. corporations and shareholders, including, among others, differences relating to interested director and officer transactions and shareholder lawsuits. Likewise, the duties of directors and officers of an Irish company generally are owed to the company only. Shareholders of Irish companies generally do not have a personal right of action against directors or officers of the company and may exercise such rights of action on behalf of the company only in limited circumstances. Accordingly, holders of our securities may have more difficulty protecting their interests than would holders of securities of a corporation incorporated in a jurisdiction of the United States.

Our shareholders should also be aware that Irish law does not allow for any form of legal proceedings directly equivalent to the class action available in the United States.

We have incurred and will continue to incur increased costs as a result of operating as a public company, and our management is required to devote substantial time and attention to our public reporting obligations.

As a publicly-traded company, we have incurred and will continue to incur significant additional legal, accounting and other expenses compared to historical levels. In addition, new and changing laws, regulations and standards relating to corporate governance and public disclosure, including the Dodd-Frank Wall Street Reform and Consumer Protection Act and the rules and regulations promulgated and to be promulgated thereunder, as well as under the Sarbanes-Oxley Act of 2002 (the Sarbanes-Oxley Act), the Jumpstart Our Business Startups Act of 2012 (the JOBS Act) and the rules and regulations of the SEC and the Nasdaq Capital Market, have created uncertainty for public companies and increased our costs and time that our board of directors and management must devote to complying with these rules and regulations. We expect these rules and regulations to continue to increase our legal and financial compliance costs substantially and lead to diversion of management time and attention from revenue-generating activities.

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

We are an "emerging growth company" as defined in the JOBS Act, and, therefore, we may take advantage of reduced disclosure and regulatory requirements that are otherwise generally applicable to public companies, including not being required to have our internal control over financial reporting audited by our independent registered public accounting firm pursuant to Section 404 of the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and any golden parachute payments. We may take advantage of these reduced disclosure and regulatory requirements until we are no longer an "emerging growth company." We may remain an "emerging growth company" until as late as December 31, 2023 (the fiscal year-end following the fifth anniversary of our IPO), although we may cease to be an "emerging growth company" earlier under certain circumstances, including if the market value of our ordinary shares that is held by non-affiliates exceeds $700 million as of any June 30, in which case we would cease to be an "emerging growth company" as of the following December 31, or if our gross revenue exceeds $1.07 billion in any fiscal year. In addition, the JOBS Act provides that an emerging growth company can delay adopting new or revised accounting standards until those standards apply to private companies. We have irrevocably elected not to avail ourselves of this delayed adoption of new or revised accounting standards and, therefore, we are subject to the same new or revised accounting standards as public companies that are not emerging growth companies.

We are also a "smaller reporting company" as defined in Rule 12b-2 promulgated under the Exchange Act. We may remain a smaller reporting company until we have a non-affiliate public float in excess of $250 million and annual revenues in excess of $100 million, or a non-affiliate public float in excess of $700 million, each as determined on an annual basis. Even after we no longer qualify as an "emerging growth company", we may still qualify as a smaller reporting company, which would allow us to take advantage of many of the same exemptions from disclosure requirements as those allowed for an emerging growth company.

Investors may find our ordinary shares less attractive if we rely on certain or all of these exemptions. If some investors find our ordinary shares less attractive as a result, there may be a less active trading market for our ordinary shares and our share price may decline or become more volatile.

If we fail to maintain an effective system of disclosure controls and internal control over financial reporting, our ability to produce timely and accurate financial statements or comply with applicable regulations could be impaired.

As a public company, we are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act, the Sarbanes-Oxley Act, and the rules and regulations of the applicable listing standards of the Nasdaq Capital Market. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting. Our current controls and any new controls that we develop may become inadequate because of changes in conditions in our business. Further, weaknesses in our disclosure controls and internal control over financial reporting may be discovered in the future. Any failure to develop or maintain effective controls or any difficulties encountered in their implementation or improvement could harm our results of operations or cause us to fail to meet our reporting obligations and may result in a restatement of our consolidated financial statements for prior periods. Any failure to implement and maintain effective internal control over financial reporting could also adversely affect the results of periodic management evaluations and annual independent registered public accounting firm attestation reports regarding the effectiveness of our internal control over financial reporting that we will eventually be required to include in our periodic reports that will be filed with the SEC. Ineffective disclosure controls and procedures and internal control over financial reporting could also cause investors to lose confidence in our reported financial and other information, which would likely have a negative effect on the trading price of our ordinary shares. In addition, if we are unable to continue to meet these requirements, we may not be able to remain listed on the Nasdaq Capital Market.

Pursuant to Section 404 of the Sarbanes-Oxley Act, we are required to furnish a report by our management on our internal control over financial reporting. However, while we remain an emerging growth company and/or smaller reporting company with less than $100 million in revenue, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404, we engaged and continue to engage in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements. Additionally, we will be unable to issue securities in the public markets through the use of a shelf registration if we are not in compliance with Section 404.

Any failure to maintain effective disclosure controls and internal control over financial reporting could have a material and adverse effect on our business, results of operations and financial condition and could cause a decline in the trading price of our ordinary shares.

We have never paid cash dividends, do not anticipate paying any cash dividends and our ability to pay dividends, or repurchase or redeem our ordinary shares, is limited by law.

We have never declared or paid cash dividends on our ordinary shares and do not anticipate paying any dividends on our ordinary shares in the foreseeable future. Any determination to pay dividends in the future will be at the sole discretion of our board of directors after considering our financial condition, results of operations, capital requirements, contractual restrictions, general business conditions and other factors our board of directors deems relevant, and subject to compliance with applicable laws, including the Irish Companies Act which requires Irish companies to have distributable reserves available for distribution equal to or greater than the amount of the proposed dividend. Distributable reserves are the accumulated realized profits of the company that have not previously been utilized in a distribution or capitalization less accumulated realized losses that have not previously been written off in a reduction or reorganization of capital. Unless the company creates sufficient distributable reserves from its business activities, the creation of such distributable reserves would involve a reduction of the company's share premium account, which would require the approval of (i) 75% of our shareholders present and voting at a shareholder meeting, and (ii) the Irish High Court. In the event that we do not undertake a reduction of capital to create distributable reserves, no distributions by way of dividends, share repurchases or otherwise will be permitted under Irish law until such time as the company has created sufficient distributable reserves from its business activities.

Accordingly, the only opportunity for a shareholder to achieve a return on their investment in our company is expected to be if the market price of our ordinary shares appreciates and they sell their ordinary shares at a profit.

Anti-takeover provisions in our Articles of Association and under Irish law could make an acquisition of us more difficult, limit attempts by our shareholders to replace or remove our current directors and management team, and limit the market price of our ordinary shares.

Our Articles of Association contain provisions that may delay or prevent a change of control, discourage bids at a premium over the market price of our ordinary shares, and adversely affect the market price of our ordinary shares and the voting and other rights of the holders of our ordinary shares. These provisions include:

- dividing our board of directors into three classes, with each class serving a staggered three-year term;
- permitting our board of directors to adopt a shareholder rights plan upon such terms and conditions as it deems expedient and in our best interests;
- permitting our board of directors to issue preference shares, with such rights, preferences and privileges as they may designate;
- establishing an advance notice procedure for shareholder proposals to be brought before an annual meeting, including proposed nominations of persons for election to our board of directors; and
- imposing particular approval and other requirements in relation to certain business combinations.

These provisions would apply even if the offer may be considered beneficial by some shareholders. In addition, these provisions may frustrate or prevent any attempts by our shareholders to replace or remove our current management team by making it more difficult for shareholders to replace members of our board of directors, which is responsible for appointing the members of our management.

Provisions in the EN Indenture and RLN Indenture may deter or prevent a business combination that may be favorable to the holders of our ordinary shares.

If a fundamental change occurs prior to the interest record date of the Exchangeable Notes, holders of the Exchangeable Notes will have the right, at their option, to require us to repurchase for cash all or a portion of their Exchangeable Notes. The negative covenants in the EN Indenture also prohibit us from undergoing a change of control transaction, other than a transaction in which each Exchangeable Note holder receives cash consideration of at least 300% of the outstanding principal amount of its notes. Furthermore, the EN Indenture prohibits us from engaging in certain mergers or acquisitions unless, among other things, the surviving entity assumes our obligations under the Exchangeable Notes, the EN Indenture and the guarantees. In addition, the RLN Indenture prohibits us from engaging in certain mergers or acquisitions unless, among other things, the surviving entity assumes our obligations under the RLNs, the RLN Indenture and the guarantees and the RLN Indenture prohibits us from selling, transferring or assigning certain assets and prohibits Iterum Bermuda, the Guarantors or any of our significant subsidiaries from undergoing a change of control, other than in connection with a change of control of us. These and other provisions in the EN Indenture and the RLN Indenture could deter or prevent a third party from acquiring us even when the acquisition may be favorable to the holders of our ordinary shares.

Irish law differs from the laws in effect in the United States with respect to defending unwanted takeover proposals and may give our board of directors less ability to control negotiations with hostile offerors.

Following the authorization for trading of our ordinary shares on the Nasdaq Global Market on May 25, 2018, we became subject to the Irish Takeover Panel Act, 1997, Irish Takeover Rules 2013 (Irish Takeover Rules). Under the Irish Takeover Rules, our board of directors is not permitted to take any action that might frustrate an offer for our ordinary shares once our board of directors has received an approach that may lead to an offer or has reason to believe that such an offer is or may be imminent, subject to certain exceptions. Potentially frustrating actions such as (i) the issue of shares, options, restricted share units or convertible securities, (ii) material acquisitions or disposals, (iii) entering into contracts other than in the ordinary course of business or (iv) any action, other than seeking alternative offers, which may result in frustration of an offer, are prohibited during the course of an offer or at any earlier time during which our board of directors has reason to believe an offer is or may be imminent. These provisions may give our board of directors less ability to control negotiations with hostile offerors than would be the case for a corporation incorporated in a jurisdiction of the United States.

The operation of the Irish Takeover Rules may affect the ability of certain parties to acquire our ordinary shares.

Under the Irish Takeover Rules, if an acquisition of ordinary shares were to increase the aggregate holding of the acquirer and its concert parties to ordinary shares that represent 30% or more of the voting rights of the company, then the acquirer and/or, in certain circumstances, its concert parties would be required (except with the consent of the Irish Takeover Panel) to make an offer for all of the outstanding ordinary shares at a price not less than the highest price paid for the ordinary shares by the acquirer or its concert parties during the previous 12 months (known as a mandatory cash offer). This requirement would also be triggered by an acquisition of ordinary shares by a person holding (together with its concert parties) ordinary shares that represent between 30% and 50% of the voting rights in the company, if the effect of such acquisition was to increase that person's percentage of the voting rights by 0.05% within any 12 month period. The EN Indenture provides that if a holder of Exchangeable Notes notifies us that they would be subject to this mandatory offer requirement, we will only issue to such holder such number of ordinary shares that can be issued without triggering a mandatory cash offer on an exchange with the remaining ordinary shares to be delivered as promptly as practicable after the holder notifies us that they would no longer be subject to a mandatory cash offer request.

Under the Irish Takeover Rules, certain separate concert parties are presumed to be acting in concert. Our board of directors and their relevant family members, related trusts and "controlled companies" are presumed to be acting in concert with any corporate shareholder who holds 20% or more of our shares. The application of these presumptions may result in restrictions upon the ability of any such concert parties and/or members of our board of directors and the other holders of the Exchangeable Notes to acquire more of our securities, including under the terms of the Exchangeable Notes and any executive incentive arrangements. We, or any such holders, may consult with the Irish Takeover Panel from time to time with respect to the application of this presumption and the restrictions on the ability to acquire further securities, although we are unable to provide any assurance as to whether the Irish Takeover Panel would overrule this presumption. Accordingly, the application of the Irish Takeover Rules may restrict the ability of certain of our shareholders and directors to acquire our ordinary shares.

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

Under Irish law, our authorized share capital can be increased by an ordinary resolution of our shareholders and the directors may issue new ordinary or preferred shares up to a maximum amount equal to the authorized but unissued share capital, without shareholder approval, once authorized to do so by our Articles of Association or by a resolution approved by not less than 50% of the votes cast at a general meeting of our shareholders. Additionally, subject to specified exceptions, Irish law grants statutory preemption rights to existing shareholders where shares are being issued for cash consideration but allows shareholders to disapply such statutory preemption rights either in our Articles of Association or by way of a resolution approved by not less than 75% of the votes cast at a general meeting of our shareholders. Such disapplication can either be generally applicable or be in respect of a particular allotment of shares. Accordingly, at an extraordinary meeting of our shareholders on January 28, 2021, our shareholders authorized the board to issue new shares, and to disapply statutory preemption rights for such issuances up to the amount of our authorized but unissued share capital until January 26, 2026. The authorization of the directors to issue shares and the disapplication of statutory preemption rights must both be renewed by the shareholders at least every five years, and we cannot provide any assurance that these authorizations will always be approved, or be approved without limitations, which could limit our ability to issue equity and thereby adversely affect the holders of our securities.

Item 2. Unregistered Sales of Equity Securities

Recent Sales of Unregistered Securities

We did not issue any securities that were not registered under the Securities Act during the three months ended September 30, 2022.

Item 6. Exhibits.

The following is a list of exhibits filed or furnished as part of this Quarterly Report on Form 10-Q:

Exhibit No.	Description of Document	Filed with this report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File Number
1.1	At the Market Offering Agreement by and between Iterum Therapeutics plc and H.C. Wainwright & Co., LLC, dated as of October 7, 2022		Form S-3	October 7, 2022	333-267795
3.1	Amended and Restated Constitution of Iterum Therapeutics plc.		Form 8-K (Exhibit 3.1)	August 19, 2022	001-38503
10.1	2015 Equity Incentive Plan, as amended	X			
10.2	Amended and Restated 2018 Equity Incentive Plan, as amended	X			
10.3	Iterum Therapeutics plc 2021 Inducement Equity Incentive Plan, as amended	X			
31.1	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	X			
31.2	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	X			
32.1	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	X			
32.2	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	X			
101.INS	Inline XBRL Instance Document	X			
101.SCH	Inline XBRL Taxonomy Extension Schema Document	X			
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document	X			
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document	X			
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document	X			
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document	X			
104	Cover Page Interactive Data File (formatted as Inline XBRL with applicable taxonomy extension information contained in Exhibits 101)	X			

SIGNATURES

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.

ITERUM THERAPEUTICS PLC

Date: November 10, 2022 By: /s/ Corey Fishman
Corey Fishman
President and Chief Executive Officer

Date: November 10, 2022 By: /s/ Judith Matthews
Judith Matthews
Chief Financial Officer

EXHIBIT 10.1

ITERUM THERAPEUTICS LIMITED

2015 EQUITY INCENTIVE PLAN

ADOPTED BY THE BOARD OF DIRECTORS: November 18, 2015
APPROVED BY THE SHAREHOLDERS: November 18, 2015
AMENDED AND RESTATED BY THE BOARD OF DIRECTORS: December 7, 2016
AMENDED BY THE BOARD OF DIRECTORS: May 17, 2017
AMENDED BY THE SHAREHOLDERS: May 17, 2017
TERMINATION DATE: November 17, 2025

1. GENERAL.

(a) Eligible Stock Award Recipients. Employees, Directors and Consultants are eligible to receive Stock Awards.

(b) Available Stock Awards. The Plan provides for the grant of the following types of Stock Awards: (i) Incentive Stock Options, (ii) Nonstatutory Stock Options, (iii) Stock Appreciation Rights, (iv) Restricted Stock Awards, (v) Restricted Stock Unit Awards and (vi) Other Stock Awards.

(c) Purpose. The Plan, through the grant of Stock Awards, is intended to help the Company secure and retain the services of eligible award recipients, provide incentives for such persons to exert maximum efforts for the success of the Company and any Affiliate and provide a means by which the eligible recipients may benefit from increases in value of the Ordinary Shares.

(d) Definitions. All capitalized terms in this document are defined in Section 13 below.

2. ADMINISTRATION.

(a) Administration by the Board. The Board will administer the Plan. The Board may delegate administration of the Plan to a Committee or Committees, as provided in Section 2(c).

(b) Powers of the Board. The Board will have the power, subject to, and within the limitations of, the express provisions of the Plan:

(i) To determine (A) who will be granted Stock Awards; (B) when and how each Stock Award will be granted; (C) what type of Stock Award will be granted; (D) the provisions of each Stock Award (which need not be identical), including when a person will be permitted to exercise or otherwise receive cash or Ordinary Shares under the Stock Award; (E) the number of Ordinary Shares subject to, or the cash value of, a Stock Award; and (F) the Fair Market Value applicable to a Stock Award.

(ii) To construe and interpret the Plan and Stock Awards granted under it, and to establish, amend and revoke rules and regulations for administration of the Plan and Stock Awards. The Board, in the exercise of these powers, may correct any defect, omission or inconsistency in the Plan or in any Award Agreement, in a manner and to the extent it will deem necessary or expedient to make the Plan or Stock Award fully effective.

(iii) To settle all controversies regarding the Plan and Stock Awards granted under it.

(iv) To accelerate, in whole or in part, the time at which a Stock Award may be exercised or vest (or the time at which cash or Ordinary Shares may be issued in settlement thereof).

(v) To suspend or terminate the Plan at any time. Except as otherwise provided in the Plan or a Award Agreement, suspension or termination of the Plan will not impair a Participant's rights under the Participant's then-outstanding Stock Award without the Participant's written consent except as provided in subsection (viii) below.

(vi) To amend the Plan in any respect the Board deems necessary or advisable, subject to the limitations, if any, of applicable law. Except as otherwise provided in the Plan or an Award Agreement, no

amendment of the Plan will materially impair a Participant's rights under an outstanding Stock Award without the Participant's written consent.

(vii) To submit any amendment to the Plan for shareholder approval, including, but not limited to, amendments to the Plan intended to satisfy the requirements of Section 422 of the Code regarding Incentive Stock Options.

(viii) To approve forms of Award Agreements for use under the Plan and to amend the terms of any one or more Stock Awards, including, but not limited to, amendments to provide terms more favorable to the Participant than previously provided in the Award Agreement, subject to any specified limits in the Plan that are not subject to Board discretion; *provided however,* that a Participant's rights under any Stock Award will not be impaired by any such amendment unless (A) the Company requests the consent of the affected Participant, and (B) such Participant consents in writing. Notwithstanding the foregoing, (1) a Participant's rights will not be deemed to have been impaired by any such amendment if the Board, in its sole discretion, determines that the amendment, taken as a whole, does not materially impair the Participant's rights, and (2) subject to the limitations of applicable law, if any, the Board may amend the terms of any one or more Stock Awards without the affected Participant's consent (A) to maintain the qualified status of the Stock Award as an Incentive Stock Option under Section 422 of the Code; (B) to change the terms of an Incentive Stock Option, if such change results in impairment of the Stock Award solely because it impairs the qualified status of the Stock Award as an Incentive Stock Option under Section 422 of the Code; (C) to clarify the manner of exemption from, or to bring the Stock Award into compliance with, Section 409A of the Code; or (D) to comply with other applicable laws.

(ix) Generally, to exercise such powers and to perform such acts as the Board deems necessary or expedient to promote the best interests of the Company and that are not in conflict with the provisions of the Plan or Stock Awards.

(x) To adopt such procedures and sub-plans as are necessary or appropriate to permit participation in the Plan by Employees, Directors or Consultants who are foreign nationals or employed outside Ireland or the United States (provided that Board approval will not be necessary for immaterial modifications to the Plan or any Award Agreement that are required for compliance with the laws of the relevant foreign jurisdiction).

(xi) To effect, with the consent of any adversely affected Participant, (A) the alteration of the exercise, purchase or strike price of any outstanding Stock Award (unless this is in the context of a Capitalization Adjustment in which case Participant consent is not required); (B) the cancellation of any outstanding Stock Award and the grant in substitution therefor of a new (1) Option or SAR, (2) Restricted Stock Award, (3) Restricted Stock Unit Award, (4) Other Stock Award, (5) cash and/or (6) other valuable consideration determined by the Board, in its sole discretion, with any such substituted award (x) covering the same or a different number of Ordinary Shares as the cancelled Stock Award and (y) granted under the Plan or another equity or compensatory plan of the Company; or (C) any other action that is treated as a repricing under generally accepted accounting principles.

(c) Delegation to Committee. The Board may delegate some or all of the administration of the Plan to a Committee or Committees. If administration of the Plan is delegated to a Committee, the Committee will have, in connection with the administration of the Plan, the powers theretofore possessed by the Board that have been delegated to the Committee, including the power to delegate to a subcommittee of the Committee any of the administrative powers the Committee is authorized to exercise (and references in this Plan to the Board will thereafter be to the Committee or subcommittee, as applicable). Any delegation of administrative powers will be reflected in resolutions, not inconsistent with the provisions of the Plan, adopted from time to time by the Board or Committee (as applicable). The Board may retain the authority to concurrently administer the Plan with the Committee and may, at any time, revest in the Board some or all of the powers previously delegated.

(d) Effect of Board's Decision. All determinations, interpretations and constructions made by the Board in good faith will not be subject to review by any person and will be final, binding and conclusive on all persons.

3. SHARES SUBJECT TO THE PLAN.

(a) Limit on Share Capital Available under Plan.

(i) Subject to Section 9(a) relating to Capitalization Adjustments, the aggregate number of Ordinary Shares that may be issued pursuant to Stock Awards from and after the Effective Date will not exceed 464,000 shares.

(ii) For clarity, the limit in this Section 3(a) is a limitation on the number of Ordinary Shares that may be issued pursuant to the Plan. Accordingly, this Section 3(a) does not limit the granting of Stock Awards except as provided in Section 7(a).

(b) Calculating Limits. If a Stock Award or any portion thereof (i) expires or otherwise terminates without all of the shares covered by such Stock Award having been issued or (ii) is settled in cash (*i.e.*, the Participant receives cash rather than stock), such expiration, termination or settlement will not reduce (or otherwise offset) the number of Ordinary Shares that may be available for issuance under the Plan under Section 3(a). If any Ordinary Shares issued pursuant to a Stock Award are forfeited back to or repurchased by the Company because of the failure to meet a contingency or condition required to vest such shares in the Participant, then the number of such shares will not be taken into account for purposes of the limit in Section 3(a) and will become available for issuance under the Plan. Any shares reacquired by the Company in satisfaction of tax withholding obligations on a Stock Award or as consideration for the exercise or purchase price of a Stock Award will again become available for issuance under the Plan.

(c) then the number of such shares will not be taken into account for the purposes and will become available for issuance under the Plan

(d) Incentive Stock Option Limit. Subject to the limit in Section 3(a), and Section 9(a) relating to Capitalization Adjustments, the aggregate maximum number of Ordinary Shares that may be issued pursuant to the exercise of Incentive Stock Options will be a number of Ordinary Shares equal to the limit in Section 3(a).

(e) Source of Shares. The stock issuable under the Plan will be shares of authorized but unissued Ordinary Shares.

4. ELIGIBILITY.

(a) Eligibility for Specific Stock Awards. Incentive Stock Options may be granted only to employees of the Company or a "parent corporation" or "subsidiary corporation" thereof (as such terms are defined in Sections 424(e) and 424(f) of the Code). Stock Awards other than Incentive Stock Options may be granted to Employees, Directors and Consultants; *provided, however*, that Stock Awards may not be granted to Employees, Directors and Consultants who are providing Continuous Service only to any "parent" of the Company, as such term is defined in Rule 405, unless (i) the stock underlying such Stock Awards is treated as "service recipient stock" under Section 409A of the Code (for example, because the Stock Awards are granted pursuant to a corporate transaction such as a spin off transaction), (ii) the Company, in consultation with its legal counsel, has determined that such Stock Awards are otherwise exempt from Section 409A of the Code, or (iii) the Company, in consultation with its legal counsel, has determined that such Stock Awards comply with the distribution requirements of Section 409A of the Code.

(b) Ten Percent Shareholders. A Ten Percent Shareholder will not be granted an Incentive Stock Option unless the exercise price of such Option is at least 110% of the Fair Market Value on the date of grant and the Option is not exercisable after the expiration of five years from the date of grant.

(c) Consultants. A Consultant will not be eligible for the grant of a Stock Award if, at the time of grant, either the offer or sale of the Company's securities to such Consultant is not exempt under Rule 701 because of the nature of the services that the Consultant is providing to the Company, because the Consultant is not a natural person, or because of any other provision of Rule 701, unless the Company determines that such grant need not comply with the requirements of Rule 701 and will satisfy another exemption under the Securities Act as well as comply with the securities laws of all other relevant jurisdictions.

5. PROVISIONS RELATING TO OPTIONS AND STOCK APPRECIATION RIGHTS.

Each Option or SAR will be in such form and will contain such terms and conditions as the Board deems appropriate. All Options will be separately designated Incentive Stock Options or Nonstatutory Stock Options at the time of grant, and, if certificates are issued, a separate certificate or certificates will be issued for Ordinary Shares purchased on exercise of each type of Option. If an Option is not specifically designated as an Incentive

Stock Option, or if an Option is designated as an Incentive Stock Option but some portion or all of the Option fails to qualify as an Incentive Stock Option under the applicable rules, then the Option (or portion thereof) will be a Nonstatutory Stock Option. The provisions of separate Options or SARs need not be identical; *provided, however*, that each Award Agreement will conform to (through incorporation of provisions hereof by reference in the applicable Award Agreement or otherwise) the substance of each of the following provisions:

(a) Term. Subject to the provisions of Section 4(b) regarding Ten Percent Shareholders, no Option or SAR will be exercisable after the expiration of 10 years from the date of its grant or such shorter period specified in the Award Agreement.

(b) Exercise Price. Subject to the provisions of Section 4(b) regarding Ten Percent Shareholders, the exercise or strike price of each Option or SAR will be not less than the greater of (i) the nominal value of an Ordinary Share or (ii) 100% of the Fair Market Value of the Ordinary Shares subject to the Option or SAR on the date the Stock Award is granted. Notwithstanding the foregoing, an Option or SAR may be granted with an exercise or strike price lower than 100% of the Fair Market Value of the Ordinary Shares subject to the Stock Award if such Stock Award is granted pursuant to an assumption of or substitution for another option or stock appreciation right pursuant to a Corporate Transaction and in a manner consistent with the provisions of Section 409A of the Code and, if applicable, Section 424(a) of the Code, *provided that* in all cases it will not be less than the nominal value of an Ordinary Share. Each SAR will be denominated in Ordinary Share equivalents.

(c) Exercise and Purchase Price for Options. To exercise any outstanding Option, the Participant must provide written notice of exercise to the Company in compliance with the provisions of the Award Agreement evidencing such Option. The purchase price of Ordinary Shares acquired pursuant to the exercise of an Option may be paid, to the extent permitted by applicable law and as determined by the Board in its sole discretion, by any combination of the methods of payment set forth below. The Board will have the authority to grant Options that do not permit all of the following methods of payment (or otherwise restrict the ability to use certain methods) and to grant Options that require the consent of the Company to use a particular method of payment. In all cases the Company shall require that the nominal value of each newly issued Ordinary Share is paid up. The permitted methods of payment are as follows:

(i) by cash, check, bank draft or money order payable to the Company;

(ii) pursuant to a program developed under Regulation T as promulgated by the U.S. Federal Reserve Board that, prior to the issuance of the stock subject to the Option, results in either the receipt of cash (or check) by the Company or the receipt of irrevocable instructions to pay the aggregate exercise price to the Company from the sales proceeds;

(iii) by delivery to the Company (either by actual delivery or attestation) of Ordinary Shares;

(iv) if an Option is a Nonstatutory Stock Option, by a "net exercise" arrangement pursuant to which the Company will reduce the number of Ordinary Shares issuable upon exercise by the largest whole number of shares with a Fair Market Value that does not exceed the aggregate exercise price; *provided, however*, that the Company will accept a cash or other payment from the Participant to the extent of any remaining balance of the aggregate exercise price not satisfied by such reduction in the number of whole shares to be issued. Ordinary Shares will no longer be subject to an Option and will not be exercisable thereafter to the extent that (A) shares issuable upon exercise are used to pay the exercise price pursuant to the "net exercise," (B) shares are delivered to the Participant as a result of such exercise, and (C) shares are withheld to satisfy tax withholding obligations;

(v) according to a deferred payment or similar arrangement with the Participant; *provided, however*, that interest will compound at least annually and will be charged at the minimum rate of interest necessary to avoid (A) the imputation of interest income to the Company and compensation income to the Participant under any applicable provisions of the Code, and (B) the classification of the Option as a liability for financial accounting purposes; or

(vi) in any other form of legal consideration that may be acceptable to the Board and specified in the applicable Award Agreement.

(d) Exercise and Payment of a SAR. To exercise any outstanding SAR, the Participant must provide written notice of exercise to the Company in compliance with the provisions of the Award Agreement

evidencing such SAR. The appreciation distribution payable on the exercise of a SAR will be not greater than an amount equal to the excess of (A) the aggregate Fair Market Value (on the date of the exercise of the SAR) of a number of Ordinary Shares equal to the number of Ordinary Shares equivalents in which the Participant is vested under such SAR, and with respect to which the Participant is exercising the SAR on such date, over (B) the aggregate strike price of the number of Ordinary Shares equivalents with respect to which the Participant is exercising the SAR on such date. The appreciation distribution may be paid in Ordinary Shares, in cash, in any combination of the two or in any other form of consideration, as determined by the Board and contained in the Award Agreement evidencing such SAR. Where the SAR is settled using newly issued Ordinary Shares the Company shall require that the nominal value of each newly issued Ordinary Share is paid up.

(e) Transferability of Options and SARs. The Board may, in its sole discretion, impose such limitations on the transferability of Options and SARs as the Board will determine. In the absence of such a determination by the Board to the contrary, the following restrictions on the transferability of Options and SARs will apply:

(i) Restrictions on Transfer. An Option or SAR will not be transferable except by will or by the laws of descent and distribution (or pursuant to subsections (ii) and (iii) below), and will be exercisable during the lifetime of the Participant only by the Participant. The Board may permit transfer of the Option or SAR in a manner that is not prohibited by applicable tax and securities laws. Except as explicitly provided in the Plan, neither an Option nor a SAR may be transferred for consideration.

(ii) Domestic Relations Orders. Subject to the approval of the Board or a duly authorized Officer, an Option or SAR may be transferred pursuant to the terms of a domestic relations order, official marital settlement agreement or other divorce or separation instrument which contains the information required by the Company to effect the transfer. If an Option is an Incentive Stock Option, such Option may be deemed to be a Nonstatutory Stock Option as a result of such transfer.

(iii) Beneficiary Designation. Subject to the approval of the Board or a duly authorized Officer, a Participant may, by delivering written notice to the Company, in a form approved by the Company (or the designated broker), designate a third party who, upon the death of the Participant, will thereafter be entitled to exercise the Option or SAR and receive the Ordinary Shares or other consideration resulting from such exercise. In the absence of such a designation, upon the death of the Participant, the executor or administrator of the Participant's estate will be entitled to exercise the Option or SAR and receive the Ordinary Shares or other consideration resulting from such exercise. However, the Company may prohibit designation of a beneficiary at any time, including due to any conclusion by the Company that such designation would be inconsistent with the provisions of applicable laws whether in the United States or any other jurisdiction in which a Participant resides.

(f) Vesting Generally. The total number of Ordinary Shares subject to an Option or SAR may vest and therefore become exercisable in periodic installments that may or may not be equal. The Option or SAR may be subject to such other terms and conditions on the time or times when it may or may not be exercised (which may be based on the satisfaction of performance goals or other criteria) as the Board may deem appropriate. The vesting provisions of individual Options or SARs may vary. The provisions of this Section 5(f) are subject to any Option or SAR provisions governing the minimum number of Ordinary Shares as to which an Option or SAR may be exercised.

(g) Termination of Continuous Service. Except as otherwise provided in the applicable Award Agreement or other agreement between the Participant and the Company, if a Participant's Continuous Service terminates (other than for Cause and other than upon the Participant's death or Disability), the Participant may exercise his or her Option or SAR (to the extent that the Participant was entitled to exercise such Stock Award as of the date of termination of Continuous Service) within the period of time ending on the earlier of (i) the date three months following the termination of the Participant's Continuous Service (or such longer or shorter period specified in the applicable Award Agreement, which period will not be less than 30 days if necessary to comply with applicable laws unless such termination is for Cause) and (ii) the expiration of the term of the Option or SAR as set forth in the Award Agreement. If, after termination of Continuous Service, the Participant does not exercise his or her Option or SAR (as applicable) within the applicable time frame, the Option or SAR will terminate.

(h) Extension of Termination Date. If the exercise of an Option or SAR following the termination of the Participant's Continuous Service (other than for Cause and other than upon the Participant's death or

Disability) would be prohibited at any time solely because the issuance of Ordinary Shares would violate the registration requirements under the Securities Act, then the Option or SAR will terminate on the earlier of (i) the expiration of a total period of time (that need not be consecutive) equal to the applicable post-termination exercise period after the termination of the Participant's Continuous Service during which the exercise of the Option or SAR would not be in violation of such registration requirements, and (ii) the expiration of the term of the Option or SAR as set forth in the applicable Award Agreement. In addition, unless otherwise provided in a Participant's Award Agreement, if the sale of any Ordinary Shares received upon exercise of an Option or SAR following the termination of the Participant's Continuous Service (other than for Cause) would violate the Company's insider trading policy, then the Option or SAR will terminate on the earlier of (i) the expiration of the period of time (that need not be consecutive) equal to the applicable post-termination exercise period after the termination of the Participant's Continuous Service during which the sale of the Ordinary Shares received upon exercise of the Option or SAR would not be in violation of the Company's insider trading policy, and (ii) the expiration of the term of the Option or SAR as set forth in the applicable Award Agreement.

(i) Disability of Participant. Except as otherwise provided in the applicable Award Agreement or other agreement between the Participant and the Company, if a Participant's Continuous Service terminates as a result of the Participant's Disability, the Participant may exercise his or her Option or SAR (to the extent that the Participant was entitled to exercise such Option or SAR as of the date of termination of Continuous Service), but only within such period of time ending on the earlier of (i) the date 12 months following such termination of Continuous Service (or such longer or shorter period specified in the Award Agreement, which period will not be less than six months if necessary to comply with applicable laws unless such termination is for Cause), and (ii) the expiration of the term of the Option or SAR as set forth in the Award Agreement. If, after termination of Continuous Service, the Participant does not exercise his or her Option or SAR within the applicable time frame, the Option or SAR (as applicable) will terminate.

(j) Death of Participant. Except as otherwise provided in the applicable Award Agreement or other agreement between the Participant and the Company, if (i) a Participant's Continuous Service terminates as a result of the Participant's death, or (ii) the Participant dies within the period (if any) specified in the Award Agreement for exercisability after the termination of the Participant's Continuous Service (for a reason other than death), then the Option or SAR may be exercised (to the extent the Participant was entitled to exercise such Option or SAR as of the date of death) by the Participant's estate, by a person who acquired the right to exercise the Option or SAR by bequest or inheritance or by a person designated to exercise the Option or SAR upon the Participant's death, but only within the period ending on the earlier of (i) the date 18 months following the date of death (or such longer or shorter period specified in the Award Agreement, which period will not be less than six months if necessary to comply with applicable laws unless such termination is for Cause), and (ii) the expiration of the term of such Option or SAR as set forth in the Award Agreement. If, after the Participant's death, the Option or SAR is not exercised within the applicable time frame, the Option or SAR (as applicable) will terminate.

(k) Termination for Cause. Except as explicitly provided otherwise in a Participant's Award Agreement or other individual written agreement between the Company or any Affiliate and the Participant, if a Participant's Continuous Service is terminated for Cause, the Option or SAR will terminate immediately upon such Participant's termination of Continuous Service, and the Participant will be prohibited from exercising his or her Option or SAR from and after the date of such termination of Continuous Service.

(l) Non-Exempt Employees. If an Option or SAR is granted to an Employee who is a non-exempt employee for purposes of the U.S. Fair Labor Standards Act of 1938, as amended, the Option or SAR will not be first exercisable for any Ordinary Shares until at least six months following the date of grant of the Option or SAR (although the Stock Award may vest prior to such date). Consistent with the provisions of the U.S. Worker Economic Opportunity Act, (i) if such non-exempt Employee dies or suffers a Disability, (ii) upon a Corporate Transaction in which such Option or SAR is not assumed, continued, or substituted, (iii) upon a Change in Control, or (iv) upon the Participant's retirement (as such term may be defined in the Participant's Award Agreement, in another agreement between the Participant and the Company, or, if no such definition, in accordance with the Company's then current employment policies and guidelines), the vested portion of any Options and SARs may be exercised earlier than six months following the date of grant. The foregoing provision is intended to operate so that any income derived by a non-exempt employee in connection with the exercise or vesting of an Option or SAR will be exempt from his or her regular rate of pay. To the extent permitted and/or required for compliance with the U.S. Worker Economic Opportunity Act to ensure that any income derived by a non-exempt employee in connection with the exercise, vesting or issuance of any shares under any other Stock Award will be exempt from the employee's regular rate of pay, the provisions of this

Section 5(l) will apply to all Stock Awards and are hereby incorporated by reference into such Award Agreements.

(m) Early Exercise of Options. An Option may, but need not, include a provision whereby the Participant may elect at any time before the Participant's Continuous Service terminates to exercise the Option as to any part or all of the Ordinary Shares subject to the Option prior to the full vesting of the Option.

(n) Right of Repurchase; Right of First Refusal. Subject to the "Repurchase Limitation" in Section 8(l), and subject to applicable Irish company law, the Option or SAR may include a provision whereby (i) the Company may elect to repurchase all or any part of the vested or unvested Ordinary Shares acquired by the Participant pursuant to the exercise of the Option or SAR, and/or (ii) the Company may elect to exercise a right of first refusal following receipt of notice from the Participant of the intent to transfer all or any part of the Ordinary Shares received upon the exercise of the Option or SAR.

6. PROVISIONS OF STOCK AWARDS OTHER THAN OPTIONS AND SARS.

(a) Restricted Stock Awards. Each Restricted Stock Award will be in such form and will contain such terms and conditions as the Board will deem appropriate. To the extent consistent with the Company's Constitution, at the Board's election, Ordinary Shares underlying a Restricted Stock Award may be (i) held in book entry form subject to the Company's instructions until any restrictions relating to the Restricted Stock Award lapse; or (ii) evidenced by a certificate, which certificate will be held in such form and manner as determined by the Board. The terms and conditions of Restricted Stock Awards may change from time to time, and the terms and conditions of separate Restricted Stock Awards need not be identical; *provided, however*, that each Award Agreement will conform to (through incorporation of the provisions hereof by reference in the agreement or otherwise) the substance of each of the following provisions:

(i) Consideration. A Restricted Stock Award may be awarded in consideration for (A) cash, check, bank draft or money order payable to the Company, (B) past services to the Company or an Affiliate, or (C) any other form of legal consideration (including future services) that may be acceptable to the Board, in its sole discretion, and permissible under applicable law. In all cases the Company shall require that the nominal value of each newly issued Ordinary Share issued in satisfaction of a Restricted Stock Award is paid up.

(ii) Vesting. Subject to the "Repurchase Limitation" in Section 8(l), and applicable Irish company law, Ordinary Shares awarded under the Award Agreement may be subject to forfeiture to the Company in accordance with a vesting schedule to be determined by the Board.

(iii) Termination of Participant's Continuous Service. If a Participant's Continuous Service terminates, the Company may receive through a forfeiture condition or a repurchase right, any or all of the Ordinary Shares held by the Participant that have not vested as of the date of termination of Continuous Service under the terms of the Award Agreement.

(iv) Transferability. Rights to acquire Ordinary Shares under the Restricted Stock Award will be transferable by the Participant only upon such terms and conditions as are set forth in the Award Agreement, as the Board will determine in its sole discretion, so long as Ordinary Shares awarded under the Restricted Stock Award remain subject to the terms of the Award Agreement.

(v) Dividends. An Award Agreement may provide that any dividends paid on Restricted Stock will be subject to the same vesting and forfeiture restrictions as apply to the shares subject to the Restricted Stock Award to which they relate.

(b) Restricted Stock Unit Awards. Each Restricted Stock Unit Award will be in such form and will contain such terms and conditions as the Board will deem appropriate. The terms and conditions of Restricted Stock Unit Awards may change from time to time, and the terms and conditions of separate Restricted Stock Unit Awards need not be identical; *provided* that each Restricted Stock Unit Award Agreement will conform to (through incorporation of the provisions hereof by reference in the Agreement or otherwise) the substance of each of the following provisions:

(i) Consideration. At the time of grant of a Restricted Stock Unit Award, the Board will determine the consideration, if any, to be paid by the Participant upon delivery of each share of Ordinary Shares subject to the Restricted Stock Unit Award. The consideration to be paid (if any) by the Participant for each

share of Ordinary Shares subject to a Restricted Stock Unit Award may be paid in any form of legal consideration that may be acceptable to the Board, in its sole discretion, and permissible under applicable law.

(ii) Vesting. At the time of the grant of a Restricted Stock Unit Award, the Board may impose such restrictions on or conditions to the vesting of the Restricted Stock Unit Award as it, in its sole discretion, deems appropriate.

(iii) Payment. A Restricted Stock Unit Award may be settled by the delivery of Ordinary Shares, their cash equivalent, any combination thereof or in any other form of consideration, as determined by the Board and contained in the Restricted Stock Unit Award Agreement. In all cases the Company shall require that the nominal value of each newly issued Ordinary Share issued in satisfaction of a Restricted Stock Unit Award is paid up.

(iv) Additional Restrictions. At the time of the grant of a Restricted Stock Unit Award, the Board, as it deems appropriate, may impose such restrictions or conditions that delay the delivery of the Ordinary Shares (or their cash equivalent) subject to a Restricted Stock Unit Award to a time after the vesting of such Restricted Stock Unit Award.

(v) Dividend Equivalents. Dividend equivalents may be credited in respect of Ordinary Shares covered by a Restricted Stock Unit Award, as determined by the Board and contained in the Restricted Stock Unit Award Agreement. At the sole discretion of the Board, such dividend equivalents may be converted into additional Ordinary Shares covered by the Restricted Stock Unit Award in such manner as determined by the Board. Any additional shares covered by the Restricted Stock Unit Award credited by reason of such dividend equivalents will be subject to all of the same terms and conditions of the underlying Award Agreement to which they relate.

(vi) Termination of Participant's Continuous Service. Except as otherwise provided in the applicable Award Agreement, such portion of the Restricted Stock Unit Award that has not vested will be forfeited upon the Participant's termination of Continuous Service.

(vii) Compliance with Section 409A of the Code. Notwithstanding anything to the contrary set forth herein, any Restricted Stock Unit Award granted under the Plan that is not exempt from the requirements of Section 409A of the Code shall contain such provisions so that such Restricted Stock Unit Award will comply with the requirements of Section 409A of the Code. Such restrictions, if any, shall be determined by the Board and contained in the Restricted Stock Unit Award Agreement evidencing such Restricted Stock Unit Award. For example, such restrictions may include, without limitation, a requirement that any Ordinary Shares that are to be issued in a year following the year in which the Restricted Stock Unit Award vests must be issued in accordance with a fixed pre-determined schedule.

(c) Other Stock Awards. Other forms of Stock Awards valued in whole or in part by reference to, or otherwise based on, Ordinary Shares, including the appreciation in value thereof (e.g., options or stock rights with an exercise price or strike price less than 100% of the Fair Market Value of the Ordinary Shares at the time of grant) may be granted either alone or in addition to Stock Awards provided for under Section 5 and the preceding provisions of this Section 6. Subject to the provisions of the Plan, the Board will have sole and complete authority to determine the persons to whom and the time or times at which such Other Stock Awards will be granted, the number of Ordinary Shares (or the cash equivalent thereof) to be granted pursuant to such Other Stock Awards and all other terms and conditions of such Other Stock Awards.

7. COVENANTS OF THE COMPANY.

(a) Availability of Shares. The Company will maintain sufficient authorized and unissued Ordinary Shares to satisfy then-outstanding Stock Awards in full.

(b) Securities Law Compliance. The Company will seek to obtain from each regulatory commission or agency having jurisdiction over the Plan such authority as may be required to grant Stock Awards and to issue and sell Ordinary Shares upon exercise of the Stock Awards; *provided, however,* that this undertaking will not require the Company to register under the Securities Act, the Plan, any Stock Award or any Ordinary Shares issued or issuable pursuant to any such Stock Award. If, after reasonable efforts and at a reasonable cost, the Company is unable to obtain from any such regulatory commission or agency the authority that counsel for the Company deems necessary for the lawful issuance and sale of Ordinary Shares under the Plan, the Company

will be relieved from any liability for failure to issue and sell Ordinary Shares upon exercise of such Stock Awards unless and until such authority is obtained. A Participant will not be eligible for the grant of a Stock Award or the subsequent issuance of cash or Ordinary Shares pursuant to the Stock Award if such grant or issuance would be in violation of any applicable securities law.

(c) No Obligation to Notify or Minimize Taxes. The Company will have no duty or obligation to any Participant to advise such holder as to the time or manner of exercising such Stock Award. Furthermore, the Company will have no duty or obligation to warn or otherwise advise such holder of a pending termination or expiration of a Stock Award or a possible period in which the Stock Award may not be exercised. The Company has no duty or obligation to minimize the tax consequences of a Stock Award to the holder of such Stock Award.

8. MISCELLANEOUS.

(a) Use of Proceeds from Sales of Ordinary Shares. Proceeds from the sale of Ordinary Shares pursuant to Stock Awards will constitute general funds of the Company.

(b) Corporate Action Constituting Grant of Stock Awards. Corporate action constituting a grant by the Company of a Stock Award to any Participant will be deemed completed as of the date of such corporate action, unless otherwise determined by the Board, regardless of when the instrument, certificate, or letter evidencing the Stock Award is communicated to, or actually received or accepted by, the Participant. In the event that the corporate records (e.g., Board consents, resolutions or minutes) documenting the corporate action constituting the grant contain terms (e.g., exercise price, vesting schedule or number of shares) that are inconsistent with those in the Award Agreement or related grant documents as a result of a clerical error in the papering of the Award Agreement or related grant documents, the corporate records will control and the Participant will have no legally binding right to the incorrect term in the Award Agreement or related grant documents.

(c) Shareholder Rights. No Participant will be deemed to be the holder of, or to have any of the rights of a holder with respect to, any Ordinary Shares subject to a Stock Award unless and until (i) such Participant has satisfied all requirements for exercise of, or the issuance of Ordinary Shares under, the Stock Award pursuant to its terms, and (ii) the issuance of the Ordinary Shares subject to the Stock Award has been entered into the books and records of the Company.

(d) No Employment or Other Service Rights. Nothing in the Plan, any Award Agreement or any other instrument executed thereunder or in connection with any Award granted pursuant thereto will confer upon any Participant any right to continue to serve the Company or an Affiliate in the capacity in effect at the time the Stock Award was granted or will affect any right that the Company or an Affiliate may have to terminate (i) the employment of an Employee with or without notice and with or without cause, subject to the employment laws of the country in which the Employee is employed, (ii) the service of a Consultant pursuant to the terms of such Consultant's agreement with the Company or an Affiliate, or (iii) the service of a Director pursuant to the Constitution of the Company or an Affiliate, and any applicable provisions of the corporate law of the country or state in which the Company or the Affiliate is incorporated, as the case may be.

(e) Change in Time Commitment. In the event a Participant's regular level of time commitment in the performance of his or her services for the Company and any Affiliates is reduced (for example, and without limitation, if the Participant is an Employee of the Company and the Employee has a change in status from a full-time Employee to a part-time Employee or takes an extended leave of absence) after the date of grant of any Stock Award to the Participant, the Board has the right in its sole discretion to (x) make a corresponding reduction in the number of shares subject to any portion of such Stock Award that is scheduled to vest or become payable after the date of such change in time commitment, and (y) in lieu of or in combination with such a reduction, extend the vesting or payment schedule applicable to such Stock Award. In the event of any such reduction, the Participant will have no right with respect to any portion of the Stock Award that is so reduced or extended.

(f) Incentive Stock Option Limitations. To the extent that the aggregate Fair Market Value (determined at the time of grant) of Ordinary Shares with respect to which Incentive Stock Options are exercisable for the first time by any Participant during any calendar year (under all plans of the Company and any Affiliates) exceeds $100,000 (or such other limit established in the Code) or otherwise does not comply with the rules governing Incentive Stock Options, the Options or portions thereof that exceed such limit

(according to the order in which they were granted) or otherwise do not comply with such rules will be treated as Nonstatutory Stock Options, notwithstanding any contrary provision of the applicable Award Agreement(s).

(g) Investment Assurances. The Company may require a Participant, as a condition of exercising or acquiring Ordinary Shares under any Stock Award, (i) to give written assurances satisfactory to the Company as to the Participant's knowledge and experience in financial and business matters and/or to employ a purchaser representative reasonably satisfactory to the Company who is knowledgeable and experienced in financial and business matters and that the Participant is capable of evaluating, alone or together with the purchaser representative, the merits and risks of exercising the Stock Award; and (ii) to give written assurances satisfactory to the Company stating that the Participant is acquiring Ordinary Shares subject to the Stock Award for the Participant's own account and not with any present intention of selling or otherwise distributing the Ordinary Shares. The foregoing requirements, and any assurances given pursuant to such requirements, will be inoperative if (A) the issuance of the shares upon the exercise or acquisition of Ordinary Shares under the Stock Award has been registered under a then currently effective registration statement under the Securities Act, or (B) as to any particular requirement, a determination is made by counsel for the Company that such requirement need not be met in the circumstances under the then applicable securities laws. The Company may, upon advice of counsel to the Company, place legends on stock certificates issued under the Plan as such counsel deems necessary or appropriate in order to comply with applicable securities laws, including, but not limited to, legends restricting the transfer of the Ordinary Shares.

(h) Withholding Obligations. Unless prohibited by the terms of a Award Agreement, the Company may, in its sole discretion, but subject always to applicable law, satisfy any federal, state or local tax withholding obligation relating to a Stock Award by any of the following means or by a combination of such means: (i) causing the Participant to tender a cash payment; (ii) withholding Ordinary Shares from the Ordinary Shares issued or otherwise issuable to the Participant in connection with the Stock Award; *provided, however*, that no Ordinary Shares are withheld with a value exceeding the minimum amount of tax required to be withheld by law (or such lesser amount as may be necessary to avoid classification of the Stock Award as a liability for financial accounting purposes); (iii) withholding cash from a Stock Award settled in cash; (iv) withholding payment from any amounts otherwise payable to the Participant; or (v) by such other method as may be set forth in the Award Agreement.

(i) Electronic Delivery. Any reference herein to a "written" agreement or document will include any agreement or document delivered electronically or posted on the Company's intranet (or other shared electronic medium controlled by the Company to which the Participant has access).

(j) Deferrals. To the extent permitted by applicable law, the Board, in its sole discretion, may determine that the delivery of Ordinary Shares or the payment of cash, upon the exercise, vesting or settlement of all or a portion of any Stock Award may be deferred and may establish programs and procedures for deferral elections to be made by Participants. Deferrals by Participants will be made in accordance with Section 409A of the Code. Consistent with Section 409A of the Code, the Board may provide for distributions while a Participant is still an employee or otherwise providing services to the Company. The Board is authorized to make deferrals of Stock Awards and determine when, and in what annual percentages, Participants may receive payments, including lump sum payments, following the Participant's termination of Continuous Service, and implement such other terms and conditions consistent with the provisions of the Plan and in accordance with applicable law.

(k) Compliance with Section 409A of the Code. To the extent that the Board determines that any Stock Award granted hereunder is subject to Section 409A of the Code, the Award Agreement evidencing such Stock Award shall incorporate the terms and conditions necessary to avoid the consequences specified in Section 409A(a)(1) of the Code. To the extent applicable, the Plan and Award Agreements shall be interpreted in accordance with Section 409A of the Code. Notwithstanding anything to the contrary in the Plan (and unless the Award Agreement specifically provides otherwise), if the Ordinary Shares are publicly traded, and if a Participant holding a Stock Award that constitutes "deferred compensation" under Section 409A of the Code is a "specified employee" for purposes of Section 409A of the Code, no distribution or payment of any amount that is due because of a "separation from service" (as defined in Section 409A of the Code without regard to alternative definitions thereunder) will be issued or paid before the date that is six months following the date of such Participant's "separation from service" (as defined in Section 409A of the Code without regard to alternative definitions thereunder) or, if earlier, the date of the Participant's death, unless such distribution or payment can be made in a manner that complies with Section 409A of the Code, and any amounts so deferred

will be paid in a lump sum on the day after such six month period elapses, with the balance paid thereafter on the original schedule.

(l) Repurchase Limitation. The terms of any repurchase right will be specified in the Award Agreement or a separate shareholders' agreement. The repurchase price for vested Ordinary Shares will be the Fair Market Value of the Ordinary Shares on the date of repurchase. The repurchase price for unvested Ordinary Shares will be the lower of (i) the Fair Market Value of the Ordinary Shares on the date of repurchase or (ii) their original purchase price. However, the Company will not exercise its repurchase right until at least six months (or such longer or shorter period of time necessary to avoid classification of the Stock Award as a liability for financial accounting purposes) have elapsed following delivery of Ordinary Shares subject to the Stock Award, unless otherwise specifically provided in the Award Agreement. Any repurchase rights will be subject to applicable Irish company law.

9. ADJUSTMENTS UPON CHANGES IN ORDINARY SHARES; OTHER CORPORATE EVENTS.

(a) Capitalization Adjustments. In the event of a Capitalization Adjustment, the Board will appropriately and proportionately adjust: (i) the class(es) and maximum number of securities subject to the Plan pursuant to Section 3(a), (ii) the class(es) and maximum number of securities that may be issued pursuant to the exercise of Incentive Stock Options pursuant to Section 3(c), and (iii) the class(es) and number of securities and price per share of stock subject to outstanding Stock Awards. The Board will make such adjustments, and its determination will be final, binding and conclusive; *provided always that* no adjustment may be made which reduces the price payable per Ordinary Share to an amount that is lower than the nominal value of an Ordinary Share.

(b) Dissolution or Liquidation. Except as otherwise provided in the Award Agreement, in the event of a dissolution or liquidation of the Company, all outstanding Stock Awards (other than Stock Awards consisting of vested and outstanding Ordinary Shares not subject to a forfeiture condition or the Company's right of repurchase) will terminate immediately prior to the completion of such dissolution or liquidation, and the Ordinary Shares subject to the Company's repurchase rights or subject to a forfeiture condition may be repurchased or reacquired by the Company notwithstanding the fact that the holder of such Stock Award is providing Continuous Service, *provided, however,* that the Board may, in its sole discretion, cause some or all Stock Awards to become fully vested, exercisable and/or no longer subject to repurchase or forfeiture (to the extent such Stock Awards have not previously expired or terminated) before the dissolution or liquidation is completed but contingent on its completion.

(c) Corporate Transaction. The following provisions will apply to Stock Awards in the event of a Corporate Transaction unless otherwise provided in the instrument evidencing the Stock Award or any other written agreement between the Company or any Affiliate and the Participant or unless otherwise expressly provided by the Board at the time of grant of a Stock Award. In the event of a Corporate Transaction, then, notwithstanding any other provision of the Plan, the Board may take one or more of the following actions with respect to Stock Awards, contingent upon the closing or completion of the Corporate Transaction:

(i) arrange for the surviving corporation or acquiring corporation (or the surviving or acquiring corporation's parent company) to assume or continue the Stock Award or to substitute a similar stock award for the Stock Award (including, but not limited to, an award to acquire the same consideration paid to the shareholders of the Company pursuant to the Corporate Transaction);

(ii) arrange for the assignment of any reacquisition or repurchase rights held by the Company in respect of Ordinary Shares issued pursuant to the Stock Award to the surviving corporation or acquiring corporation (or the surviving or acquiring corporation's parent company);

(iii) accelerate the vesting, in whole or in part, of the Stock Award (and, if applicable, the time at which the Stock Award may be exercised) to a date prior to the effective time of such Corporate Transaction as the Board determines (or, if the Board does not determine such a date, to the date that is five days prior to the effective date of the Corporate Transaction), with such Stock Award terminating if not exercised (if applicable) at or prior to the effective time of the Corporate Transaction; *provided, however*, that the Board may require Participants to complete and deliver to the Company a notice of exercise before the effective date of a Corporate Transaction, which exercise is contingent upon the effectiveness of such Corporate Transaction;

(iv) arrange for the lapse, in whole or in part, of any reacquisition or repurchase rights held by the Company with respect to the Stock Award;

(v) cancel or arrange for the cancellation of the Stock Award, to the extent not vested or not exercised prior to the effective time of the Corporate Transaction, in exchange for such cash consideration (including no consideration) as the Board, in its sole discretion, may consider appropriate; and

(vi) make a payment, in such form as may be determined by the Board equal to the excess, if any, of (A) the value of the property the Participant would have received upon the exercise of the Stock Award immediately prior to the effective time of the Corporate Transaction, over (B) any exercise price payable by such holder in connection with such exercise. For clarity, this payment may be zero ($0) if the value of the property is equal to or less than the exercise price. Payments under this provision may be delayed or offset to the same extent that payment of consideration to the holders of the Company's Ordinary Shares in connection with the Corporate Transaction is delayed or offset as a result of escrows, earn outs, holdbacks or any other contingencies.

The Board need not take the same action or actions with respect to all Stock Awards or portions thereof or with respect to all Participants. The Board may take different actions with respect to the vested and unvested portions of a Stock Award.

(d) Acceleration on a Qualifying Termination in Connection with a Change in Control. If during the period beginning on the date that is 30 days prior to and ending on the date that is 12 months following the consummation of a Corporate Transaction that also qualifies as a Change in Control, (i) a Participant's services to the Company (or its successor in the Change in Control) in all capacities are involuntarily terminated without Cause, or (ii) a Participant resigns service to the Company (or its successor in the Change in Control) in all capacities for Good Reason, and in either case other than as a result of death or Disability, then as of the date of Participant's termination of Continuous Service, the vesting and exercisability of any then-unvested Stock Award held by a Participant shall be accelerated in full.

10. PLAN TERM; EARLIER TERMINATION OR SUSPENSION OF THE PLAN.

(a) Plan Term. The Board may suspend or terminate the Plan at any time. Unless terminated sooner by the Board, the Plan will automatically terminate on the day before the 10th anniversary of the earlier of the Effective Date. No Stock Awards may be granted under the Plan while the Plan is suspended or after it is terminated.

(b) No Impairment of Rights. Suspension or termination of the Plan will not impair rights and obligations under any Stock Award granted while the Plan is in effect except with the written consent of the affected Participant or as otherwise permitted in the Plan.

11. EFFECTIVE DATE OF PLAN.

This Plan will become effective on the Effective Date.

12. CHOICE OF LAW.

This Plan shall be governed by and construed in accordance with the Irish Companies Act 2014 (as same may be amended, replaced and/or consolidated in the future) as to matters within the scope thereof, and as to all other matters shall be governed by and construed in accordance with the internal laws of the State of Delaware, without regard to its principles of conflicts of laws.

13. DEFINITIONS. As used in the Plan, the following definitions will apply to the capitalized terms indicated below:

(a) "***Affiliate***" means, at the time of determination, any "parent" or "majority-owned subsidiary" of the Company, as such terms are defined in Rule 405 or, as the context so requires, means a "holding company" or "subsidiary" of the Company as such terms are defined in Irish company law. The Board will have the authority to determine the time or times at which an entity's status is determined within the foregoing definition.

(b) "***Award Agreement***" means a written agreement between the Company and a holder of an Award evidencing the terms and conditions of an Award grant. Each Award Agreement will be subject to the terms and conditions of the Plan.

(c) "***Board***" means the Board of Directors of the Company.

(d) "***Capitalization Adjustment***" means any change that is made in, or other events that occur with respect to, the Ordinary Shares subject to the Plan or subject to any Stock Award after the Effective Date without the receipt of consideration by the Company through merger, consolidation, reorganization, recapitalization, reincorporation, stock dividend, dividend in property other than cash, large nonrecurring cash dividend, stock split, reverse stock split, liquidating dividend, combination of shares, exchange of shares, change in corporate structure, or any similar equity restructuring transaction, as that term is used in Statement of Financial Accounting Standards Board Accounting Standards Codification Topic 718 (or any successor thereto). Notwithstanding the foregoing, the conversion of any convertible securities of the Company will not be treated as a Capitalization Adjustment.

(e) "***Cause***" will have the meaning ascribed to such term in any written agreement between the Participant and the Company defining such term and, in the absence of such agreement, such term means, with respect to a Participant, the occurrence of any of the following events: (i) such Participant's commission of any felony or any crime involving fraud, dishonesty or moral turpitude under the laws of the United States or any state thereof or any country in which a Participant is employed; (ii) such Participant's attempted commission of, or participation in, a fraud or act of dishonesty against the Company; (iii) such Participant's intentional, material violation of any contract or agreement between the Participant and the Company or of any statutory duty owed to the Company; (iv) such Participant's unauthorized use or disclosure of the Company's confidential information or trade secrets; or (v) such Participant's gross misconduct. The determination that a termination of the Participant's Continuous Service is either for Cause or without Cause will be made by the Company, in its sole discretion. Any determination by the Company that the Continuous Service of a Participant was terminated with or without Cause for the purposes of outstanding Stock Awards held by such Participant will have no effect upon any determination of the rights or obligations of the Company or such Participant for any other purpose.

(f) "***Change in Control***" means the consummation, in a single transaction or in a series of related transactions, of any one or more of the following events:

(i) a merger or consolidation in which the Company is a constituent party (or a subsidiary of the Company is a constituent party and the Company issues shares pursuant to such merger or consolidation), other than a merger or consolidation in which the voting securities of the Company outstanding immediately prior to such merger or consolidation continue to represent (either by remaining outstanding or by being converted into voting securities of the surviving entity) more than 50% of the combined voting power of the voting securities of the surviving entity outstanding immediately after such merger or consolidation;

(ii) any transaction or series of related transactions in which in excess of 50% of the Company's voting power is transferred, other than the issue by the Company of shares in transactions the primary purpose of which is to raise capital for the Company's operations and activities; or

(iii) a sale, lease, exclusive license or other disposition of all or substantially all (as determined by the Board in its sole discretion) of the assets of the Company other than a sale, lease, license or other disposition of all or substantially all of the consolidated assets of the Company to an entity, more than 50% of the combined voting power of the voting securities of which are beneficially owned by shareholders of the Company in substantially the same proportions as their beneficial ownership of the outstanding voting securities of the Company immediately prior to such sale, lease, exclusive license or other disposition.

(g) "***Code***" means the U.S. Internal Revenue Code of 1986, as amended, including any applicable regulations and guidance thereunder.

(h) "***Committee***" means a committee of one or more Directors to whom authority has been delegated by the Board in accordance with Section 2(c).

(i) "***Company***" means Iterum Therapeutics Limited, a company incorporated under the laws of the Republic of Ireland.

(j) "***Consultant***" means any person, including an advisor, who is (i) engaged by the Company or an Affiliate to render consulting or advisory services and is compensated for such services, or (ii) serving as a member of the board of directors of an Affiliate and is compensated for such services. However, service solely as a Director, or payment of a fee for such service, will not cause a Director to be considered a "Consultant" for purposes of the Plan.

(k) "***Continuous Service***" means that the Participant's service with the Company or an Affiliate, whether as an Employee, Director or Consultant, is not interrupted or terminated. A change in the capacity in which the Participant renders service to the Company or an Affiliate as an Employee, Director or Consultant or a change in the Entity for which the Participant renders such service, provided that there is no interruption or termination of the Participant's service with the Company or an Affiliate, will not terminate a Participant's Continuous Service; *provided, however*, that if the Entity for which a Participant is rendering services ceases to qualify as an Affiliate, as determined by the Board in its sole discretion, such Participant's Continuous Service will be considered to have terminated on the date such Entity ceases to qualify as an Affiliate. For example, a change in status from an Employee of the Company to a Consultant of an Affiliate or to a Director will not constitute an interruption of Continuous Service. To the extent permitted by law, the Board or an Officer of the Company, in that party's sole discretion, may determine whether Continuous Service will be considered interrupted in the case of (i) any leave of absence approved by the Board or chief executive officer, including sick leave, military leave or any other personal leave, or (ii) transfers between the Company, an Affiliate, or their successors. Notwithstanding the foregoing, a leave of absence will be treated as Continuous Service for purposes of vesting in a Stock Award only to such extent as may be provided in the Company's leave of absence policy, in the written terms of any leave of absence agreement or policy applicable to the Participant, or as otherwise required by law.

(l) "***Corporate Transaction***" means the consummation, in a single transaction or in a series of related transactions, of any one or more of the following events:

(i) a sale or other disposition of all or substantially all, as determined by the Board in its sole discretion, of the consolidated assets of the Company and its Subsidiaries;

(ii) a sale or other disposition of at least 50% of the outstanding securities of the Company;

(iii) a merger, consolidation or similar transaction following which the Company is not the surviving corporation; or

(iv) a merger, consolidation or similar transaction following which the Company is the surviving corporation but the Ordinary Shares outstanding immediately preceding the merger, consolidation or similar transaction are converted or exchanged by virtue of the merger, consolidation or similar transaction into other property, whether in the form of securities, cash or otherwise.

For the avoidance of doubt, any one or more of the above events may be effected pursuant to (x) a takeover under Irish takeover rules; (y) a compromise or arrangement under Chapter 1 of Part 9 of the Companies Act 2014 of the Republic of Ireland or (z) Chapter 2 of Part 9 of the Companies Act 2014 of the Republic of Ireland.

(m) "***Director***" means a member of the Board.

(n) "***Disability***" means, with respect to a Participant, the inability of such Participant to engage in any substantial gainful activity by reason of any medically determinable physical or mental impairment that can be expected to result in death or that has lasted or can be expected to last for a continuous period of not less than twelve (12) months as provided in Sections 22(e)(3) and 409A(a)(2)(c)(i) of the Code, and will be determined by the Board on the basis of such medical evidence as the Board deems warranted under the circumstances.

(o) "***Effective Date***" means the effective date of this Plan, which is November 18, 2015.

(p) "***Employee***" means any person employed by the Company or an Affiliate. However, service solely as a Director, or payment of a fee for such services, will not cause a Director to be considered an "Employee" for purposes of the Plan.

(q) "***Entity***" means a corporation, partnership, limited liability company or other entity.

(r) "***Exchange Act***" means the U.S. Securities Exchange Act of 1934, as amended, and the rules and regulations promulgated thereunder.

(s) "***Fair Market Value***" means, as of any date, the value of the Ordinary Shares determined by the Board in compliance with Section 409A of the Code or, in the case of an Incentive Stock Option, in compliance with Section 422 of the Code.

(t) "***Good Reason***" will have the meaning ascribed to such term in any written agreement between the Participant and the Company or a successor corporation defining such term and, in the absence of such agreement, such term means, with respect to a Participant, any of the following actions taken without Cause without Participant's consent:

(i) A material reduction of the Participant's base compensation, other than a reduction that applies generally to all executives;

(ii) A material reduction in the Participant's authority, duties or responsibilities, provided, however, that a change in job position (including a change in title) shall not be deemed a "material reduction" unless the Participant's new authority, duties or responsibilities are materially reduced from the prior authority, duties or responsibilities;

(iii) failure or refusal of a successor to the Company to materially assume the Company's obligations under the Participant's offer letter and/or employment agreement, if applicable, in the event of a Change in Control; or

(iv) relocation of the Participant's principal place of employment that results in an increase in the Participant's one-way driving distance by more than 50 miles from the Participant's then current principal residence.

In order to resign for Good Reason, the Participant must provide written notice of the event giving rise to Good Reason to the Company within 90 days after the condition arises, allow the Company at least 30 days to cure such condition, and if the Company fails to cure the condition within such period, then Participant's resignation from all positions the Participant then holds with the Company must be effective not later than 90 days after the end of the Company's cure period.

(u) "***Incentive Stock Option***" means an option granted pursuant to Section 5 of the Plan that is intended to be, and that qualifies as, an "incentive stock option" within the meaning of Section 422 of the Code.

(v) "***Nonstatutory Stock Option***" means an option granted pursuant to Section 5 of the Plan that does not qualify as an Incentive Stock Option.

(w) "***Officer***" means the chief executive officer or the chief financial officer of the Company.

(x) "***Option***" means an Incentive Stock Option or a Nonstatutory Stock Option to purchase Ordinary Shares granted pursuant to the Plan.

(y) "***Ordinary Shares***" means the Ordinary Shares of the Company.

(z) "***Other Stock Award***" means an award based in whole or in part by reference to the Ordinary Shares which is granted pursuant to the terms and conditions of Section 6(c).

(aa) "***Participant***" means a person to whom a Stock Award is granted pursuant to the Plan or, if applicable, such other person who holds an outstanding Stock Award.

(bb) "***Plan***" means this 2015 Equity Incentive Plan.

(cc) "***Restricted Stock Award***" means an award of Ordinary Shares which is granted pursuant to the terms and conditions of Section 6(a).

(dd) "***Restricted Stock Unit Award***" means a right to receive Ordinary Shares which is granted pursuant to the terms and conditions of Section 6(b).

(ee) "***Rule 405***" means Rule 405 promulgated under the Securities Act.

(ff) "***Rule 701***" means Rule 701 promulgated under the Securities Act.

(gg) "***Securities Act***" means the U.S. Securities Act of 1933, as amended.

(hh) "***Stock Appreciation Right***" or "***SAR***" means a right to receive the appreciation on Ordinary Shares that is granted pursuant to the terms and conditions of Section 5.

(ii) "***Stock Award***" means any right to receive Ordinary Shares granted under the Plan, including an Incentive Stock Option, a Nonstatutory Stock Option, a Restricted Stock Award, a Restricted Stock Unit Award, a Stock Appreciation Right or any Other Stock Award.

(jj) "***Subsidiary***" means, with respect to the Company, (i) any corporation of which more than 50% of the outstanding capital stock having ordinary voting power to elect a majority of the board of directors of such corporation (irrespective of whether, at the time, stock of any other class or classes of such corporation will have or might have voting power by reason of the happening of any contingency) is at the time, directly or indirectly, Owned by the Company, and (ii) any partnership, limited liability company or other entity in which the Company has a direct or indirect interest (whether in the form of voting or participation in profits or capital contribution) of more than 50%, or, where the context so requires, the definition of "subsidiary" in Irish company law.

(kk) "***Ten Percent Shareholder***" means a person who Owns (or is deemed to Own pursuant to Section 424(d) of the Code) stock possessing more than 10% of the total combined voting power of all classes of stock of the Company or any Affiliate.

EXHIBIT 10.2

ITERUM THERAPEUTICS PUBLIC LIMITED COMPANY
AMENDED AND RESTATED 2018 EQUITY INCENTIVE PLAN

1. GENERAL.

(a) Relationship to Prior Plan.

(i) This Plan is intended as the successor to the Iterum Therapeutics Public Limited Company (formerly Iterum Therapeutics Limited) 2015 Equity Incentive Plan (the "Prior Plan") with respect to grants to Employees. From and after 12:01 a.m. Central time on the IPO Date, no additional awards will be granted under the Prior Plan, and any shares that would otherwise remain available for future grants under the Prior Plan as of 12:01 a.m. Central time on the IPO Date will cease to be available under the Prior Plan at such time. All Awards granted on or after 12:01 a.m. Central time on the IPO Date will be granted under this Plan. All awards granted under the Prior Plan will remain subject to the terms of the Prior Plan.

(ii) From and after 12:01 a.m. Central time on the IPO Date, any shares subject, at such time, to outstanding stock awards granted under the Prior Plan that (i) are no longer required to satisfy such awards because the awards will expire or terminate for any reason prior to exercise or settlement; (ii) are forfeited because of the failure to meet a contingency or condition required to vest such shares or otherwise return to the Company; or (iii) subject to compliance with Irish company law are reacquired, withheld (or not issued) to satisfy a tax withholding obligation in connection with an award or to satisfy the purchase price or exercise price of a stock award (such shares the "Returning Shares") will immediately be added to the Share Reserve (as further described in Section 3(a) below) as and when such shares become Returning Shares, up to the maximum number set forth in Section 3(a) below.

(b) Eligible Award Recipients. The persons eligible to receive Awards are Employees.

(c) Available Awards. The Plan provides for the grant of the following Awards: (i) Incentive Stock Options, (ii) Nonstatutory Stock Options, (iii) Stock Appreciation Rights (iv) Restricted Stock Awards, (v) Restricted Stock Unit Awards, (vi) Performance Stock Awards, (vii) Performance Cash Awards, and (viii) Other Stock Awards.

(d) Purpose. The Plan, through the grant of Awards, is intended to help the Company secure and retain the services of eligible award recipients, provide incentives for such persons to exert maximum efforts for the success of the Company and any Affiliate and provide a means by which the eligible recipients may benefit from increases in value of the Ordinary Shares.

(e) Definitions. All capitalized terms in this document are defined in Section 13 below.

2. ADMINISTRATION.

(a) Administration by the Board. The Board will administer the Plan. The Board may delegate administration of the Plan to a Committee or Committees, as provided in Section 2(c). In addition, the Board or a Committee may appoint a Stock Plan Administrator with the authority to administer the day to day operations of the Plan, and to make decisions with respect to the Plan and Awards.

(b) Powers of the Board. The Board will have the power, subject to, and within the limitations of, the express provisions of the Plan:

(i) To determine from time to time (A) which of the persons eligible under the Plan will be granted Awards; (B) when and how each Award will be granted; (C) what type or combination of types of Award will be granted; (D) the provisions of each Award granted (which need not be identical), including the time or times when a person will be permitted to exercise or otherwise receive cash or Ordinary Shares under the Stock Award; (E) the number of Ordinary Shares with respect to which a Stock Award shall be granted to each such person; and (F) the Fair Market Value applicable to a Stock Award.

(ii) To construe and interpret the Plan and Awards granted under it, to establish, amend and revoke rules and regulations for its administration, and to settle all controversies regarding the Plan and Awards granted under it. The Board, in the exercise of this power, may correct any defect, omission or inconsistency in the Plan or in any Award Agreement or in the written terms of a Performance Cash Award, in a manner and to the extent it will deem necessary or expedient to make the Plan or Award fully effective.

(iii) To prohibit (or delegate to the Stock Plan Administrator the authority to prohibit) the exercise of any Option, SAR or other exercisable Award during a period of up to thirty days prior to the consummation of any pending share dividend, share split, combination or exchange of shares, merger, consolidation or other distribution (other than normal cash dividends) of Company assets to shareholders, or any other change affecting the Ordinary Shares or the share price of the Ordinary Shares, including any Corporate Transaction, for reasons of administrative convenience.

(iv) To accelerate the time at which an Award may be exercised or the time during which an Award or any part thereof will vest.

(v) To approve forms of Award Agreements for use under the Plan and to amend the terms of any one or more Awards, subject to any specified limits in the Plan that are not subject to Board discretion; provided however, that a Participant's rights under any Award will not be materially impaired by any such amendment unless (A) the Company requests the consent of the affected Participant, and (B) such Participant consents in writing. Notwithstanding the foregoing, and subject to the limitations of applicable law, if any, the Board may amend the terms of any one or more Awards without the affected Participant's consent (w) to maintain the qualified status of the Award as an Incentive Stock Option under Section 422 of the Code; (x) to change the terms of an Incentive Stock Option, if such change results in impairment of the Stock Award solely because it impairs the qualified status of the Stock Award as an Incentive Stock Option under Section 422 of the Code; (y) to clarify the manner of exemption from, or to bring the Award into compliance with, Section 409A of the Code; or (z) to comply with other applicable laws.

(vi) To amend, suspend or terminate the Plan as provided by Section 10.

(vii) To effect, with the consent of any adversely affected Participant, (A) the alteration of the exercise, purchase or strike price of any outstanding Stock Award (unless this is in the context of a Capitalization Adjustment in which case Participant consent is not required); (B) the cancellation of any outstanding Stock Award and the grant in substitution therefor of a new (1) Option or SAR, (2) Restricted Stock Award, (3) Restricted Stock Unit Award, (4) Other Stock Award, (5) cash and/or (6) other valuable consideration determined by the Board, in its sole discretion, with any such substituted award (x) covering the same or a different number of Ordinary Shares as the cancelled Stock Award and (y) granted under the Plan or another equity or compensatory plan of the Company; or (C) any other action that is treated as a repricing under generally accepted accounting principles or applicable stock exchange rules. For the avoidance of doubt, shareholder approval will not be required to give effect to any action approved by the Board pursuant to this Section 2(b)(vii).

(viii) Generally, to exercise such powers and to perform such acts as the Board deems necessary or expedient to promote the best interests of the Company and any Affiliates and that are not in conflict with the provisions of the Plan or Awards.

(c) Delegation to Committee. The Board may delegate some or all of the administration of the Plan to a Committee or Committees. If administration of the Plan is delegated to a Committee, the Committee will have, in connection with the administration of the Plan, the powers theretofore possessed by the Board that have been delegated to the Committee, including the power to delegate to a subcommittee of the Committee any of the administrative powers the Committee is authorized to exercise (and references in this Plan to the Board will thereafter be to the Committee or subcommittee, as applicable). Any delegation of administrative powers will be reflected in resolutions, not inconsistent with the provisions of the Plan, adopted from time to time by the Board or Committee (as applicable). The Board may retain the authority to concurrently administer the Plan with the Committee and may, at any time, revest in the Board some or all of the powers previously delegated. The Committee may consist solely of two or more Non-Employee Directors, in accordance with Rule 16b-3.

(d) Delegation to an Officer. Subject to compliance with Irish law, the Board may delegate to one or more Officers the authority to do one or both of the following: (i) designate Employees who are providing Continuous Service to the Company or any of its Subsidiaries who are not Officers to be recipients of Stock Awards and the terms thereof, and (ii) determine the number of Ordinary Shares to be subject to such Stock Awards granted to such Employees; provided, however, that the Board resolutions regarding such delegation shall specify the total number of Ordinary Shares that may be subject to the Stock Awards granted by such Officer and that such Officer may not grant a Stock Award to himself or herself. Notwithstanding the foregoing, the Board may not delegate authority to an Officer to determine the Fair Market Value of the Ordinary Shares.

(e) Effect of Board's Decision. All determinations, interpretations and constructions made by the Board in good faith will not be subject to review by any person and will be final, binding and conclusive on all persons.

3. SHARES SUBJECT TO THE PLAN.

(a) Share Reserve.

(i) Subject to the provisions of this Section 3(a), and Section 9(a) relating to Capitalization Adjustments, the aggregate number of Ordinary Shares reserved for issuance pursuant to Stock Awards is 295,819 shares (the "Share Reserve"), which number shall include (i) any shares remaining for issuance pursuant to the Prior Plan as of the IPO Date and (ii) any Returning Shares. For clarity, the limit in this Section 3(a) is a limit on the number of Ordinary Shares that may be issued pursuant to the Plan. Accordingly, this Section 3(a) does not limit the granting of Stock Awards except as provided in Section 7(a).

(ii) In addition, subject to compliance with Irish law shares may be issued in connection with a merger or acquisition as permitted by, as applicable, NASDAQ Marketplace Rule 4350(i)(1)(A)(iii), NYSE Listed Company Manual Section 303A.08, AMEX Company Guide Section 711 or other applicable stock exchange rules, and such issuance shall not reduce the number of Ordinary Shares available for issuance under the Plan.

(b) Reversion of Shares to the Share Reserve. If subject to compliance with Irish law (i) any Ordinary Shares issued pursuant to a Stock Award are forfeited back to or repurchased by the Company or any Affiliate because of the failure to meet a contingency or condition required for the vesting of such Ordinary Shares, or (ii) any Ordinary Shares are cancelled in accordance with the cancellation and regrant provisions of Section 2(b)(vii), then the Ordinary Shares that are forfeited,

repurchased or canceled shall revert to and again become available for issuance under the Plan. If any Ordinary Shares subject to a Stock Award are not delivered to a Participant because such Ordinary Shares are withheld for the payment of taxes pursuant to Section 8(g) or a Stock Award is exercised through a reduction of Ordinary Shares subject to the Stock Award (i.e., "net exercised") or an appreciation distribution in respect of a Stock Appreciation Right is paid in Ordinary Shares, the number of Ordinary Shares subject to the Stock Award that are not delivered to the Participant shall remain available for subsequent issuance under the Plan. If the exercise price of any Stock Award is satisfied by tendering Ordinary Shares held by the Participant (either by actual delivery or attestation), then the number of Ordinary Shares so tendered shall remain available for issuance under the Plan.

(c) Incentive Stock Option Limit. Subject to the limit in Section 3(a), and Section 9(a) relating to Capitalization Adjustments, the aggregate maximum number of Ordinary Shares that may be issued pursuant to the exercise of Incentive Stock Options will be a number of Ordinary Shares equal to the number of Shares available for issuance under the Plan.

(d) Source of Shares. The Ordinary Shares issuable under the Plan shall be authorized but unissued or reacquired Ordinary Shares, including Ordinary Shares redeemed or repurchased by the Company or any Affiliate on the open market or otherwise, in accordance with applicable Irish law. For the avoidance of doubt, Ordinary Shares purchased by the Company in the open market or otherwise will not increase the number of Ordinary Shares available for issuance under the Plan.

4. ELIGIBILITY.

(a) Eligibility for Specific Stock Awards. Incentive Stock Options may be granted only to employees of the Company or a "parent corporation" or "subsidiary corporation" thereof (as such terms are defined in Sections 424(e) and 424(f) of the Code). Stock Awards other than Incentive Stock Options may be granted to any Employee.

(b) Ten Percent Shareholders. A Ten Percent Shareholder will not be granted an Incentive Stock Option unless the exercise price of such Option is at least 110% of the Fair Market Value on the date of grant and the Option is not exercisable after the expiration of five (5) years from the date of grant.

5. PROVISIONS RELATING TO OPTIONS AND STOCK APPRECIATION RIGHTS.

Each Option or SAR will be in such form and will contain such terms and conditions as the Board deems appropriate. All Options will be separately designated Incentive Stock Options or Nonstatutory Stock Options at the time of grant, and, if certificates are issued, a separate certificate or certificates will be issued for Ordinary Shares purchased on exercise of each type of Option. If an Option is not specifically designated as an Incentive Stock Option, or if an Option is designated as an Incentive Stock Option but some portion or all of the Option fails to qualify as an Incentive Stock Option under the applicable rules, then the Option (or portion thereof) will be a Nonstatutory Stock Option. The provisions of separate Options or SARs need not be identical; provided, however, that each Award Agreement will conform to (through incorporation of provisions hereof by reference in the applicable Award Agreement or otherwise) the substance of each of the following provisions:

(a) Term. Subject to the provisions of Section 4(b) regarding Ten Percent Shareholders, no Option or SAR will be exercisable after the expiration of 10 years from the date of its grant or such shorter period specified in the Award Agreement.

(b) Exercise Price. Subject to the provisions of Section 4(b) regarding Ten Percent Shareholders, the exercise or strike price of each Award will be not less than the greater of (i) the nominal value of an Ordinary Share or (ii) 100% of the Fair Market Value of the Ordinary Shares subject to the Option or SAR on the date the Stock Award is granted. Notwithstanding the foregoing, an Option or SAR may be granted with an exercise or strike price lower than 100% of the Fair Market Value of the Ordinary

Shares subject to the Award if such Award is granted pursuant to an assumption of or substitution for another option or stock appreciation right pursuant to a Corporate Transaction and in a manner consistent with the provisions of Section 409A of the Code and, if applicable, Section 424(a) of the Code, provided that in all cases it will not be less than the nominal value of an Ordinary Share. Each SAR will be denominated in Ordinary Share equivalents.

(c) Exercise and Purchase Price for Options. To exercise any outstanding Option, the Participant must provide written notice of exercise to the Company in the manner determined by the Stock Plan Administrator. The purchase price of Ordinary Shares acquired pursuant to the exercise of an Option may be paid, to the extent permitted by applicable law and as determined by the Board in its sole discretion, by any combination of the methods of payment set forth below. The Board will have the authority to grant Options that do not permit all of the following methods of payment (or otherwise restrict the ability to use certain methods) and to grant Options that require the consent of the Company to use a particular method of payment. In all cases the Company shall require that the nominal value of each newly issued Ordinary Share is fully paid up. The permitted methods of payment are as follows:

(i) by cash, check, bank draft or money order payable to the Company;

(ii) pursuant to a program developed under Regulation T as promulgated by the U.S. Federal Reserve Board that, prior to the issuance of Ordinary Shares subject to the Option, results in either the receipt of cash (or check) by the Company or the receipt of irrevocable instructions to pay the aggregate exercise price to the Company from the sales proceeds;

(iii) by delivery to the Company (either by actual delivery or attestation) of Ordinary Shares;

(iv) if the option is a Nonstatutory Stock Option, by a "net exercise" arrangement pursuant to which the Company will reduce the number of Ordinary Shares issuable upon exercise by the largest whole number of Ordinary Shares with a Fair Market Value that does not exceed the aggregate exercise price; provided, however, that:

(1) the Company will accept a cash or other payment from the Participant to the extent of any remaining balance of the aggregate exercise price not satisfied by such reduction in the number of whole Ordinary Shares to be issued;

(2) irrespective of whether a "net exercise" arrangement is used, the nominal value of each newly issued Ordinary Shares will be fully paid up in cash; and

(3) Ordinary Shares will no longer be subject to an Option and will not be exercisable thereafter to the extent that (A) Ordinary Shares issuable upon exercise are used to pay the exercise price pursuant to the "net exercise," (B) Ordinary Shares are delivered to the Participant as a result of such exercise, and (C) Ordinary Shares are withheld to satisfy tax withholding obligations;

(v) deduction from salary due and payable to an Employee by the Company or any Affiliate; or

(vi) in any other form of legal consideration that may be acceptable to the Board or the Stock Plan Administrator and permissible under applicable law.

(d) Exercise and Payment of a SAR. To exercise any outstanding SAR, the Participant must provide written notice of exercise to the Company in compliance with the provisions of the Award Agreement evidencing such SAR. The appreciation distribution payable on the exercise of a SAR will be not greater than an amount equal to the excess of (A) the aggregate Fair Market Value (on the date of the exercise of the SAR) of a number of Ordinary Shares equal to the number of Ordinary Shares

equivalents in which the Participant is vested under such SAR, and with respect to which the Participant is exercising the SAR on such date, over (B) the aggregate strike price of the number of Ordinary Shares equivalents with respect to which the Participant is exercising the SAR on such date . The appreciation distribution may be paid in Ordinary Shares, in cash, in any combination of the two or in any other form of consideration, as determined by the Board and contained in the Award Agreement evidencing such SAR. Where the SAR is settled using newly issued Ordinary Shares the Company shall require that the nominal value of each newly issued Ordinary Share is fully paid up.

(e) Transferability of Options and SARs. The Board may, in its sole discretion, impose such limitations on the transferability of Options and SARs as the Board will determine. In the absence of such a determination by the Board to the contrary, the following restrictions on the transferability of Options and SARs will apply:

(i) Restrictions on Transfer. An Option or SAR will not be transferable except by will or by the laws of descent and distribution (or pursuant to subsections (ii) and (iii) below), and will be exercisable during the lifetime of the Participant only by the Participant; provided, however, that the Board or the Stock Plan Administrator may, in its sole discretion, permit transfer of the Option or SAR in a manner that is not prohibited by applicable tax and securities laws upon the Participant's request. Except as explicitly provided in the Plan, neither an Option nor a SAR may be transferred for consideration.

(ii) Domestic Relations Orders. Subject to the approval of the Board or the Stock Plan Administrator, an Option or SAR may be transferred pursuant to the terms of a domestic relations order, official marital settlement agreement or other divorce or separation instrument which contains the information required by the Company to effect the transfer. If an Option is an Incentive Stock Option, such Option may be deemed to be a Nonstatutory Stock Option as a result of such transfer.

(iii) Beneficiary Designation. Subject to the approval of the Board or the Stock Plan Administrator, a Participant may, by delivering written notice to the Company, in a form provided by or otherwise satisfactory to the Stock Plan Administrator and any broker designated by the Company to effect Option exercises, designate a third party who, in the event of the death of the Participant, will thereafter be entitled to exercise the Option or SAR and receive the Ordinary Shares or other consideration resulting from such exercise. In the absence of such a designation, upon the death of the Participant, the executor or administrator of the Participant's estate will be entitled to exercise the Option or SAR and receive the Ordinary Shares or other consideration resulting from such exercise in accordance with the Participants will or the laws of intestacy as applicable. However, the Company may prohibit designation of a beneficiary at any time, including due to any conclusion by the Company that such designation would be inconsistent with the provisions of applicable laws whether in the United States or any other jurisdiction in which a Participant resides.

(f) Vesting Generally. The total number of Ordinary Shares subject to an Option or SAR may vest and therefore become exercisable in periodic installments that may or may not be equal. The Option or SAR may be subject to such other terms and conditions on the time or times when it may or may not be exercised (which may be based on the satisfaction of Performance Goals or other criteria) as the Board may deem appropriate. The vesting provisions of individual Options or SARs may vary. The provisions of this Section 5(f) are subject to any Option or SAR provisions governing the minimum number of Ordinary Shares as to which an Option or SAR may be exercised.

(g) Termination of Continuous Service. If a Participant's Continuous Service terminates, the Participant may exercise his or her Option or SAR (to the extent that the Participant was entitled to exercise the vested portion of such Award as of the date of termination of Continuous Service) but only within such period of time following the termination of the Participant's Continuous Service as set forth in the Award Agreement. Unless otherwise provided in the Award Agreement, the Option or SAR will be exercisable for a period of three (3) months following a termination of a Participant's

Continuous Service by the Company without Cause or by the Participant for any reason; provided, however that such post-termination exercise period will instead be for the twelve (12) month period following a termination due to the Participant's Disability or death. Additionally, if the Participant's death occurs within the applicable post-termination of Continuous Service period during which the Option was exercisable, the Option will be exercisable for a twelve (12) month period following the Participant's death. If, after termination of Continuous Service, the Participant does not exercise his or her Option or SAR prior to the applicable deadline the Option or SAR will terminate.

(h) Automatic Extension of Termination Date. If the exercise of an Option or SAR following the termination of the Participant's Continuous Service (other than for Cause and other than upon the Participant's death or Disability) would be prohibited at any time solely because the issuance of Ordinary Shares would violate the registration requirements under the Securities Act, then the Option or SAR will terminate on the earlier of (i) the expiration of a total period of time (that need not be consecutive) equal to the applicable post-termination exercise period after the termination of the Participant's Continuous Service during which the exercise of the Option or SAR would not be in violation of such registration requirements, and (ii) the expiration of the term of the Option or SAR as set forth in the applicable Award Agreement. In addition, unless otherwise provided in a Participant's Award Agreement, if the sale of any Ordinary Shares received upon exercise of an Option or SAR following the termination of the Participant's Continuous Service (other than for Cause) would violate the Company's insider trading policy, then the Option or SAR will terminate on the earlier of (i) the expiration of the period of time (that need not be consecutive) equal to the applicable post-termination exercise period after the termination of the Participant's Continuous Service during which the sale of the Ordinary Shares received upon exercise of the Option or SAR would not be in violation of the Company's insider trading policy, and (ii) the expiration of the term of the Option or SAR as set forth in the applicable Award Agreement.

(i) Termination for Cause. Except as explicitly provided otherwise in a Participant's Award Agreement or other individual written agreement between the Company or any Affiliate and the Participant, if a Participant's Continuous Service is terminated for Cause, the Option or SAR will terminate immediately upon such Participant's termination of Continuous Service, and the Participant will be prohibited from exercising his or her Option or SAR from and after the date of such termination of Continuous Service.

(j) Non-Exempt Employees under U.S. Law. If an Option or SAR is granted to an Employee who is a non-exempt employee for purposes of the U.S. Fair Labor Standards Act of 1938, as amended, the Option or SAR will not be first exercisable for any Ordinary Shares until at least six months following the date of grant of the Option or SAR (although the Award may vest prior to such date). Consistent with the provisions of the U.S. Worker Economic Opportunity Act, (i) if such non-exempt Employee dies or suffers a Disability, (ii) upon a Corporate Transaction in which such Option or SAR is not assumed, continued, or substituted, (iii) upon a Change in Control, or (iv) upon the Participant's retirement (as such term may be defined in the Participant's Award Agreement in another agreement between the Participant and the Company, or, if no such definition, in accordance with the Company's then current employment policies and guidelines), the vested portion of any Options and SARs may be exercised earlier than six months following the date of grant. The foregoing provision is intended to operate so that any income derived by a non-exempt employee in connection with the exercise or vesting of an Option or SAR will be exempt from his or her regular rate of pay. To the extent permitted and/or required for compliance with the U.S. Worker Economic Opportunity Act to ensure that any income derived by a non-exempt employee in connection with the exercise, vesting or issuance of any shares under any other Stock Award will be exempt from the employee's regular rate of pay, the provisions of this Section 5(j) will apply to all Stock Awards and are hereby incorporated by reference into such Award Agreements.

(k) Incentive Stock Option Limitations. To the extent that the aggregate Fair Market Value (determined at the time of grant) of an Ordinary Share with respect to which Incentive Stock Options

are exercisable for the first time by any Participant during any calendar year (under all plans of the Company and any Affiliates) exceeds U.S. $100,000 (or such other limit established in the Code) or otherwise does not comply with the rules governing Incentive Stock Options, the Options or portions thereof that exceed such limit (according to the order in which they were granted) or otherwise do not comply with such rules will be treated as Nonstatutory Stock Options, notwithstanding any contrary provision of an applicable Award Agreement.

(l) Whole Shares. Options and SARs may be exercised only with respect to whole shares.

(m) No Reload Options. No Option or SAR granted under the Plan shall contain any provision entitling the Participant to the automatic grant of additional Options or SARs in connection with any exercise of the original award.

(n) No Dividend Equivalents. No Option or SAR shall provide for the payment or accrual of dividend equivalents.

6. PROVISIONS OF STOCK AWARDS OTHER THAN OPTIONS AND SARS.

(a) Restricted Stock Awards. Each Restricted Stock Award will be in such form and will contain such terms and conditions as the Board will deem appropriate. To the extent consistent with the Company's Constitution, at the Board's election, Ordinary Shares underlying a Restricted Stock Award may be (i) held in book entry form subject to the Company's instructions until any restrictions relating to the Restricted Stock Award lapse; or (ii) evidenced by a certificate, which certificate will be held in such form and manner as determined by the Board. The terms and conditions of Restricted Stock Awards may change from time to time, and the terms and conditions of separate Restricted Stock Awards need not be identical; provided, however, that each Award Agreement will conform to (through incorporation of the provisions hereof by reference in the agreement or otherwise) the substance of each of the following provisions:

(i) Consideration. A Restricted Stock Award may be awarded in consideration for (A) cash, check, bank draft or money order payable to the Company, (B) past services to the Company or an Affiliate, or (C) any other form of legal consideration (including future services) that may be acceptable to the Board, in its sole discretion, and permissible under applicable law. In all cases the Company shall require that the nominal value of each newly issued Ordinary Share issued in satisfaction of a Restricted Stock Award is fully paid up.

(ii) Vesting. Ordinary Shares awarded under a Restricted Stock Award may be subject to forfeiture to the Company in accordance with a vesting schedule to be determined by the Board and subject to compliance with Irish law.

(iii) Termination of Participant's Continuous Service. If a Participant's Continuous Service terminates, the Company may receive through a forfeiture condition or a repurchase right subject to compliance with Irish law, any or all of the Ordinary Shares held by the Participant that have not vested as of the date of termination of Continuous Service under the terms of the Award Agreement.

(iv) Transferability. Rights to acquire Ordinary Shares under the Restricted Stock Award will be transferable by the Participant only upon such terms and conditions as are set forth in the Award Agreement, as the Board will determine in its sole discretion, so long as Ordinary Shares awarded under the Restricted Stock Award remain subject to the terms of the Award Agreement.

(v) Dividends. An Award Agreement will provide that any dividends paid on Restricted Stock will be subject to the same vesting and forfeiture restrictions as apply to the shares subject to the Restricted Stock Award to which they relate.

(b) Restricted Stock Unit Awards. Each Restricted Stock Unit Award will be in such form and will contain such terms and conditions as the Board will deem appropriate. The terms and conditions of Restricted Stock Unit Awards may change from time to time, and the terms and conditions of separate Restricted Stock Unit Awards need not be identical; provided that each Restricted Stock Unit Award Agreement will conform to (through incorporation of the provisions hereof by reference in the Agreement or otherwise) the substance of each of the following provisions:

(i) Consideration. At the time of grant of a Restricted Stock Unit Award, the Board will determine the consideration, if any, to be paid by the Participant upon delivery of each share of Ordinary Shares subject to the Restricted Stock Unit Award. The consideration to be paid (if any) by the Participant for each share of Ordinary Shares subject to a Restricted Stock Unit Award may be paid in any form of legal consideration that may be acceptable to the Board, in its sole discretion, and permissible under applicable law.

(ii) Vesting. At the time of the grant of a Restricted Stock Unit Award, the Board may impose such restrictions on or conditions to the vesting of the Restricted Stock Unit Award as it, in its sole discretion, deems appropriate.

(iii) Payment. A Restricted Stock Unit Award may be settled by the delivery of Ordinary Shares, their cash equivalent, any combination thereof or in any other form of consideration, as determined by the Board and contained in the Restricted Stock Unit Award Agreement. In all cases the Company shall require that the nominal value of each newly issued Ordinary Share issued in satisfaction of a Restricted Stock Unit Award is fully paid up.

(iv) Additional Restrictions. At the time of the grant of a Restricted Stock Unit Award, the Board, as it deems appropriate, may impose such restrictions or conditions that delay the delivery of the Ordinary Shares (or their cash equivalent) subject to a Restricted Stock Unit Award to a time after the vesting of such Restricted Stock Unit Award.

(v) Dividend Equivalents. Dividend equivalents may be credited in respect of Ordinary Shares covered by a Restricted Stock Unit Award, as determined by the Board and contained in the Restricted Stock Unit Award Agreement. At the sole discretion of the Board, such dividend equivalents may be converted into additional Ordinary Shares covered by the Restricted Stock Unit Award in such manner as determined by the Board. Any such dividend equivalents will be subject to all of the same terms and conditions, including vesting and forfeiture provisions, of the underlying Award Agreement to which they relate.

(vi) Termination of Participant's Continuous Service. Except as otherwise provided in the applicable Award Agreement, such portion of the Restricted Stock Unit Award that has not vested will be forfeited upon the Participant's termination of Continuous Service.

(c) Performance Awards.

(i) Performance Stock Awards. A Performance Stock Award is a Stock Award that may vest or may be exercised contingent upon the attainment during a Performance Period of certain Performance Goals. A Performance Stock Award may, but need not, require the completion of a specified period of Continuous Service. The length of any Performance Period, the Performance Goals to be achieved during the Performance Period, and the measure of whether and to what degree such Performance Goals have been attained shall be conclusively determined by the Committee, in its sole discretion. The Board may provide for or, subject to such terms and conditions as the Board may specify, may permit a Participant to elect for, the payment of any Performance Stock Award to be deferred to a specified date or event. In addition, to the extent permitted by applicable law and the

applicable Award Agreement, the Board may determine that cash may be used in payment of Performance Stock Awards.

(ii) Performance Cash Awards. A Performance Cash Award is a cash award that may be paid contingent upon the attainment during a Performance Period of certain Performance Goals. A Performance Cash Award may also require the completion of a specified period of Continuous Service. At the time of grant of a Performance Cash Award, the length of any Performance Period, the Performance Goals to be achieved during the Performance Period, and the measure of whether and to what degree such Performance Goals have been attained shall be conclusively determined by the Committee, in its sole discretion. The Committee may specify the form of payment of Performance Cash Awards, which may be cash or other property, or may provide for a Participant to have the option for his or her Performance Cash Award, or such portion thereof as the Board may specify, to be paid in whole or in part in cash or other property.

(iii) Board Discretion. The Board retains the discretion to amend the compensation or economic benefit due upon attainment of Performance Goals and to define the manner of calculating the Performance Criteria it selects to use for a Performance Period; provided that any Dividend equivalents with respect to Performance Stock Awards or Performance Cash Awards shall be subject to the same terms and conditions, including vesting and forfeiture provisions, of the underlying Award Agreement to which they relate.

(d) Other Stock Awards. Other forms of Stock Awards valued in whole or in part by reference to, or otherwise based on, Ordinary Shares, including the appreciation in value thereof (e.g., options or share rights with an exercise price or strike price less than 100% of the Fair Market Value of the Ordinary Shares at the time of grant) may be granted either alone or in addition to Stock Awards provided for under Section 5 and the preceding provisions of this Section 6. Subject to the provisions of the Plan, the Board will have sole and complete authority to determine the persons to whom and the time or times at which such Other Stock Awards will be granted, the number of Ordinary Shares (or the cash equivalent thereof) to be granted pursuant to such Other Stock Awards and all other terms and conditions of such Other Stock Awards; *provided*, *however*, that where Ordinary Shares are issued pursuant to any Other Stock Award, the nominal value of each newly issued Ordinary Share is fully paid up; *and, provided, further, however, that* provided that any Dividend equivalents with respect to such other Stock Awards or shall be subject to the same terms and conditions of the underlying Award Agreement to which they relate.

7. COVENANTS OF THE COMPANY.

(a) Availability of Shares. During the terms of the Stock Awards, the Company shall keep available at all times the authorized but unissued Ordinary Shares reasonably required to satisfy such Stock Awards.

(b) Securities Law Compliance. The Company will seek to obtain from each regulatory commission or agency having jurisdiction over the Plan such authority as may be required to grant Stock Awards and to issue and sell Ordinary Shares upon exercise of the Stock Awards; provided, however, that this undertaking will not require the Company to register under the Securities Act, the Plan, any Stock Award or any Ordinary Shares issued or issuable pursuant to any such Stock Award. If, after reasonable efforts and at a reasonable cost, the Company is unable to obtain from any such regulatory commission or agency the authority that counsel for the Company deems necessary for the lawful issuance and sale of Ordinary Shares under the Plan, the Company will be relieved from any liability for failure to issue and sell Ordinary Shares upon exercise of such Stock Awards unless and until such authority is obtained. A Participant will not be eligible for the grant of a Stock Award or the subsequent issuance of cash or Ordinary Shares pursuant to the Stock Award if such grant or issuance would be in violation of any applicable securities law.

(c) No Obligation to Notify or Minimize Taxes. The Company and its Affiliates shall have no duty or obligation to any Participant to advise such holder as to the time or manner of exercising such Stock Award. Furthermore, the Company and its Affiliates shall have no duty or obligation to warn or otherwise advise such holder of a pending termination or expiration of a Stock Award or a possible period in which the Stock Award may not be exercised. The Company and its Affiliates have no duty or obligation to minimize the tax consequences of a Stock Award to the holder of such Stock Award.

8. GENERAL TERMS OF AWARDS.

(a) Use of Proceeds from Sales of Ordinary Shares. Proceeds from the sale of Ordinary Shares pursuant to Stock Awards will constitute general funds of the Company.

(b) Corporate Action Constituting Grant of Stock Awards. Corporate action constituting a grant by the Company of a Stock Award to any Participant will be deemed completed as of the date of such corporate action, unless otherwise determined by the Board, regardless of when the instrument, certificate, or letter evidencing the Stock Award is communicated to, or actually received or accepted by, the Participant. In the event that the corporate records (e.g., Board consents, resolutions or minutes) documenting the corporate action constituting the grant contain terms (e.g., exercise price, vesting schedule or number of shares) that are inconsistent with those in the Award Agreement or related grant documents as a result of a clerical error in the papering of the Award Agreement or related grant documents, the corporate records will control and the Participant will have no legally binding right to the incorrect term in the Award Agreement or related grant documents.

(c) Shareholder Rights. No Participant will be deemed to be the holder of, or to have any of the rights of a holder with respect to, any Ordinary Shares subject to a Stock Award unless and until (i) such Participant has satisfied all requirements for exercise of, or the issuance of Ordinary Shares under, the Stock Award pursuant to its terms, and (ii) the issuance of the Ordinary Shares subject to the Stock Award has been entered into the books and records of the Company.

(d) No Employment or Other Service Rights. Nothing in the Plan, any Award Agreement or any other instrument executed thereunder or in connection with any Award granted pursuant thereto will confer upon any Participant any right to continue to serve the Company or an Affiliate in the capacity in effect at the time the Award was granted or will affect any right that the Company or an Affiliate may have to terminate (i) the employment of an Employee with or without notice and with or without cause, subject to the employment laws of the country in which the Employee is employed, subject to any applicable provisions of the corporate law of the country or state in which the Company or the Affiliate is incorporated, as the case may be.

(e) Change in Time Commitment. In the event a Participant's regular level of time commitment in the performance of his or her services for the Company and any Affiliates is reduced (for example, and without limitation, if the Participant is an Employee of the Company and the Employee has a change in status from a full-time Employee to a part-time Employee or takes an extended leave of absence) after the date of grant of any Award to the Participant, the Board has the right in its sole discretion to (x) make a corresponding reduction in the number of shares subject to any portion of such Award that is scheduled to vest or become payable after the date of such change in time commitment, and (y) in lieu of or in combination with such a reduction, extend the vesting or payment schedule applicable to such Award. In the event of any such reduction, the Participant will have no right with respect to any portion of the Award that is so reduced or extended.

(f) Investment Assurances. The Company may require a Participant, as a condition of exercising or acquiring Ordinary Shares under any Stock Award, (i) to give written assurances satisfactory to the Company as to the Participant's knowledge and experience in financial and business matters and/or to employ a purchaser representative reasonably satisfactory to the Company who is knowledgeable and experienced in financial and business matters and that the Participant is capable of evaluating, alone

or together with the purchaser representative, the merits and risks of exercising the Stock Award; and (ii) to give written assurances satisfactory to the Company stating that the Participant is acquiring Ordinary Shares subject to the Stock Award for the Participant's own account and not with any present intention of selling or otherwise distributing the Ordinary Shares. The foregoing requirements, and any assurances given pursuant to such requirements, will be inoperative if (A) the issuance of the shares upon the exercise or acquisition of Ordinary Shares under the Stock Award has been registered under a then currently effective registration statement under the Securities Act, or (B) as to any particular requirement, a determination is made by counsel for the Company that such requirement need not be met in the circumstances under the then applicable securities laws. The Company may, upon advice of counsel to the Company, place legends on share certificates issued under the Plan as such counsel deems necessary or appropriate in order to comply with applicable securities laws, including, but not limited to, legends restricting the transfer of the Ordinary Shares.

(g) Withholding Obligations. Unless prohibited by the terms of an Award Agreement, the Company or any Affiliate may, in its sole discretion, but subject always to applicable law, satisfy any federal, state, local or foreign tax withholding obligation, or levies or social security deduction obligation relating to an Award by any of the following means or by a combination of such means: (i) causing the Participant to tender a cash payment; (ii) withholding Ordinary Shares from the Ordinary Shares issued or otherwise issuable to the Participant in connection with the Award; provided, however, that no Ordinary Shares are withheld with a value exceeding the maximum amount of tax, levies and social security contribution permitted to be withheld by law or the practice of any revenue authority (or such lesser amount as may be necessary to avoid classification of the Stock Award as a liability for financial accounting purposes); (iii) withholding cash from an Award settled in cash; (iv) withholding payment from any amounts otherwise payable to the Participant; or (v) by such other method as may be set forth in the Award Agreement.

(h) Electronic Delivery. Any reference herein to a "written" agreement or document will include any agreement or document delivered electronically, filed publicly at www.sec.gov (or any successor website thereto) or posted on the Company's intranet (or other shared electronic medium controlled by the Company to which the Participant has access).

(i) Deferrals. To the extent permitted by applicable law, the Board, in its sole discretion, may determine that the delivery of Ordinary Shares or the payment of cash, upon the exercise, vesting or settlement of all or a portion of any Award may be deferred and may establish programs and procedures for deferral elections to be made by Participants. Deferrals by Participants will be made in accordance with Section 409A of the Code. Consistent with Section 409A of the Code, the Board may provide for distributions while a Participant is still an employee or otherwise providing services to the Company or an Affiliate. The Board is authorized to make deferrals of Awards and determine when, and in what annual percentages, Participants may receive payments, including lump sum payments, following the Participant's termination of Continuous Service, and implement such other terms and conditions consistent with the provisions of the Plan and in accordance with applicable law.

(j) Compliance with Section 409A of the Code. To the extent that the Board determines that any Award granted hereunder is subject to Section 409A of the Code, the Award Agreement evidencing such Award shall incorporate the terms and conditions necessary to avoid the consequences specified in Section 409A(a)(1) of the Code. To the extent applicable, the Plan and Award Agreements shall be interpreted in accordance with Section 409A of the Code. If required for compliance with Section 409A of the Code, in no event will a Corporate Transaction or a Change in Control, as applicable, be deemed to have occurred if such transaction is not also a "change in the ownership or effective control of" the Company or "a change in the ownership of a substantial portion of the assets of" the Company as determined under Treasury Regulation Section 1.409A-3(i)(5) (without regard to any alternative definition thereunder). Notwithstanding anything to the contrary in the Plan (and unless the Award Agreement specifically provides otherwise), if the Ordinary Shares are publicly traded, and if a Participant holding an Award that constitutes "deferred compensation" under Section 409A of the

Code is a "specified employee" for purposes of Section 409A of the Code, no distribution or payment of any amount that is due because of a "separation from service" (as defined in Section 409A of the Code without regard to alternative definitions thereunder) will be issued or paid before the date that is six months following the date of such Participant's "separation from service" (as defined in Section 409A of the Code without regard to alternative definitions thereunder) or, if earlier, the date of the Participant's death, unless such distribution or payment can be made in a manner that complies with Section 409A of the Code, and any amounts so deferred will be paid in a lump sum on the day after such six month period elapses, with the balance paid thereafter on the original schedule.

(k) Clawback/Recovery. All Awards granted under the Plan will be subject to recoupment in accordance with any clawback policy that the Company is required to adopt pursuant to the listing standards of any national securities exchange or association on which the Company's securities are listed or as is otherwise required by the U.S. Dodd-Frank Wall Street Reform and Consumer Protection Act or other applicable law. In addition, the Board may impose such other clawback, recovery or recoupment provisions in an Award Agreement as the Board determines necessary or appropriate, including but not limited to a reacquisition right in respect of previously acquired Ordinary Shares or other cash or property upon the occurrence of an event constituting Cause. No recovery of compensation under such a clawback policy will be an event giving rise to a right to resign for "good reason" or "constructive termination" (or similar term) under any agreement with the Company or an Affiliate.

(l) Securities Compliance. A Participant will not be issued any shares in respect of an Award unless either (i) the shares are registered under the Securities Act; or (ii) the Company has determined that such issuance would be exempt from the registration requirements of the Securities Act. Each Award also must comply with other applicable laws and regulations governing the Award, and a Participant will not receive such shares if the Company determines that such receipt would not be in material compliance with such laws and regulations.

(m) Effect on Other Benefit Plans. The value of any Award granted under the Plan, as determined upon grant, vesting or settlement, will not be included as compensation, earnings, salaries, or other similar terms used when calculating any Participant's benefits under any employee benefit plan sponsored by the Company or any Affiliate, except as such plan otherwise expressly provides. The Company expressly reserves its rights to amend, modify, or terminate any of the Company's or any Affiliate's benefit plans.

9. ADJUSTMENTS UPON CHANGES IN ORDINARY SHARES; OTHER CORPORATE EVENTS.

(a) Capitalization Adjustments. In the event of a Capitalization Adjustment, the Board will appropriately and proportionately adjust: (i) the class(es) and maximum number of securities subject to the Plan pursuant to Section 3(a), (ii) the class(es) and maximum number of securities that may be issued pursuant to the exercise of Incentive Stock Options pursuant to Section 3(c), and (iii) the class(es) and number of securities and price per share subject to outstanding Awards. The Board will make such adjustments, and its determination will be final, binding and conclusive; provided always that no adjustment may be made which reduces the price payable per Ordinary Share to an amount that is lower than the nominal value of an Ordinary Share.

(b) Dissolution. Except as otherwise provided in the Award Agreement, in the event of a dissolution or liquidation of the Company, all outstanding Stock Awards (other than Stock Awards consisting of vested and outstanding Ordinary Shares not subject to a forfeiture condition or the Company's or any Affiliate's right of repurchase) will terminate immediately prior to the completion of such dissolution or liquidation, and the Ordinary Shares subject to the Company's or any Affiliate's repurchase rights or subject to a forfeiture condition may be repurchased or reacquired by the Company or an Affiliate in accordance with Irish company law notwithstanding the fact that the holder of such Stock Award is

providing Continuous Service, provided, however, that the Board may, in its sole discretion, cause some or all Stock Awards to become fully vested, exercisable and/or no longer subject to repurchase or forfeiture (to the extent such Stock Awards have not previously expired or terminated) before the dissolution or liquidation is completed but contingent on its completion.

(c) Corporate Transaction. Notwithstanding any other provision of the Plan, the Board may take one or more of the following actions in the event of a Corporate Transaction with respect to Stock Awards, contingent upon the closing or completion of the Corporate Transaction, unless otherwise provided in the instrument evidencing the Stock Award or any other written agreement between the Company or any Affiliate and the Participant or unless otherwise expressly provided by the Board at the time of grant of a Stock Award:

(i) arrange for the surviving corporation or acquiring corporation (or the surviving or acquiring corporation's parent company) to assume or continue the Stock Award or to substitute a similar stock award for the Stock Award (including, but not limited to, an award to acquire the same consideration paid to the shareholders of the Company pursuant to the Corporate Transaction);

(ii) arrange for the assignment of any reacquisition or repurchase rights held by the Company in respect of Ordinary Shares issued pursuant to the Stock Award to the surviving corporation or acquiring corporation (or the surviving or acquiring corporation's parent company);

(iii) accelerate the vesting, in whole or in part, of the Stock Award (and, if applicable, the time at which the Stock Award may be exercised) to a date prior to the effective time of such Corporate Transaction as the Board determines (or, if the Board does not determine such a date, to the date that is five days prior to the effective date of the Corporate Transaction), with such Stock Award terminating if not exercised (if applicable) at or prior to the effective time of the Corporate Transaction; provided, however, that the Board may require Participants to complete and deliver to the Company a notice of exercise before the effective date of a Corporate Transaction, which exercise is contingent upon the effectiveness of such Corporate Transaction; provided, however, that the Board may require Participants to complete and deliver to the Company a notice of exercise before the effective date of a Corporate Transaction;

(iv) arrange for the lapse, in whole or in part, of any reacquisition or repurchase rights held by the Company with respect to the Stock Award;

(v) cancel or arrange for the cancellation of the Stock Award, to the extent not vested or not exercised prior to the effective time of the Corporate Transaction, in exchange for no consideration (U.S. $0) or such cash consideration, if any, as the Board, in its sole discretion, may consider appropriate; and

(vi) cancel or arrange for the cancellation of the Stock Award, to the extent not exercised prior to the effective time of the Corporate Transaction, in exchange for a payment, in such form as may be determined by the Board equal to the excess, if any, of (A) the per share amount (or value of property per share) payable to holders of Ordinary Shares in connection with the Corporate Transaction, over (B) the per share exercise price under the applicable Stock Award, multiplied by the number of vested shares subject to the Stock Award. For clarity, this payment may be zero (U.S. $0) if the amount per share (or value of property per share) payable to the holders of Ordinary Shares is equal to or less than the per share exercise price of the Stock Award. In addition, any escrow, holdback, earnout or similar provisions in the definitive agreement for the Corporate Transaction may apply to such payment to the holder of the Stock Award to the same extent and in the same manner as such provisions apply generally to the holders of Ordinary Shares.

The Board need not take the same action or actions with respect to all Stock Awards or portions thereof or with respect to all Participants. The Board may take different actions with respect to the vested and unvested portions of a Stock Award.

(d) Acceleration on a Qualifying Termination in Connection with a Change in Control. If during the period beginning on the date that is 30 days prior to and ending on the date that is 12 months following the consummation of a Corporate Transaction that also qualifies as a Change in Control, (i) a Participant's services to the Company (or its successor in the Change in Control) in all capacities are involuntarily terminated without Cause, or (ii) a Participant resigns service to the Company (or its successor in the Change in Control) in all capacities for Good Reason, and in either case other than as a result of death or Disability, then as of the date of Participant's termination of Continuous Service, the vesting and exercisability of any then-unvested Stock Award held by a Participant shall be accelerated in full.

10. AMENDMENT, TERMINATION SUSPENSION OF THE PLAN OR ADOPTION OF SUB-PLANS.

(a) Plan Term. The Board may suspend or terminate the Plan at any time. No Incentive Stock Options may be granted after the tenth anniversary of the earlier of (i) the Adoption Date and (ii) the Effective Date. No Awards may be granted under the Plan while the Plan is suspended or after it is terminated.

(b) Amendments. To amend the Plan in any respect the Board deems necessary or advisable. However, except as provided in Section 9(a) relating to Capitalization Adjustments, to the extent required by applicable law or listing requirements, shareholder approval shall be required for any amendment of the Plan that either (A) materially increases the number of Ordinary Shares available for issuance under the Plan, (B) materially expands the class of individuals eligible to receive Awards under the Plan, (C) materially increases the benefits accruing to Participants under the Plan or materially reduces the price at which Ordinary Shares may be issued or purchased under the Plan, (D) materially extends the term of the Plan, or (E) expands the types of Awards available for issuance under the Plan. Except as provided above, rights under any Award granted before amendment of the Plan shall not be impaired by any amendment of the Plan unless (1) the Company requests the consent of the affected Participant, and (2) such Participant consents in writing.

(c) No Impairment of Rights. Amendment, suspension or termination of the Plan will not materially impair rights and obligations under any Award granted while the Plan is in effect except with the written consent of the affected Participant or as otherwise permitted in the Plan.

(d) Sub-Plans. The Board shall be entitled to adopt sub-plans to the Plan pursuant to which Awards may be made on such terms and conditions different from those specified in the Plan as may, in the judgment of the Board, be necessary or desirable in order to recognize differences in local law, tax policy or practices, subject to any required shareholder approval as contemplated in Section 9(b).

11. EFFECTIVE DATE OF PLAN.

The Amended and Restated 2018 Equity Incentive Plan will become effective on the date of the Company's 2020 Annual General Meeting of Shareholders, provided that the shareholders approve the Plan at such meeting (the "Effective Date").

12. CHOICE OF LAW.

This Plan shall be governed by and construed in accordance with the Irish Companies Act 2014 (as same may be amended, replaced and/or consolidated in the future) as to matters within the scope

thereof, and as to all other matters shall be governed by and construed in accordance with the internal laws of the State of Delaware, without regard to its principles of conflicts of laws.

13. DEFINITIONS. As used in the Plan, the following definitions will apply to the capitalized terms indicated below:

(a) "***Adoption Date***" means the date that the Amended and Restated 2018 Equity Incentive Plan was first adopted by the Board.

(b) "***Affiliate***" means, at the time of determination, any "parent" or "majority-owned subsidiary" of the Company, as such terms are defined in Rule 405 of the Securities Act or, as the context so requires, means a "holding company" or "subsidiary" of the Company as such terms are defined in Irish company law. The Board will have the authority to determine the time or times at which "parent" or "subsidiary" status is determined within the foregoing definition.

(c) "***Award***" means a Stock Award or a Performance Cash Award.

(d) "***Award Agreement***" means a written agreement between the Company and a Participant evidencing the terms and conditions of an Award.

(e) "***Board***" means the Board of Directors of the Company.

(f) "***Capitalization Adjustment***" means any change that is made in, or other events that occur with respect to, the Ordinary Shares subject to the Plan or subject to any Stock Award after the Effective Date without the receipt of consideration by the Company through merger, consolidation, reorganization, recapitalization, reincorporation, share dividend, dividend in property other than cash, large nonrecurring cash dividend, share split or reverse share split, liquidating dividend, combination of shares, exchange of shares, change in corporate structure, or any similar equity restructuring transaction, as that term is used in Statement of Financial Accounting Standards Board Accounting Standards Codification Topic 718 (or any successor thereto). Notwithstanding the foregoing, the conversion of any convertible securities of the Company will not be treated as a Capitalization Adjustment.

(g) "***Cause***" will have the meaning ascribed to such term in any written agreement between the Participant and the Company defining such term and, in the absence of such agreement, such term means, with respect to a Participant, the occurrence of any of the following events: (i) such Participant's commission of any felony or any crime involving fraud, dishonesty or moral turpitude under the laws of the United States or any state thereof or any country in which a Participant is employed; (ii) such Participant's attempted commission of, or participation in, a fraud or act of dishonesty against the Company or an Affiliate; (iii) such Participant's intentional, material violation of any contract or agreement between the Participant and the Company or an Affiliate, of any statutory duty owed to the Company or an Affiliate; (iv) such Participant's unauthorized use or disclosure of the confidential information or trade secrets of the Company or an Affiliate; or (v) such Participant's gross misconduct. The determination that a termination of the Participant's Continuous Service is either for Cause or without Cause will be made by the Company, in its sole discretion. Any determination by the Company that the Continuous Service of a Participant was terminated with or without Cause for the purposes of outstanding Stock Awards held by such Participant will have no effect upon any determination of the rights or obligations of the Company or an Affiliate or such Participant for any other purpose.

(h) "***Change in Control***" means the consummation, in a single transaction or in a series of related transactions, of any one or more of the following events:

(i) any Exchange Act Person becomes the Owner, directly or indirectly, of securities of the Company representing more than 50% of the combined voting power of the Company's then outstanding securities other than by virtue of a merger, consolidation or similar transaction. Notwithstanding the foregoing, a Change in Control shall not be deemed to occur (A) on account of the acquisition of securities of the Company directly from the Company, (B) on account of the acquisition of securities of the Company by an investor, any affiliate thereof or any other Exchange Act Person that acquires the Company's securities in a transaction or series of related transactions the primary purpose of which is to obtain financing for the Company through the issuance of equity securities, or (C) solely because the level of Ownership held by any Exchange Act Person (the "Subject Person") exceeds the designated percentage threshold of the outstanding voting securities as a result of a repurchase or other acquisition of voting securities by the Company or any Affiliate reducing the number of shares outstanding, provided that if a Change in Control would occur (but for the operation of this sentence) as a result of the acquisition of voting securities by the Company or any Affiliate, and after such share acquisition, the Subject Person becomes the Owner of any additional voting securities that, assuming the repurchase or other acquisition had not occurred, increases the percentage of the then outstanding voting securities Owned by the Subject Person over the designated percentage threshold, then a Change in Control shall be deemed to occur;

(ii) a merger, consolidation or similar transaction involving (directly or indirectly) the Company and, immediately after the consummation of such merger, consolidation or similar transaction, the shareholders of the Company immediately prior thereto do not Own, directly or indirectly, either (A) outstanding voting securities representing more than 50% of the combined outstanding voting power of the surviving Entity in such merger, consolidation or similar transaction or (B) more than 50% of the combined outstanding voting power of the parent of the surviving Entity in such merger, consolidation or similar transaction, in each case in substantially the same proportions as their Ownership of the outstanding voting securities of the Company immediately prior to such transaction;

(iii) the shareholders of the Company approve or the Board approves a plan of complete dissolution or liquidation of the Company, or a complete dissolution or liquidation of the Company shall otherwise occur, except for a liquidation into a parent corporation;

(iv) a sale, lease, exclusive license or other disposition of all or substantially all (as determined by the Board in its sole discretion) of the consolidated assets of the Company and its Subsidiaries, other than a sale, lease, license or other disposition of all or substantially all of the consolidated assets of the Company and its Subsidiaries to an Entity, more than 50% of the combined voting power of the voting securities of which are Owned by shareholders of the Company in substantially the same proportions as their Ownership of the outstanding voting securities of the Company immediately prior to such sale, lease, license or other disposition; or

(v) individuals who, on the date the Plan is adopted by the Board, are members of the Board (the "Incumbent Board") cease for any reason to constitute at least a majority of the members of the Board; provided, however, that if the appointment or election (or nomination for election) of any new Board member was approved or recommended by a majority vote of the members of the Incumbent Board then still in office, such new member shall, for purposes of this Plan, be considered as a member of the Incumbent Board.

For the avoidance of doubt, any one or more of the above events may be effected pursuant to (i) a compromise or arrangement sanctioned by the Irish courts under section 450 of the Irish Companies Act 2014 (as may be amended, updated or replaced from time to time) (the "2014 Act") or (ii) a scheme, contract or offer which has become binding on all shareholders pursuant to Section 609 of the 2014 Act, or (iii) a bid pursuant to Regulation 23 or 24 of the European Communities (Takeover Bids (Directive 2004/25/EC)) Regulations 2006.

Notwithstanding the foregoing or any other provision of this Plan, (A) the term Change in Control shall not include a sale of assets, merger or other transaction effected exclusively for the purpose of changing the domicile of the Company, and (B) the definition of Change in Control (or any analogous term) in an individual written agreement between the Company or any Affiliate and the Participant shall supersede the foregoing definition with respect to Awards subject to such agreement; provided, however, that if no definition of Change in Control or any analogous term is set forth in such an individual written agreement, the foregoing definition shall apply.

(i) "***Code***" means the U.S. Internal Revenue Code of 1986, as amended, including any applicable regulations and guidance thereunder.

(j) "***Committee***" means a committee of one or more Directors to whom authority has been delegated by the Board in accordance with Section 2(c).

(k) "***Company***" means Iterum Therapeutics Public Limited Company, a company incorporated under the laws of the Republic of Ireland.

(l) "***Continuous Service***" means that the Participant's service with the Company or an Affiliate, whether as an Employee or Director is not interrupted or terminated. A change in the capacity in which the Participant renders service to the Company or an Affiliate as an Employee or Director or a change in the Entity for which the Participant renders such service, provided that there is no interruption or termination of the Participant's service with the Company or an Affiliate, will not terminate a Participant's Continuous Service; provided, however, that if the Entity for which a Participant is rendering services ceases to qualify as an Affiliate, as determined by the Board in its sole discretion, such Participant's Continuous Service will be considered to have terminated on the date such Entity ceases to qualify as an Affiliate. To the extent permitted by law, the Board, the chief executive officer of the Company (or an Affiliate, if applicable) or the Stock Plan Administrator, in that party's sole discretion, may determine whether Continuous Service will be considered interrupted in the case of (i) any leave of absence approved by the Company (or an Affiliate, if applicable), including sick leave, military leave or any other personal leave, or (ii) transfers between the Company, an Affiliate, or their successors. Notwithstanding the foregoing, a leave of absence will be treated as Continuous Service for purposes of vesting in a Stock Award only to such extent as may be provided in the Company's (or an Affiliate's, if applicable) leave of absence policy, in the written terms of any leave of absence agreement or policy applicable to the Participant, or as otherwise required by law.

(m) "***Corporate Transaction***" means the consummation, in a single transaction or in a series of related transactions, of any one or more of the following events:

(i) a sale or other disposition of all or substantially all, as determined by the Board, in its sole discretion, of the consolidated assets of the Company and its Subsidiaries;

(ii) a sale or other disposition of at least 50% of the outstanding securities of the Company;

(iii) a merger, consolidation or similar transaction following which the Company is not the surviving corporation; or

(iv) a merger, consolidation or similar transaction following which the Company is the surviving corporation but the Ordinary Shares outstanding immediately preceding the merger, consolidation or similar transaction are converted or exchanged by virtue of the merger, consolidation or similar transaction into other property, whether in the form of securities, cash or otherwise.

For the avoidance of doubt, any one or more of the above events may be effected pursuant to (x) a takeover under Irish takeover rules; (y) a compromise or arrangement under Chapter 1 of Part 9 of the 2014 Act or (z) Chapter 2 of Part 9 of the 2014 Act.

(n) "***Director***" means a member of the Board.

(o) "***Disability***" means, with respect to a Participant, the inability of such Participant to engage in any substantial gainful activity by reason of any medically determinable physical or mental impairment that can be expected to result in death or that has lasted or can be expected to last for a continuous period of not less than twelve (12) months as provided in Sections 22(e)(3) and 409A(a)(2)(c)(i) of the Code, and will be determined by the Board on the basis of such medical evidence as the Board deems warranted under the circumstances.

(p) "***Employee***" means any person employed by the Company or an Affiliate.

(q) "***Entity***" means a corporation, partnership, limited liability company or other entity.

(r) "***Exchange Act***" means the U.S. Securities Exchange Act of 1934, as amended, and the rules and regulations promulgated thereunder.

(s) "***Exchange Act Person***" means any natural person, Entity or "group" (within the meaning of Section 13(d) or 14(d) of the Exchange Act), except that "Exchange Act Person" shall not include (i) the Company or any Subsidiary of the Company, (ii) any employee benefit plan of the Company or any Subsidiary of the Company or any trustee or other fiduciary holding securities under an employee benefit plan of the Company or any Subsidiary of the Company, (iii) an underwriter temporarily holding securities pursuant to a registered public offering of such securities, (iv) an Entity Owned, directly or indirectly, by the shareholders of the Company in substantially the same proportions as their Ownership of Ordinary Shares of the Company; or (v) any natural person, Entity or "group" (within the meaning of Section 13(d) or 14(d) of the Exchange Act) that, as of the Effective Date, is the Owner, directly or indirectly, of securities of the Company representing more than 50% of the combined voting power of the Company's then outstanding securities.

(t) "***Fair Market Value***" means, as of any date, the value of the Ordinary Shares determined as follows:

(i) If the Ordinary Shares is listed on any established stock exchange or traded on the NASDAQ Global Market or the NASDAQ Global Select Market, the Fair Market Value of a share of Ordinary Shares, unless otherwise determined by the Board, shall be the closing sales price for such Ordinary Shares as quoted on such exchange or market (or the exchange or market with the greatest volume of trading in the Ordinary Shares) on the day of determination, as reported in a source the Board deems reliable.

(ii) Unless otherwise provided by the Board, if there is no closing sales price for the Ordinary Shares on the day of determination, then the Fair Market Value shall be the closing selling price on the last preceding date for which such quotation exists.

(iii) In the absence of such markets for the Ordinary Shares, the Fair Market Value shall be determined by the Board in good faith and in a manner that complies with Sections 409A and 422 of the Code.

(a) "***Good Reason***" will have the meaning ascribed to such term in any written agreement between the Participant and the Company or a successor corporation defining such term and, in the absence of such agreement, such term means, with respect to a Participant, any of the following actions taken without Cause without Participant's consent:

(i) A material reduction of the Participant's base compensation, other than a reduction that applies generally to all executives;

(ii) A material reduction in the Participant's authority, duties or responsibilities, provided, however, that a change in job position (including a change in title) shall not be deemed a "material reduction" unless the Participant's new authority, duties or responsibilities are materially reduced from the prior authority, duties or responsibilities;

(iii) failure or refusal of a successor to the Company to materially assume the Company's obligations under the Participant's offer letter and/or employment agreement, if applicable, in the event of a Change in Control; or

(iv) relocation of the Participant's principal place of employment that results in an increase in the Participant's one-way driving distance by more than 50 miles from the Participant's then current principal residence.

In order to resign for Good Reason, the Participant must provide written notice of the event giving rise to Good Reason to the Company within 90 days after the condition arises, allow the Company at least 30 days to cure such condition, and if the Company fails to cure the condition within such period, then Participant's resignation from all positions the Participant then holds with the Company must be effective not later than 90 days after the end of the Company's cure period.

(u) "***Incentive Stock Option***" means an option granted pursuant to Section 5 of the Plan that is intended to be, and that qualifies as, an "incentive stock option" within the meaning of Section 422 of the Code.

(v) "***IPO Date***" means the date of the underwriting agreement between the Company and the underwriter(s) managing the initial public offering of the Ordinary Shares, pursuant to which the Ordinary Shares are priced for the initial public offering.

(w) "***Non-Employee Director***" means a Director who either (i) is not a current employee or officer of the Company or an Affiliate, does not receive compensation, either directly or indirectly, from the Company or an Affiliate for services rendered as a consultant or in any capacity other than as a Director (except for an amount as to which disclosure would not be required under Item 404(a) of Regulation S-K promulgated pursuant to the Securities Act ("Regulation S-K")), does not possess an interest in any other transaction for which disclosure would be required under Item 404(a) of Regulation S-K, and is not engaged in a business relationship for which disclosure would be required pursuant to Item 404(b) of Regulation S-K; or (ii) is otherwise considered a "non-employee director" for purposes of Rule 16b-3.

(x) "***Nonstatutory Stock Option***" means an option granted pursuant to Section 5 of the Plan that does not qualify as an Incentive Stock Option.

(y) "***Officer***" means a person who is an officer of the Company within the meaning of Section 16 of the Exchange Act.

(z) "***Option***" means an Incentive Stock Option or a Nonstatutory Stock Option to purchase Ordinary Shares granted pursuant to the Plan.

(aa) "***Ordinary Shares***" or "***Shares***" means the Ordinary Shares in the capital of the Company.

(bb) "***Other Stock Award***" means an award based in whole or in part by reference to the Ordinary Shares which is granted pursuant to the terms and conditions of Section 6(d).

(cc) "***Own***," "***Owned***," "***Owner***," "***Ownership***" A person or Entity shall be deemed to "Own," to have "Owned," to be the "Owner" of, or to have acquired "Ownership" of securities if such person or Entity, directly or indirectly, through any contract, arrangement, understanding, relationship or

otherwise, has or shares voting power, which includes the power to vote or to direct the voting, with respect to such securities.

(dd) "***Participant***" means a person to whom an Award is granted pursuant to the Plan or, if applicable, such other person who holds an outstanding Stock Award.

(ee) "***Performance Cash Award***" means an award of cash granted pursuant to the terms and conditions of Section 6(c)(ii).

(ff) "***Performance Criteria***" means one or more criteria that the Board will select for purposes of establishing the Performance Goals for a Performance Period. The Performance Criteria that will be used to establish such Performance Goals may be based on any one of, or combination of, the following as determined by the Board: (1) earnings (including earnings per share and net earnings); (2) earnings before interest, taxes and depreciation; (3) earnings before interest, taxes, depreciation and amortization; (4) earnings before interest, taxes, depreciation, amortization and legal settlements; (5) earnings before interest, taxes, depreciation, amortization, legal settlements and other income (expense); (6) earnings before interest, taxes, depreciation, amortization, legal settlements, other income (expense) and stock-based compensation; (7) earnings before interest, taxes, depreciation, amortization, legal settlements, other income (expense), stock-based compensation and changes in deferred revenue; (8) total stockholder return; (9) return on equity or average stockholder's equity; (10) return on assets, investment, or capital employed; (11) stock price; (12) margin (including gross margin); (13) income (before or after taxes); (14) operating income; (15) operating income after taxes; (16) pre-tax profit; (17) operating cash flow; (18) sales or revenue targets; (19) increases in revenue or product revenue; (20) expenses and cost reduction goals; (21) improvement in or attainment of working capital levels; (22) economic value added (or an equivalent metric); (23) market share; (24) cash flow; (25) cash flow per share; (26) share price performance; (27) debt reduction; (28) implementation or completion of projects or processes (including, without limitation, clinical trial initiation, clinical trial enrollment, clinical trial results, new and supplemental indications for existing products, regulatory filing submissions, regulatory filing acceptances, regulatory or advisory committee interactions, regulatory approvals, and product supply); (29) stockholders' equity; (30) capital expenditures; (31) debt levels; (32) operating profit or net operating profit; (33) workforce diversity; (34) growth of net income or operating income; (35) billings; (36) bookings; (37) employee retention; (38) initiation of phases of clinical trials and/or studies by specific dates; (39) patient enrollment rates; (40) budget management; (41) submission to, or approval by, a regulatory body (including, but not limited to the U.S. Food and Drug Administration) of an applicable filing or a product candidate; (42) regulatory milestones; (43) progress of internal research or clinical programs; (44) progress of partnered programs; (45) partner satisfaction; (46) timely completion of clinical trials; (47) submission of INDs and NDAs and other regulatory achievements; (48) research progress, including the development of programs; (49) strategic partnerships or transactions (including in-licensing and out-licensing of intellectual property; (50) customer satisfaction; and (51) other measures of performance selected by the Board.

(gg) "***Performance Goals***" means, one or more goals established by the Board for the Performance Period based upon the Performance Criteria. Performance Goals may be based on a Company-wide basis, with respect to one or more business units, divisions, Affiliates, or business segments, and in either absolute terms or relative to the performance of one or more comparable companies or the performance of one or more relevant indices. Unless specified otherwise by the Board (i) in the Award Agreement at the time the Award is granted or (ii) in such other document setting forth the Performance Goals at the time the Performance Goals are established, the Board will appropriately make adjustments in the method of calculating the attainment of Performance Goals for a Performance Period as follows: (1) to exclude restructuring and/or other nonrecurring charges; (2) to exclude exchange rate effects; (3) to exclude the effects of changes to generally accepted accounting principles; (4) to exclude the effects of any statutory adjustments to corporate tax rates; (5) to exclude the effects of any items that are unusual in nature or occur infrequently as determined under generally

accepted accounting principles; (6) to exclude the dilutive effects of acquisitions or joint ventures; (7) to assume that any business divested by the Company achieved performance objectives at targeted levels during the balance of a Performance Period following such divestiture; (8) to exclude the effect of any change in the outstanding shares of common stock of the Company by reason of any stock dividend or split, stock repurchase, reorganization, recapitalization, merger, consolidation, spin-off, combination or exchange of shares or other similar corporate change, or any distributions to common stockholders other than regular cash dividends; (9) to exclude the effects of stock based compensation and the award of bonuses under the Company's bonus plans; (10) to exclude costs incurred in connection with potential acquisitions or divestitures that are required to be expensed under generally accepted accounting principles; (11) to exclude the goodwill and intangible asset impairment charges that are required to be recorded under generally accepted accounting principles; and (12) to exclude the effect of any other unusual, non-recurring gain or loss or other extraordinary item. In addition, the Board retains the discretion to increase, to reduce or to eliminate the compensation or economic benefit due upon attainment of Performance Goals and to define the manner of calculating the Performance Criteria it selects to use for such Performance Period. Partial achievement of the specified criteria may result in the payment or vesting corresponding to the degree of achievement as specified in the Award Agreement or the written terms of a Performance Cash Award.

(hh) "***Performance Period***" means the period of time selected by the Board over which the attainment of one or more Performance Goals will be measured for the purpose of determining a Participant's right to and the payment of a Stock Award or a Performance Cash Award. Performance Periods may be of varying and overlapping duration, at the sole discretion of the Board.

(ii) "***Performance Stock Award***" means a Stock Award granted under the terms and conditions of Section 6(c)(i).

(jj) "***Personal Data***" has the same meaning as defined in the Data Protection Acts 1988 and 2003.

(kk) "***Plan***" means this Amended and Restated Iterum Therapeutics Public Limited Company 2018 Equity Incentive Plan.

(ll) "***Restricted Stock Award***" means an award of Ordinary Shares which is granted pursuant to the terms and conditions of Section 6(a).

(mm) "***Restricted Stock Unit Award***" means a right to receive Ordinary Shares which is granted pursuant to the terms and conditions of Section 6(b).

(nn) "***Rule 16b-3***" means Rule 16b-3 promulgated under the Exchange Act or any successor to Rule 16b-3, as in effect from time to time.

(oo) "***Securities Act***" means the U.S. Securities Act of 1933, as amended.

(pp) "***Stock Appreciation Right***" or "***SAR***" means a right to receive the appreciation on Ordinary Shares that is granted pursuant to the terms and conditions of Section 5.

(qq) "***Stock Award***" means any right to receive Ordinary Shares granted under the Plan, including an Incentive Stock Option, a Nonstatutory Stock Option, a Restricted Stock Award, a Restricted Stock Unit Award, a Stock Appreciation Right, a Performance Stock Award or any Other Stock Award.

(rr) "***Stock Plan Administrator***" means one or more Officers or Employees designated by the Board pursuant to Section 2(a).

(ss) "***Subsidiary***" means, with respect to the Company, (i) any corporation of which more than 50% of the outstanding capital stock having ordinary voting power to elect a majority of the board of directors

of such corporation (irrespective of whether, at the time, stock of any other class or classes of such corporation will have or might have voting power by reason of the happening of any contingency) is at the time, directly or indirectly, Owned by the Company, and (ii) any partnership, limited liability company or other entity in which the Company has a direct or indirect interest (whether in the form of voting or participation in profits or capital contribution) of more than 50%, or, where the context so requires, the definition of "subsidiary" in Irish company law.

(tt) "***Ten Percent Shareholder***" means a person who Owns (or is deemed to Own pursuant to Section 424(d) of the Code) shares possessing more than 10% of the total combined voting power of all classes of shares of the Company or any Affiliate.

PLAN ADOPTION AND AMENDMENTS

Adopted by the Board of Directors of Iterum Therapeutics Public Limited Company on March 14, 2018.

Approved by the shareholders of Iterum Therapeutics Public Limited Company on May 14, 2018.

Amended and Restated Plan adopted by Board of Directors of Iterum Therapeutics Public Limited Company March 11, 2020.

Approved by the shareholders of Iterum Therapeutics Public Limited Company on June 10, 2020.

AMENDMENT TO
AMENDED AND RESTATED 2018 EQUITY INCENTIVE PLAN

The Amended and Restated 2018 Equity Incentive Plan (the "Plan") of Iterum Therapeutics plc is hereby further amended as follows:

1. Section 3(a)(i) is hereby deleted and a new Section 3(a)(i) is inserted in lieu thereof which shall read as follows:

> "(i) Subject to the provisions of this Section 3(a), and Section 9(a) relating to Capitalization Adjustments, the aggregate number of Ordinary Shares reserved for issuance pursuant to Stock Awards is 1,295,819 shares (the "Share Reserve"), which number shall include (i) any shares remaining for issuance pursuant to the Prior Plan as of the IPO Date and (ii) any Returning Shares. For clarity, the limit in this Section 3(a) is a limit on the number of Ordinary Shares that may be issued pursuant to the Plan. Accordingly, this Section 3(a) does not limit the granting of Stock Awards except as provided in Section 7(a)."

Except as set forth above, the remainder of the Plan remains in full force and effect

Amendment to Amended and Restated Plan adopted by Board of Directors of Iterum Therapeutics Public Limited Company March 11, 2021.

Approved by the shareholders of Iterum Therapeutics Public Limited Company on June 23, 2021.

ITERUM THERAPEUTICS PUBLIC LIMITED COMPANY
2018 EQUITY INCENTIVE PLAN – SUB PLAN FOR NON-EMPLOYEE DIRECTORS AND CONSULTANTS

1 ESTABLISHMENT AND PURPOSE

This sub-plan is established by the Board in accordance with Section 10(d) of the Iterum Therapeutics Public Limited Company Amended and Restated 2018 Incentive Plan (the "Plan") for the purposes of granting Awards to Non—Employee Directors and Consultants of Iterum Therapeutics Public Limited Company and its Subsidiaries. This sub-plan shall be known as the "NED and Consultant Sub-Plan" or "Sub-Plan".

2 RULES

2.1 The provisions of the Plan shall apply in their entirety to Awards made under this Sub-Plan save and expect only as set out in Sections 3 and 4 below. Capitalized terms contained in this Sub-Plan that are not defined herein shall have the same meanings given to them in the Plan.

2.2 The terms of this Sub-Plan shall also apply to Awards originally granted under the Plan to Employees, if such individual subsequently experiences a change in status from an Employee to either a Consultant or a Non-Employee Director without a break in Continuous Service.

2.3 For clarity, any Awards granted under this Sub-Plan will be deemed to be granted from the Plan for purposes of reducing the number of shares available under the Share Reserve. Shares subject to Awards that are forfeited, cancelled or expire in the manner contemplated by Section 3(b) of the Plan will be added back to the Share Reserve as provided therein.

3 DEFINITIONS

3.1 The following definition shall be inserted for the purposes of this Sub-Plan:
"Consultant" means any person, including an advisor, who is (i) engaged by the Company or an Affiliate to render consulting or advisory services and is compensated for such services, or (ii) serving as a member of the board of directors of an Affiliate and is compensated for such services. However, service solely as a Non-Employee Director, or payment of a fee for such service, will not cause a Non-Employee Director to be considered a "Consultant" for purposes of the Plan. Notwithstanding the foregoing, a person is treated as a Consultant under this Plan only if a Form S-8 Registration Statement under the Securities Act is available to register either the offer or the sale of the Company's securities to such person;

3.2 The following definitions shall be deleted and replaced with the following for the purposes if this Sub-Plan:

"Continuous Service" means that the Participant's service with the Company or an Affiliate, whether as a Director or Consultant, is not interrupted or terminated. A change in the capacity in which the Participant renders service to the Company or an Affiliate as Director or Consultant or a change in the Entity for which the Participant renders such service, provided that there is no interruption or termination of the Participant's service with the Company or an Affiliate, will not terminate a Participant's Continuous Service; provided, however, that if the Entity for which a Participant is rendering services ceases to qualify as an Affiliate, as determined by the Board in its sole discretion, such Participant's Continuous Service will be considered to have terminated on the date such Entity ceases to qualify as an Affiliate. To the extent permitted by law, the Board, the chief executive officer of the Company (or an Affiliate, if applicable) or the Stock Plan Administrator, in that party's sole discretion, may determine whether Continuous Service will be considered interrupted in the case of (i) any interruption of service approved by the Company (or an Affiliate, if applicable), including sick

leave, interruption of service or any other personal leave, or (ii) transfers of service between the Company, an Affiliate, or their successors. Notwithstanding the foregoing, a leave of absence will be treated as Continuous Service for purposes of vesting in a Stock Award only to such extent as may be provided in the Company's (or an Affiliate's, if applicable) leave of absence policy, in the written terms of any agreement or policy applicable to the Participant, or as otherwise required by law;

"Good Reason" will have the meaning ascribed to such term in any written agreement between the Participant and the Company or a successor corporation defining such term and, in the absence of such agreement, such term means, with respect to a Participant, any of the following actions taken without Cause without Participant's consent:

(i) a material reduction of the Participant's base service fee, other than a reduction that applies generally to all Non-Employee Directors or Consultants;

(ii) a material reduction in the Participant's authority, duties or responsibilities; or

(iii) failure or refusal of a successor to the Company to materially assume the Company's obligations under the Participant's service agreement, if applicable, in the event of a Change in Control;

In order to terminate service for Good Reason, the Participant must provide written notice of the event giving rise to Good Reason to the Company within 90 days after the condition arises, allow the Company at least 30 days to cure such condition, and if the Company fails to cure the condition within such period, then Participant's termination of service must be effective not later than 90 days after the end of the Company's cure period; and

4 SECTIONS

In this Sub-Plan:

4.1 Section 1(b) of the Plan shall be deleted and replaced with the following:
1(b)—Eligible Awards Recipients. The person eligible to receive Awards are Non-Employee Directors and Consultants.

4.2 Section 2(d) shall be deleted and replaced with the following:
2(d) – Delegation to an Officer. Subject to compliance with Irish law, the Board may delegate to one of more Officers the authority to do one or both of the following: (i) designate Non-Employee Directors and Consultants who are providing Continuous Service to the Company or any of its Subsidiaries to be recipients of Stock Awards and the terms thereof, and (ii) determine the number of Ordinary Shares to be subject to Board resolutions regarding such delegation shall specify the total number of Ordinary Shares that may be subject to the Stock Awards granted by such Officer and that such Officer many not grant a Stock Awards to himself or herself. Notwithstanding the foregoing, the Board may not delegate authority to an Officer to determine the fair Market Value of the Ordinary Shares.

4.3 Section 3(b) of the Plan shall be deleted and replaced with the following:

3(b)—Reversion of Shares to the Share Reserve. If subject to compliance with Irish law (i) any Ordinary Shares issued pursuant to a Stock Award are forfeited back to or repurchased by the Company or any Affiliate because of the failure to meet a contingency or condition required for the vesting of such Ordinary Shares, or (ii) any Ordinary Shares are cancelled in accordance with the cancellation and regrant provisions of Section 2(b)(vii), then the Ordinary Shares that are forfeited, repurchased or cancelled shall revert to and again become available for issuance under the Plan. If any Ordinary Shares subject to a Stock Award are not delivered to a Participant because an appreciation

distribution in respect of a Stock Appreciation Right is paid in Ordinary Shares, the number of Ordinary Shares subject to the Stock Award that are not delivered to the Participant shall remain available for subsequent issuance under the Plan.

4.4 Section 5(c) of the Plan shall be deleted and replaced with the following:

5(c)—Exercise and Purchase Price for Options. To exercise any outstanding Option, the Participant must provide written notice of exercise to the Company in the manner determined by the Stock Plan Administrator. The purchase price of Ordinary Shares acquired pursuant to the exercise of an Option may be paid, to the extent permitted by applicable law and as determined by the Board in its sole discretion, by any combination of the methods of payment set forth below. The Board will have the authority to grant Options that do not permit all of the following methods of payment (or otherwise restrict the ability to use certain methods) and to grant Options that require the consent of the Company to use a particular method of payment. In all cases the Company shall require that the nominal value of each newly issued Ordinary Share is fully paid up. The permitted methods of payment are as follows:

(i) by cash, check, bank draft or money order payable to the Company;

(ii) pursuant to a program developed under Regulation T as promulgated by the U.S. Federal Reserve Board that, prior to the issuance of Ordinary Shares subject to the Option, results in either the receipt of cash (or check) by the Company or the receipt of irrevocable instructions to pay the aggregate exercise price to the Company from the sales proceeds;

(iii) deduction from service fees due and payable to a Non-Employee Director or Consultant by the Company or any Affiliate; or
(iv) in any other form of legal consideration that may be acceptable to the Board or the Stock Plan Administration and permissible under applicable law.

4.5 Section 8(d) shall be deleted and replaces with the following:

8(d) – No Service Rights. Nothing in the Plan, any Award Agreement or any other instrument executed thereunder or in connection with any Award granted pursuant thereto will confer upon any Participant any right to continue to serve the Company or an Affiliate in the capacity in effect at the time the Award was granted or will affect any right that the Company or an Affiliate may have to terminate (i) the service of a Director pursuant to the Constitution of the Company or an Affiliate, or (ii) the service of a Consultant pursuant to the terms of such Consultant's agreement with the Company or and Affiliate, or any applicable provisions of the corporate law of the country or state in which the Company or the Affiliate is incorporated as the case may be.

4.6 Rule 8 (g) of the Plan shall be deleted and replaced with the following:

8(g)—Withholding Obligations. Unless prohibited by the terms of an Award Agreement, the Company or any Affiliate may, in its sole discretion, but subject always to applicable law, satisfy any federal, state, local or foreign tax withholding obligation, or levies or social security deduction obligation relating to an Award by any of the following means or by a combination of such means: (i) causing the Participant to tender a cash payment; (ii) implementing a sell-to cover arrangement (iii) withholding cash from an Award settled in cash; (iv) withholding payment from any amounts otherwise payable to the Participant; or (v) by such other method as may be set forth in the Award Agreement subject to compliance with applicable law.

EXHIBIT 10.3

ITERUM THERAPEUTICS PUBLIC LIMITED COMPANY
2021 INDUCEMENT EQUITY INCENTIVE PLAN

1.GENERAL.

(a)Eligible Award Recipients. Awards under the 2021 Inducement Equity Incentive Plan (the "Plan") may only be granted to persons who (a) were not previously an Employee or Director of the Company or an Affiliate or (b) are commencing employment with the Company or an Affiliate following a bona fide period of non-employment, in either case as an inducement material to the individual's entering into employment with the Company or an Affiliate and in accordance with, and solely to the extent permitted by, the requirements of Nasdaq Stock Market Rule 5635(c)(4). For the avoidance of doubt, neither consultants nor advisors shall be eligible to participate in the Plan.

(b)Available Awards. The Plan provides for the grant of the following Awards: (i) Nonstatutory Share Options, (ii) Share Appreciation Rights, (iii) Restricted Share Awards, (iv) Restricted Share Unit Awards, (v) Performance Share Awards and (vi) Other Share Awards.

(c)Purpose. The Plan, through the grant of Awards, is intended to help the Company secure and retain the services of eligible award recipients with an inducement material for such persons to enter into employment with the Company, provide incentives for such persons to exert maximum efforts for the success of the Company and any Affiliate and provide a means by which the eligible recipients may benefit from increases in value of the Ordinary Shares.

(d)Definitions. All capitalized terms in this document are defined in Section 12 below.

2.ADMINISTRATION.

(a)Administration by the Board. The Board will administer the Plan. The Board may delegate administration of the Plan to a Committee or Committees, as provided in Section 2(c). In addition, the Board or a Committee may appoint a Share Plan Administrator with the authority to administer the day to day operations of the Plan, and to make decisions with respect to the Plan and Awards. Notwithstanding the foregoing or anything in the Plan to the contrary, the grant of any Award under the Plan must be approved by the Company's independent compensation committee or a majority of the Company's independent Directors (as defined in Nasdaq Stock Market Rule 5605(a)(2)) in order to comply with the exemption from the shareholder approval requirement for "inducement grants" provided under Nasdaq Stock Market Rule 5635(c)(4).

(b)Powers of the Board. The Board will have the power, subject to, and within the limitations of, the express provisions of the Plan:

(i)To determine from time to time (A) which of the persons eligible under the Plan will be granted Awards; (B) when and how each Award will be granted; (C) what type or combination of types of Award will be granted; (D) the provisions of each Award granted (which need not be identical), including the time or times when a person will be permitted to exercise or otherwise receive cash or Ordinary Shares under the Share Award; (E) the number of Ordinary

Shares with respect to which a Share Award shall be granted to each such person; and (F) the Fair Market Value applicable to a Share Award.

(ii)To construe and interpret the Plan and Awards granted under it, to establish, amend and revoke rules and regulations for its administration, and to settle all controversies regarding the Plan and Awards granted under it. The Board, in the exercise of this power, may correct any defect, omission or inconsistency in the Plan or in any Award Agreement, in a manner and to the extent it will deem necessary or expedient to make the Plan or Award fully effective.

(iii)To prohibit (or delegate to the Share Plan Administrator the authority to prohibit) the exercise of any Option, SAR or other exercisable Award during a period of up to thirty days prior to the consummation of any pending share dividend, share split, combination or exchange of shares, merger, consolidation or other distribution (other than normal cash dividends) of Company assets to shareholders, or any other change affecting the Ordinary Shares or the share price of the Ordinary Shares, including any Corporate Transaction, for reasons of administrative convenience.

(iv)To accelerate the time at which an Award may be exercised or the time during which an Award or any part thereof will vest.

(v)To approve forms of Award Agreements for use under the Plan and to amend the terms of any one or more Awards, subject to any specified limits in the Plan that are not subject to Board discretion; provided however, that a Participant's rights under any Award will not be materially impaired by any such amendment unless (A) the Company requests the consent of the affected Participant, and (B) such Participant consents in writing. Notwithstanding the foregoing, and subject to the limitations of applicable law, if any, the Board may amend the terms of any one or more Awards without the affected Participant's consent (1) to clarify the manner of exemption from, or to bring the Award into compliance with, Section 409A of the Code; or (2) to comply with other applicable laws.

(vi)To amend, suspend or terminate the Plan as provided by Section 9.

(vii)To effect, with the consent of any adversely affected Participant, (A) the alteration of the exercise, purchase or strike price of any outstanding Share Award (unless this is in the context of a Capitalization Adjustment in which case Participant consent is not required); (B) the cancellation of any outstanding Share Award and the grant in substitution therefor of a new (1) Option or SAR, (2) Restricted Share Award, (3) Restricted Share Unit Award, (4) Other Share Award, (5) cash and/or (6) other valuable consideration determined by the Board, in its sole discretion, with any such substituted award (x) covering the same or a different number of Ordinary Shares as the cancelled Share Award and (y) granted under the Plan or another equity or compensatory plan of the Company; or (C) any other action that is treated as a repricing under generally accepted accounting principles or applicable stock exchange rules. For the avoidance of doubt, shareholder approval will not be required to give effect to any action approved by the Board pursuant to this Section 2(b)(vii).

(viii)Generally, to exercise such powers and to perform such acts as the Board deems necessary or expedient to promote the best interests of the Company and any Affiliates and that are not in conflict with the provisions of the Plan or Awards.

(c)Delegation to Committee. The Board may delegate some or all of the administration of the Plan to a Committee or Committees to the extent permitted by the Nasdaq Stock Market rules. If administration of the Plan is delegated to a Committee, the Committee will have, in connection with the administration of the Plan, the powers theretofore possessed by the Board that have been delegated to the Committee, including the power to delegate to a subcommittee of the Committee any of the administrative powers the Committee is authorized to exercise (and references in this Plan to the Board will thereafter be to the Committee or subcommittee, as applicable). Any delegation of administrative powers will be reflected in resolutions, not inconsistent with the provisions of the Plan, adopted from time to time by the Board or Committee (as applicable). The Board may retain the authority to concurrently administer the Plan with the Committee and may, at any time, revest in the Board some or all of the powers previously delegated. The Committee may consist solely of two or more Non-Employee Directors, in accordance with Rule 16b-3.

(d)Delegation to an Officer. Subject to compliance with Irish law and the Nasdaq Stock Market rules, the Board may delegate to one or more Officers the authority to determine Employees who are eligible recipients of Share Awards hereunder and the number of Ordinary Shares to be subject to such Share Awards granted to such Employees; provided, however, that the Board resolutions regarding such delegation shall specify the total number of Ordinary Shares that may be subject to the Share Awards granted by such Officer and that such Officer may not grant a Share Award to himself or herself. Notwithstanding the foregoing, the Board may not delegate authority to an Officer to determine the Fair Market Value of the Ordinary Shares.

(e)Effect of Board's Decision. All determinations, interpretations and constructions made by the Board in good faith will not be subject to review by any person and will be final, binding and conclusive on all persons.

3.SHARES SUBJECT TO THE PLAN.

(a)Share Reserve.

(i)Subject to the provisions of this Section 3(a), and Section 8(a) relating to Capitalization Adjustments, the aggregate number of Ordinary Shares reserved for issuance pursuant to Share Awards is 333,333 shares (the "Share Reserve"). For clarity, the limit in this Section 3(a) is a limit on the number of Ordinary Shares that may be issued pursuant to the Plan. Accordingly, this Section 3(a) does not limit the granting of Share Awards except as provided in Section 6(a).

(ii)In addition, subject to compliance with Irish law shares may be issued in connection with a merger or acquisition as permitted by, as applicable, Nasdaq Marketplace Rule

4350(i)(1)(A)(iii), NYSE Listed Company Manual Section 303A.08, AMEX Company Guide Section 711 or other applicable stock exchange rules, and such issuance shall not reduce the number of Ordinary Shares available for issuance under the Plan.

(b)Reversion of Shares to the Share Reserve. If subject to compliance with Irish law (i) any Ordinary Shares issued pursuant to a Share Award are forfeited back to or repurchased by the Company or any Affiliate because of the failure to meet a contingency or condition required for the vesting of such Ordinary Shares, or (ii) any Ordinary Shares are cancelled in accordance with the cancellation and regrant provisions of Section 2(b)(vii), then the Ordinary Shares that are forfeited, repurchased or canceled shall revert to and again become available for issuance under the Plan. If any Ordinary Shares subject to a Share Award are not delivered to a Participant because such Ordinary Shares are withheld for the payment of taxes pursuant to Section 7(g) or a Share Award is exercised through a reduction of Ordinary Shares subject to the Share Award (i.e., "net exercised") or an appreciation distribution in respect of a Share Appreciation Right is paid in Ordinary Shares, the number of Ordinary Shares subject to the Share Award that are not delivered to the Participant shall remain available for subsequent issuance under the Plan. If the exercise price of any Share Award is satisfied by tendering Ordinary Shares held by the Participant (either by actual delivery or attestation), then the number of Ordinary Shares so tendered shall remain available for issuance under the Plan.

(c)Source of Shares. The Ordinary Shares issuable under the Plan shall be authorized but unissued or reacquired Ordinary Shares, including Ordinary Shares redeemed or repurchased by the Company or any Affiliate on the open market or otherwise, in accordance with applicable Irish law. For the avoidance of doubt, Ordinary Shares purchased by the Company in the open market or otherwise will not increase the number of Ordinary Shares available for issuance under the Plan.

4.PROVISIONS RELATING TO OPTIONS AND SHARE APPRECIATION RIGHTS.

Each Option or SAR will be in such form and will contain such terms and conditions as the Board deems appropriate. All Options under the Plan will be Nonstatutory Share Options. The provisions of separate Options or SARs need not be identical; provided, however, that each Award Agreement will conform to (through incorporation of provisions hereof by reference in the applicable Award Agreement or otherwise) the substance of each of the following provisions:

(a)Term. No Option or SAR will be exercisable after the expiration of 10 years from the date of its grant or such shorter period specified in the Award Agreement.

(b)Exercise Price. The exercise or strike price of each Award will be not less than the greater of (i) the nominal value of an Ordinary Share or (ii) 100% of the Fair Market Value of the Ordinary Shares subject to the Option or SAR on the date the Share Award is granted. Notwithstanding the foregoing, an Option or SAR may be granted with an exercise or strike price lower than 100% of the Fair Market Value of the Ordinary Shares subject to the Award if such Award is granted pursuant to an assumption of or substitution for another option or share

appreciation right pursuant to a Corporate Transaction and in a manner consistent with the provisions of Section 409A of the Code and, if applicable, Section 424(a) of the Code, provided that in all cases it will not be less than the nominal value of an Ordinary Share. Each SAR will be denominated in Ordinary Share equivalents.

(c)Exercise and Purchase Price for Options. To exercise any outstanding Option, the Participant must provide written notice of exercise to the Company in the manner determined by the Share Plan Administrator. The purchase price of Ordinary Shares acquired pursuant to the exercise of an Option may be paid, to the extent permitted by applicable law and as determined by the Board in its sole discretion, by any combination of the methods of payment set forth below. The Board will have the authority to grant Options that do not permit all of the following methods of payment (or otherwise restrict the ability to use certain methods) and to grant Options that require the consent of the Company to use a particular method of payment. In all cases the Company shall require that the nominal value of each newly issued Ordinary Share is fully paid up. The permitted methods of payment are as follows:

(i)by cash, check, bank draft or money order payable to the Company;

(ii)pursuant to a program developed under Regulation T as promulgated by the U.S. Federal Reserve Board that, prior to the issuance of Ordinary Shares subject to the Option, results in either the receipt of cash (or check) by the Company or the receipt of irrevocable instructions to pay the aggregate exercise price to the Company from the sales proceeds;

(iii)by delivery to the Company (either by actual delivery or attestation) of Ordinary Shares;

(iv)by a "net exercise" arrangement pursuant to which the Company will reduce the number of Ordinary Shares issuable upon exercise by the largest whole number of Ordinary Shares with a Fair Market Value that does not exceed the aggregate exercise price; provided, however, that:

(1) the Company will accept a cash or other payment from the Participant to the extent of any remaining balance of the aggregate exercise price not satisfied by such reduction in the number of whole Ordinary Shares to be issued;

(2) irrespective of whether a "net exercise" arrangement is used, the nominal value of each newly issued Ordinary Shares will be fully paid up in cash; and

(3) Ordinary Shares will no longer be subject to an Option and will not be exercisable thereafter to the extent that (A) Ordinary Shares issuable upon exercise are used to pay the exercise price pursuant to the "net exercise," (B) Ordinary Shares are delivered to the Participant as a result of such exercise, and (C) Ordinary Shares are withheld to satisfy tax withholding obligations;

(v)deduction from salary due and payable to an Employee by the Company or any Affiliate; or

(vi)in any other form of legal consideration that may be acceptable to the Board or the Share Plan Administrator and permissible under applicable law.

(d)Exercise and Payment of a SAR. To exercise any outstanding SAR, the Participant must provide written notice of exercise to the Company in compliance with the provisions of the Award Agreement evidencing such SAR. The appreciation distribution payable on the exercise of a SAR will be not greater than an amount equal to the excess of (A) the aggregate Fair Market Value (on the date of the exercise of the SAR) of a number of Ordinary Shares equal to the number of Ordinary Shares equivalents in which the Participant is vested under such SAR, and with respect to which the Participant is exercising the SAR on such date, over (B) the aggregate strike price of the number of Ordinary Shares equivalents with respect to which the Participant is exercising the SAR on such date. The appreciation distribution may be paid in Ordinary Shares, in cash, in any combination of the two or in any other form of consideration, as determined by the Board and contained in the Award Agreement evidencing such SAR. Where the SAR is settled using newly issued Ordinary Shares the Company shall require that the nominal value of each newly issued Ordinary Share is fully paid up.

(e)Transferability of Options and SARs. The Board may, in its sole discretion, impose such limitations on the transferability of Options and SARs as the Board will determine. In the absence of such a determination by the Board to the contrary, the following restrictions on the transferability of Options and SARs will apply:

(i)**Restrictions on Transfer.** An Option or SAR will not be transferable except by will or by the laws of descent and distribution (or pursuant to subsections (ii) and (iii) below), and will be exercisable during the lifetime of the Participant only by the Participant; provided, however, that the Board or the Share Plan Administrator may, in its sole discretion, permit transfer of the Option or SAR in a manner that is not prohibited by applicable tax and securities laws upon the Participant's request. Except as explicitly provided in the Plan, neither an Option nor a SAR may be transferred for consideration.

(ii)**Domestic Relations Orders.** Subject to the approval of the Board or the Share Plan Administrator, an Option or SAR may be transferred pursuant to the terms of a domestic relations order, official marital settlement agreement or other divorce or separation instrument which contains the information required by the Company to effect the transfer.

(iii)**Beneficiary Designation.** Subject to the approval of the Board or the Share Plan Administrator, a Participant may, by delivering written notice to the Company, in a form provided by or otherwise satisfactory to the Share Plan Administrator and any broker designated by the Company to effect Option exercises, designate a third party who, in the event of the death of the Participant, will thereafter be entitled to exercise the Option or SAR and receive the Ordinary Shares or other consideration resulting from such exercise. In the absence of such a designation, upon the death of the Participant, the executor or administrator of the Participant's estate will be entitled to exercise the Option or SAR and receive the Ordinary Shares or other consideration resulting from such exercise in accordance with the Participants will or the laws of intestacy as applicable. However, the Company may prohibit designation of a beneficiary at any

time, including due to any conclusion by the Company that such designation would be inconsistent with the provisions of applicable laws whether in the United States or any other jurisdiction in which a Participant resides.

(f)Vesting Generally. The total number of Ordinary Shares subject to an Option or SAR may vest and therefore become exercisable in periodic installments that may or may not be equal. The Option or SAR may be subject to such other terms and conditions on the time or times when it may or may not be exercised (which may be based on the satisfaction of Performance Goals or other criteria) as the Board may deem appropriate. The vesting provisions of individual Options or SARs may vary. The provisions of this Section 4(f) are subject to any Option or SAR provisions governing the minimum number of Ordinary Shares as to which an Option or SAR may be exercised.

(g)Termination of Continuous Service. If a Participant's Continuous Service terminates, the Participant may exercise his or her Option or SAR (to the extent that the Participant was entitled to exercise the vested portion of such Award as of the date of termination of Continuous Service) but only within such period of time following the termination of the Participant's Continuous Service as set forth in the Award Agreement. Unless otherwise provided in the Award Agreement, the Option or SAR will be exercisable for a period of three (3) months following a termination of a Participant's Continuous Service by the Company without Cause or by the Participant for any reason; provided, however that such post-termination exercise period will instead be for the twelve (12) month period following a termination due to the Participant's Disability or death. Additionally, if the Participant's death occurs within the applicable post-termination of Continuous Service period during which the Option was exercisable, the Option will be exercisable for a twelve (12) month period following the Participant's death. If, after termination of Continuous Service, the Participant does not exercise his or her Option or SAR prior to the applicable deadline the Option or SAR will terminate.

(h)Automatic Extension of Termination Date. If the exercise of an Option or SAR following the termination of the Participant's Continuous Service (other than for Cause and other than upon the Participant's death or Disability) would be prohibited at any time solely because the issuance of Ordinary Shares would violate the registration requirements under the Securities Act, then the Option or SAR will terminate on the earlier of (i) the expiration of a total period of time (that need not be consecutive) equal to the applicable post-termination exercise period after the termination of the Participant's Continuous Service during which the exercise of the Option or SAR would not be in violation of such registration requirements, and (ii) the expiration of the term of the Option or SAR as set forth in the applicable Award Agreement. In addition, unless otherwise provided in a Participant's Award Agreement, if the sale of any Ordinary Shares received upon exercise of an Option or SAR following the termination of the Participant's Continuous Service (other than for Cause) would violate the Company's insider trading policy, then the Option or SAR will terminate on the earlier of (i) the expiration of the period of time (that need not be consecutive) equal to the applicable post-termination exercise period after the termination of the Participant's Continuous Service during which the sale of the Ordinary Shares received upon exercise of the Option or SAR would not be in violation of the Company's insider

trading policy, and (ii) the expiration of the term of the Option or SAR as set forth in the applicable Award Agreement.

(i)Termination for Cause. Except as explicitly provided otherwise in a Participant's Award Agreement or other individual written agreement between the Company or any Affiliate and the Participant, if a Participant's Continuous Service is terminated for Cause, the Option or SAR will terminate immediately upon such Participant's termination of Continuous Service, and the Participant will be prohibited from exercising his or her Option or SAR from and after the date of such termination of Continuous Service.

(j)Non-Exempt Employees under U.S. Law. If an Option or SAR is granted to an Employee who is a non-exempt employee for purposes of the U.S. Fair Labor Standards Act of 1938, as amended, the Option or SAR will not be first exercisable for any Ordinary Shares until at least six months following the date of grant of the Option or SAR (although the Award may vest prior to such date). Consistent with the provisions of the U.S. Worker Economic Opportunity Act, (i) if such non-exempt Employee dies or suffers a Disability, (ii) upon a Corporate Transaction in which such Option or SAR is not assumed, continued, or substituted, (iii) upon a Change in Control, or (iv) upon the Participant's retirement (as such term may be defined in the Participant's Award Agreement in another agreement between the Participant and the Company, or, if no such definition, in accordance with the Company's then current employment policies and guidelines), the vested portion of any Options and SARs may be exercised earlier than six months following the date of grant. The foregoing provision is intended to operate so that any income derived by a non-exempt employee in connection with the exercise or vesting of an Option or SAR will be exempt from his or her regular rate of pay. To the extent permitted and/or required for compliance with the U.S. Worker Economic Opportunity Act to ensure that any income derived by a non-exempt employee in connection with the exercise, vesting or issuance of any shares under any other Share Award will be exempt from the employee's regular rate of pay, the provisions of this Section 4(j) will apply to all Share Awards and are hereby incorporated by reference into such Award Agreements.

(k)Whole Shares. Options and SARs may be exercised only with respect to whole shares.

(l)No Reload Options. No Option or SAR granted under the Plan shall contain any provision entitling the Participant to the automatic grant of additional Options or SARs in connection with any exercise of the original award.

(m)No Dividend Equivalents. No Option or SAR shall provide for the payment or accrual of dividend equivalents.

5.PROVISIONS OF SHARE AWARDS OTHER THAN OPTIONS AND SARS.

(a)Restricted Share Awards. Each Restricted Share Award will be in such form and will contain such terms and conditions as the Board will deem appropriate. To the extent consistent with the Company's Constitution, at the Board's election, Ordinary Shares underlying a Restricted Share Award may be (i) held in book entry form subject to the Company's

instructions until any restrictions relating to the Restricted Share Award lapse; or (ii) evidenced by a certificate, which certificate will be held in such form and manner as determined by the Board. The terms and conditions of Restricted Share Awards may change from time to time, and the terms and conditions of separate Restricted Share Awards need not be identical; provided, however, that each Award Agreement will conform to (through incorporation of the provisions hereof by reference in the agreement or otherwise) the substance of each of the following provisions:

(i)**Consideration.** A Restricted Share Award may be awarded in consideration for (A) cash, check, bank draft or money order payable to the Company, (B) services to the Company or an Affiliate, or (C) any other form of legal consideration (including future services) that may be acceptable to the Board, in its sole discretion, and permissible under applicable law. In all cases the Company shall require that the nominal value of each newly issued Ordinary Share issued in satisfaction of a Restricted Share Award is fully paid up.

(ii)**Vesting.** Ordinary Shares awarded under a Restricted Share Award may be subject to forfeiture to the Company in accordance with a vesting schedule to be determined by the Board and subject to compliance with Irish law.

(iii)**Termination of Participant's Continuous Service.** If a Participant's Continuous Service terminates, the Company may receive through a forfeiture condition or a repurchase right subject to compliance with Irish law, any or all of the Ordinary Shares held by the Participant that have not vested as of the date of termination of Continuous Service under the terms of the Award Agreement.

(iv)**Transferability.** Rights to acquire Ordinary Shares under the Restricted Share Award will be transferable by the Participant only upon such terms and conditions as are set forth in the Award Agreement, as the Board will determine in its sole discretion, so long as Ordinary Shares awarded under the Restricted Share Award remain subject to the terms of the Award Agreement.

(v)**Dividends.** An Award Agreement will provide that any dividends paid on Restricted Shares will be subject to the same vesting and forfeiture restrictions as apply to the shares subject to the Restricted Share Award to which they relate.

(b)Restricted Share Unit Awards. Each Restricted Share Unit Award will be in such form and will contain such terms and conditions as the Board will deem appropriate. The terms and conditions of Restricted Share Unit Awards may change from time to time, and the terms and conditions of separate Restricted Share Unit Awards need not be identical; provided that each Restricted Share Unit Award Agreement will conform to (through incorporation of the provisions hereof by reference in the Agreement or otherwise) the substance of each of the following provisions:

(i)**Consideration.** At the time of grant of a Restricted Share Unit Award, the Board will determine the consideration, if any, to be paid by the Participant upon delivery of each share of Ordinary Shares subject to the Restricted Share Unit Award. The consideration to be paid (if

any) by the Participant for each share of Ordinary Shares subject to a Restricted Share Unit Award may be paid in any form of legal consideration that may be acceptable to the Board, in its sole discretion, and permissible under applicable law.

(ii)**Vesting.** At the time of the grant of a Restricted Share Unit Award, the Board may impose such restrictions on or conditions to the vesting of the Restricted Share Unit Award as it, in its sole discretion, deems appropriate.

(iii)**Payment.** A Restricted Share Unit Award may be settled by the delivery of Ordinary Shares, their cash equivalent, any combination thereof or in any other form of consideration, as determined by the Board and contained in the Restricted Share Unit Award Agreement. In all cases the Company shall require that the nominal value of each newly issued Ordinary Share issued in satisfaction of a Restricted Share Unit Award is fully paid up.

(iv)**Additional Restrictions.** At the time of the grant of a Restricted Share Unit Award, the Board, as it deems appropriate, may impose such restrictions or conditions that delay the delivery of the Ordinary Shares (or their cash equivalent) subject to a Restricted Share Unit Award to a time after the vesting of such Restricted Share Unit Award.

(v)**Dividend Equivalents.** Dividend equivalents may be credited in respect of Ordinary Shares covered by a Restricted Share Unit Award, as determined by the Board and contained in the Restricted Share Unit Award Agreement. At the sole discretion of the Board, such dividend equivalents may be converted into additional Ordinary Shares covered by the Restricted Share Unit Award in such manner as determined by the Board. Any such dividend equivalents will be subject to all of the same terms and conditions, including vesting and forfeiture provisions, of the underlying Award Agreement to which they relate.

(vi)**Termination of Participant's Continuous Service**. Except as otherwise provided in the applicable Award Agreement, such portion of the Restricted Share Unit Award that has not vested will be forfeited upon the Participant's termination of Continuous Service.

(c)Performance Awards.

(i)**Performance Share Awards**. A Performance Share Award is a Share Award that may vest or may be exercised contingent upon the attainment during a Performance Period of certain Performance Goals. A Performance Share Award may, but need not, require the completion of a specified period of Continuous Service. The length of any Performance Period, the Performance Goals to be achieved during the Performance Period, and the measure of whether and to what degree such Performance Goals have been attained shall be conclusively determined by the Board or Committee, in its sole discretion. The Board may provide for or, subject to such terms and conditions as the Board may specify, may permit a Participant to elect for, the payment of any Performance Share Award to be deferred to a specified date or event. In addition, to the extent permitted by applicable law and the applicable Award Agreement, the Board may determine that cash may be used in payment of Performance Share Awards.

(ii)**Board Discretion.** The Board retains the discretion to amend the compensation or economic benefit due upon attainment of Performance Goals and to define the manner of calculating the Performance Criteria it selects to use for a Performance Period; provided that any dividend equivalents with respect to Performance Share Awards shall be subject to the same terms and conditions, including vesting and forfeiture provisions, of the underlying Award Agreement to which they relate.

(d)Other Share Awards. Other forms of Share Awards valued in whole or in part by reference to, or otherwise based on, Ordinary Shares, including the appreciation in value thereof (e.g., options or share rights with an exercise price or strike price less than 100% of the Fair Market Value of the Ordinary Shares at the time of grant) may be granted either alone or in addition to Share Awards provided for under Section 4 and the preceding provisions of this Section 5. Subject to the provisions of the Plan, the Board will have sole and complete authority to determine the persons to whom and the time or times at which such Other Share Awards will be granted, the number of Ordinary Shares (or the cash equivalent thereof) to be granted pursuant to such Other Share Awards and all other terms and conditions of such Other Share Awards; *provided*, *however*, that where Ordinary Shares are issued pursuant to any Other Share Award, the nominal value of each newly issued Ordinary Share is fully paid up; *and, provided, further, that* any dividend equivalents with respect to such other Share Awards or shall be subject to the same terms and conditions of the underlying Award Agreement to which they relate.

6.COVENANTS OF THE COMPANY.

(a)Availability of Shares. During the terms of the Share Awards, the Company shall keep available at all times the authorized but unissued Ordinary Shares reasonably required to satisfy such Share Awards.

(b)Securities Law Compliance. The Company will seek to obtain from each regulatory commission or agency having jurisdiction over the Plan such authority as may be required to grant Share Awards and to issue and sell Ordinary Shares upon exercise of the Share Awards; provided, however, that this undertaking will not require the Company to register under the Securities Act, the Plan, any Share Award or any Ordinary Shares issued or issuable pursuant to any such Share Award. If, after reasonable efforts and at a reasonable cost, the Company is unable to obtain from any such regulatory commission or agency the authority that counsel for the Company deems necessary for the lawful issuance and sale of Ordinary Shares under the Plan, the Company will be relieved from any liability for failure to issue and sell Ordinary Shares upon exercise of such Share Awards unless and until such authority is obtained. A Participant will not be eligible for the grant of a Share Award or the subsequent issuance of cash or Ordinary Shares pursuant to the Share Award if such grant or issuance would be in violation of any applicable securities law.

(c)No Obligation to Notify or Minimize Taxes. The Company and its Affiliates shall have no duty or obligation to any Participant to advise such holder as to the time or manner of exercising such Share Award. Furthermore, the Company and its Affiliates shall have no duty or obligation to warn or otherwise advise such holder of a pending termination or expiration of a

Share Award or a possible period in which the Share Award may not be exercised. The Company and its Affiliates have no duty or obligation to minimize the tax consequences of a Share Award to the holder of such Share Award.

7.GENERAL TERMS OF AWARDS.

(a)Use of Proceeds from Sales of Ordinary Shares. Proceeds from the sale of Ordinary Shares pursuant to Share Awards will constitute general funds of the Company.

(b)Corporate Action Constituting Grant of Share Awards. Corporate action constituting a grant by the Company of a Share Award to any Participant will be deemed completed as of the date of such corporate action, unless otherwise determined by the Board, regardless of when the instrument, certificate, or letter evidencing the Share Award is communicated to, or actually received or accepted by, the Participant. In the event that the corporate records (e.g., Board consents, resolutions or minutes) documenting the corporate action constituting the grant contain terms (e.g., exercise price, vesting schedule or number of shares) that are inconsistent with those in the Award Agreement or related grant documents as a result of a clerical error in the papering of the Award Agreement or related grant documents, the corporate records will control and the Participant will have no legally binding right to the incorrect term in the Award Agreement or related grant documents.

(c)Shareholder Rights. No Participant will be deemed to be the holder of, or to have any of the rights of a holder with respect to, any Ordinary Shares subject to a Share Award unless and until (i) such Participant has satisfied all requirements for exercise of, or the issuance of Ordinary Shares under, the Share Award pursuant to its terms, and (ii) the issuance of the Ordinary Shares subject to the Share Award has been entered into the books and records of the Company.

(d)No Employment or Other Service Rights. Nothing in the Plan, any Award Agreement or any other instrument executed thereunder or in connection with any Award granted pursuant thereto will confer upon any Participant any right to continue to serve the Company or an Affiliate in the capacity in effect at the time the Award was granted or will affect any right that the Company or an Affiliate may have to terminate (i) the employment of an Employee with or without notice and with or without cause, subject to the employment laws of the country in which the Employee is employed, subject to any applicable provisions of the corporate law of the country or state in which the Company or the Affiliate is incorporated, as the case may be.

(e)Change in Time Commitment. In the event a Participant's regular level of time commitment in the performance of his or her services for the Company and any Affiliates is reduced (for example, and without limitation, if the Participant is an Employee of the Company and the Employee has a change in status from a full-time Employee to a part-time Employee or takes an extended leave of absence) after the date of grant of any Award to the Participant, the Board has the right in its sole discretion to (x) make a corresponding reduction in the number of shares subject to any portion of such Award that is scheduled to vest or become payable after the date of such change in time commitment, and (y) in lieu of or in combination with such a reduction, extend the vesting or payment schedule applicable to such Award. In the event of any

such reduction, the Participant will have no right with respect to any portion of the Award that is so reduced or extended.

(f)Investment Assurances. The Company may require a Participant, as a condition of exercising or acquiring Ordinary Shares under any Share Award, (i) to give written assurances satisfactory to the Company as to the Participant's knowledge and experience in financial and business matters and/or to employ a purchaser representative reasonably satisfactory to the Company who is knowledgeable and experienced in financial and business matters and that the Participant is capable of evaluating, alone or together with the purchaser representative, the merits and risks of exercising the Share Award; and (ii) to give written assurances satisfactory to the Company stating that the Participant is acquiring Ordinary Shares subject to the Share Award for the Participant's own account and not with any present intention of selling or otherwise distributing the Ordinary Shares. The foregoing requirements, and any assurances given pursuant to such requirements, will be inoperative if (A) the issuance of the shares upon the exercise or acquisition of Ordinary Shares under the Share Award has been registered under a then currently effective registration statement under the Securities Act, or (B) as to any particular requirement, a determination is made by counsel for the Company that such requirement need not be met in the circumstances under the then applicable securities laws. The Company may, upon advice of counsel to the Company, place legends on share certificates issued under the Plan as such counsel deems necessary or appropriate in order to comply with applicable securities laws, including, but not limited to, legends restricting the transfer of the Ordinary Shares.

(g)Withholding Obligations. Unless prohibited by the terms of an Award Agreement, the Company or any Affiliate may, in its sole discretion, but subject always to applicable law, satisfy any federal, state, local or foreign tax withholding obligation, or levies or social security deduction obligation relating to an Award by any of the following means or by a combination of such means: (i) causing the Participant to tender a cash payment; (ii) withholding Ordinary Shares from the Ordinary Shares issued or otherwise issuable to the Participant in connection with the Award; provided, however, that no Ordinary Shares are withheld with a value exceeding the maximum amount of tax, levies and social security contribution permitted to be withheld by law or the practice of any revenue authority (or such lesser amount as may be necessary to avoid classification of the Share Award as a liability for financial accounting purposes); (iii) withholding cash from an Award settled in cash; (iv) withholding payment from any amounts otherwise payable to the Participant; or (v) by such other method as may be set forth in the Award Agreement.

(h)Electronic Delivery. Any reference herein to a "written" agreement or document will include any agreement or document delivered electronically, filed publicly at www.sec.gov (or any successor website thereto) or posted on the Company's intranet (or other shared electronic medium controlled by the Company to which the Participant has access).

(i)Deferrals. To the extent permitted by applicable law, the Board, in its sole discretion, may determine that the delivery of Ordinary Shares or the payment of cash, upon the exercise, vesting or settlement of all or a portion of any Award may be deferred and may establish programs and procedures for deferral elections to be made by Participants. Deferrals by Participants will be

made in accordance with Section 409A of the Code. Consistent with Section 409A of the Code, the Board may provide for distributions while a Participant is still an employee or otherwise providing services to the Company or an Affiliate. The Board is authorized to make deferrals of Awards and determine when, and in what annual percentages, Participants may receive payments, including lump sum payments, following the Participant's termination of Continuous Service, and implement such other terms and conditions consistent with the provisions of the Plan and in accordance with applicable law.

(j)Compliance with Section 409A of the Code. To the extent that the Board determines that any Award granted hereunder is subject to Section 409A of the Code, the Award Agreement evidencing such Award shall incorporate the terms and conditions necessary to avoid the consequences specified in Section 409A(a)(1) of the Code. To the extent applicable, the Plan and Award Agreements shall be interpreted in accordance with Section 409A of the Code. If required for compliance with Section 409A of the Code, in no event will a Corporate Transaction or a Change in Control, as applicable, be deemed to have occurred if such transaction is not also a "change in the ownership or effective control of" the Company or "a change in the ownership of a substantial portion of the assets of" the Company as determined under Treasury Regulation Section 1.409A-3(i)(5) (without regard to any alternative definition thereunder). Notwithstanding anything to the contrary in the Plan (and unless the Award Agreement specifically provides otherwise), if the Ordinary Shares are publicly traded, and if a Participant holding an Award that constitutes "deferred compensation" under Section 409A of the Code is a "specified employee" for purposes of Section 409A of the Code, no distribution or payment of any amount that is due because of a "separation from service" (as defined in Section 409A of the Code without regard to alternative definitions thereunder) will be issued or paid before the date that is six months following the date of such Participant's "separation from service" (as defined in Section 409A of the Code without regard to alternative definitions thereunder) or, if earlier, the date of the Participant's death, unless such distribution or payment can be made in a manner that complies with Section 409A of the Code, and any amounts so deferred will be paid in a lump sum on the day after such six month period elapses, with the balance paid thereafter on the original schedule.

(k)Clawback/Recovery. All Awards granted under the Plan will be subject to recoupment in accordance with any clawback policy that the Company is required to adopt pursuant to the listing standards of any national securities exchange or association on which the Company's securities are listed or as is otherwise required by the U.S. Dodd-Frank Wall Street Reform and Consumer Protection Act or other applicable law. In addition, the Board may impose such other clawback, recovery or recoupment provisions in an Award Agreement as the Board determines necessary or appropriate, including but not limited to a reacquisition right in respect of previously acquired Ordinary Shares or other cash or property upon the occurrence of an event constituting Cause. No recovery of compensation under such a clawback policy will be an event giving rise to a right to resign for "good reason" or "constructive termination" (or similar term) under any agreement with the Company or an Affiliate.

(l)Securities Compliance. A Participant will not be issued any shares in respect of an Award unless either (i) the shares are registered under the Securities Act; or (ii) the Company has

determined that such issuance would be exempt from the registration requirements of the Securities Act. Each Award also must comply with other applicable laws and regulations governing the Award, and a Participant will not receive such shares if the Company determines that such receipt would not be in material compliance with such laws and regulations.

(m)Effect on Other Benefit Plans. The value of any Award granted under the Plan, as determined upon grant, vesting or settlement, will not be included as compensation, earnings, salaries, or other similar terms used when calculating any Participant's benefits under any employee benefit plan sponsored by the Company or any Affiliate, except as such plan otherwise expressly provides. The Company expressly reserves its rights to amend, modify, or terminate any of the Company's or any Affiliate's benefit plans.

(n) Press Release. Promptly following the grant of an Award hereunder, the Company must disclose in a press release the material terms of the grant, the number of shares involved, and if required by law or the rules of the Exchange Act, the identity of the Participant and each Participant, by accepting the Award, consents to the foregoing.

8.ADJUSTMENTS UPON CHANGES IN ORDINARY SHARES; OTHER CORPORATE EVENTS.

(a)Capitalization Adjustments. In the event of a Capitalization Adjustment, the Board will appropriately and proportionately adjust: (i) the class(es) and maximum number of securities subject to the Plan pursuant to Section 3(a) and (ii) the class(es) and number of securities and price per share subject to outstanding Awards. The Board will make such adjustments, and its determination will be final, binding and conclusive; provided always that no adjustment may be made which reduces the price payable per Ordinary Share to an amount that is lower than the nominal value of an Ordinary Share.

(b)Dissolution. Except as otherwise provided in the Award Agreement, in the event of a dissolution or liquidation of the Company, all outstanding Share Awards (other than Share Awards consisting of vested and outstanding Ordinary Shares not subject to a forfeiture condition or the Company's or any Affiliate's right of repurchase) will terminate immediately prior to the completion of such dissolution or liquidation, and the Ordinary Shares subject to the Company's or any Affiliate's repurchase rights or subject to a forfeiture condition may be repurchased or reacquired by the Company or an Affiliate in accordance with Irish company law notwithstanding the fact that the holder of such Share Award is providing Continuous Service, provided, however, that the Board may, in its sole discretion, cause some or all Share Awards to become fully vested, exercisable and/or no longer subject to repurchase or forfeiture (to the extent such Share Awards have not previously expired or terminated) before the dissolution or liquidation is completed but contingent on its completion.

(c)Corporate Transaction. Notwithstanding any other provision of the Plan, the Board may take one or more of the following actions in the event of a Corporate Transaction with respect to Share Awards, contingent upon the closing or completion of the Corporate Transaction, unless otherwise provided in the instrument evidencing the Share Award or any other written agreement

between the Company or any Affiliate and the Participant or unless otherwise expressly provided by the Board at the time of grant of a Share Award:

(i)arrange for the surviving corporation or acquiring corporation (or the surviving or acquiring corporation's parent company) to assume or continue the Share Award or to substitute a similar share award for the Share Award (including, but not limited to, an award to acquire the same consideration paid to the shareholders of the Company pursuant to the Corporate Transaction);

(ii)arrange for the assignment of any reacquisition or repurchase rights held by the Company in respect of Ordinary Shares issued pursuant to the Share Award to the surviving corporation or acquiring corporation (or the surviving or acquiring corporation's parent company);

(iii)accelerate the vesting, in whole or in part, of the Share Award (and, if applicable, the time at which the Share Award may be exercised) to a date prior to the effective time of such Corporate Transaction as the Board determines (or, if the Board does not determine such a date, to the date that is five days prior to the effective date of the Corporate Transaction), with such Share Award terminating if not exercised (if applicable) at or prior to the effective time of the Corporate Transaction; provided, however, that the Board may require Participants to complete and deliver to the Company a notice of exercise before the effective date of a Corporate Transaction, which exercise is contingent upon the effectiveness of such Corporate Transaction; provided, however, that the Board may require Participants to complete and deliver to the Company a notice of exercise before the effective date of a Corporate Transaction;

(iv)arrange for the lapse, in whole or in part, of any reacquisition or repurchase rights held by the Company with respect to the Share Award;

(v)cancel or arrange for the cancellation of the Share Award, to the extent not vested or not exercised prior to the effective time of the Corporate Transaction, in exchange for no consideration (U.S. $0) or such cash consideration, if any, as the Board, in its sole discretion, may consider appropriate; and

(vi)cancel or arrange for the cancellation of the Share Award, to the extent not exercised prior to the effective time of the Corporate Transaction, in exchange for a payment, in such form as may be determined by the Board equal to the excess, if any, of (A) the per share amount (or value of property per share) payable to holders of Ordinary Shares in connection with the Corporate Transaction, over (B) the per share exercise price under the applicable Share Award, multiplied by the number of vested shares subject to the Share Award. For clarity, this payment may be zero (U.S. $0) if the amount per share (or value of property per share) payable to the holders of Ordinary Shares is equal to or less than the per share exercise price of the Share Award. In addition, any escrow, holdback, earnout or similar provisions in the definitive agreement for the Corporate Transaction may apply to such payment to the holder of the Share Award to the same extent and in the same manner as such provisions apply generally to the holders of Ordinary Shares.

The Board need not take the same action or actions with respect to all Share Awards or portions thereof or with respect to all Participants. The Board may take different actions with respect to the vested and unvested portions of a Share Award.

(d)Acceleration on a Qualifying Termination in Connection with a Change in Control. If during the period beginning on the date that is 30 days prior to and ending on the date that is 12 months following the consummation of a Corporate Transaction that also qualifies as a Change in Control, (i) a Participant's services to the Company (or its successor in the Change in Control) in all capacities are involuntarily terminated without Cause, or (ii) a Participant resigns service to the Company (or its successor in the Change in Control) in all capacities for Good Reason, and in either case other than as a result of death or Disability, then as of the date of Participant's termination of Continuous Service, the vesting and exercisability of any then-unvested Share Award held by a Participant shall be accelerated in full.

9.AMENDMENT, TERMINATION SUSPENSION OF THE PLAN OR ADOPTION OF SUB-PLANS.

(a)Plan Term. The Board may suspend or terminate the Plan at any time. No Awards may be granted under the Plan while the Plan is suspended or after it is terminated.

(b)Amendments. The Board may amend the Plan in any respect the Board deems necessary or advisable. Except as provided in Section 8(a) relating to Capitalization Adjustments, rights under any Award granted before amendment of the Plan shall not be impaired by any amendment of the Plan unless (1) the Company requests the consent of the affected Participant, and (2) such Participant consents in writing; provided that no amendment that would require shareholder approval under the Nasdaq Stock Market rules may be made effective unless and until the Company's shareholders approve such amendment.

(c)No Impairment of Rights. Amendment, suspension or termination of the Plan will not materially impair rights and obligations under any Award granted while the Plan is in effect except with the written consent of the affected Participant or as otherwise permitted in the Plan.

(d)Sub-Plans. The Board shall be entitled to adopt sub-plans to the Plan pursuant to which Awards may be made on such terms and conditions different from those specified in the Plan as may, in the judgment of the Board, be necessary or desirable in order to recognize differences in local law, tax policy or practices.

10.EFFECTIVE DATE OF PLAN.

The Plan will become effective on the date on which it is adopted by the Board (the "Effective Date"). It is expressly intended that approval of the Company's shareholders not be required as a condition to the effectiveness of the Plan, and the Plan's provisions will be interpreted in a manner consistent with such intent for all purposes.

11.CHOICE OF LAW.

This Plan shall be governed by and construed in accordance with the Irish Companies Act 2014 (as the same may be amended, replaced and/or consolidated in the future) (the "2014 Act") as to matters within the scope thereof, and as to all other matters shall be governed by and construed in accordance with the internal laws of the State of Delaware, without regard to its principles of conflicts of laws.

12.DEFINITIONS. As used in the Plan, the following definitions will apply to the capitalized terms indicated below:

(a) "***Affiliate***" means, at the time of determination, any "parent" or "majority-owned subsidiary" of the Company, as such terms are defined in Rule 405 of the Securities Act or, as the context so requires, means a "holding company" or "subsidiary" of the Company as such terms are defined in Irish company law. The Board will have the authority to determine the time or times at which "parent" or "subsidiary" status is determined within the foregoing definition.

(b)"***Award***" means a Share Award.

(c)"***Award Agreement***" means a written agreement between the Company and a Participant evidencing the terms and conditions of an Award.

(d)"***Board***" means the Board of Directors of the Company.

(e)"***Capitalization Adjustment***" means any change that is made in, or other events that occur with respect to, the Ordinary Shares subject to the Plan or subject to any Share Award after the Effective Date without the receipt of consideration by the Company through merger, consolidation, reorganization, recapitalization, reincorporation, share dividend, dividend in property other than cash, large nonrecurring cash dividend, share split or reverse share split, liquidating dividend, combination of shares, exchange of shares, change in corporate structure, or any similar equity restructuring transaction, as that term is used in Statement of Financial Accounting Standards Board Accounting Standards Codification Topic 718 (or any successor thereto). Notwithstanding the foregoing, the conversion of any convertible securities of the Company will not be treated as a Capitalization Adjustment.

(f)"***Cause***" will have the meaning ascribed to such term in any written agreement between the Participant and the Company defining such term and, in the absence of such agreement, such term means, with respect to a Participant, the occurrence of any of the following events: (i) such Participant's commission of any felony or any crime involving fraud, dishonesty or moral turpitude under the laws of the United States or any state thereof or any country in which a Participant is employed; (ii) such Participant's attempted commission of, or participation in, a fraud or act of dishonesty against the Company or an Affiliate; (iii) such Participant's intentional, material violation of any contract or agreement between the Participant and the Company or an Affiliate, of any statutory duty owed to the Company or an Affiliate; (iv) such Participant's unauthorized use or disclosure of the confidential information or trade secrets of the Company or an Affiliate; or (v) such Participant's gross misconduct. The determination that a termination of the Participant's Continuous Service is either for Cause or without Cause will be

made by the Company, in its sole discretion. Any determination by the Company that the Continuous Service of a Participant was terminated with or without Cause for the purposes of outstanding Share Awards held by such Participant will have no effect upon any determination of the rights or obligations of the Company or an Affiliate or such Participant for any other purpose.

(g)"***Change in Control***" means the consummation, in a single transaction or in a series of related transactions, of any one or more of the following events:

(i)any Exchange Act Person becomes the Owner, directly or indirectly, of securities of the Company representing more than 50% of the combined voting power of the Company's then outstanding securities other than by virtue of a merger, consolidation or similar transaction. Notwithstanding the foregoing, a Change in Control shall not be deemed to occur (A) on account of the acquisition of securities of the Company directly from the Company, (B) on account of the acquisition of securities of the Company by an investor, any affiliate thereof or any other Exchange Act Person that acquires the Company's securities in a transaction or series of related transactions the primary purpose of which is to obtain financing for the Company through the issuance of equity securities, or (C) solely because the level of Ownership held by any Exchange Act Person (the "Subject Person") exceeds the designated percentage threshold of the outstanding voting securities as a result of a repurchase or other acquisition of voting securities by the Company or any Affiliate reducing the number of shares outstanding, provided that if a Change in Control would occur (but for the operation of this sentence) as a result of the acquisition of voting securities by the Company or any Affiliate, and after such share acquisition, the Subject Person becomes the Owner of any additional voting securities that, assuming the repurchase or other acquisition had not occurred, increases the percentage of the then outstanding voting securities Owned by the Subject Person over the designated percentage threshold, then a Change in Control shall be deemed to occur;

(ii)a merger, consolidation or similar transaction involving (directly or indirectly) the Company and, immediately after the consummation of such merger, consolidation or similar transaction, the shareholders of the Company immediately prior thereto do not Own, directly or indirectly, either (A) outstanding voting securities representing more than 50% of the combined outstanding voting power of the surviving Entity in such merger, consolidation or similar transaction or (B) more than 50% of the combined outstanding voting power of the parent of the surviving Entity in such merger, consolidation or similar transaction, in each case in substantially the same proportions as their Ownership of the outstanding voting securities of the Company immediately prior to such transaction;

(iii)the shareholders of the Company approve or the Board approves a plan of complete dissolution or liquidation of the Company, or a complete dissolution or liquidation of the Company shall otherwise occur, except for a liquidation into a parent corporation;

(iv)a sale, lease, exclusive license or other disposition of all or substantially all (as determined by the Board in its sole discretion) of the consolidated assets of the Company and its Subsidiaries, other than a sale, lease, license or other disposition of all or substantially all of the consolidated assets of the Company and its Subsidiaries to an Entity, more than 50% of the

combined voting power of the voting securities of which are Owned by shareholders of the Company in substantially the same proportions as their Ownership of the outstanding voting securities of the Company immediately prior to such sale, lease, license or other disposition; or

(v)individuals who, on the date the Plan is adopted by the Board, are members of the Board (the "Incumbent Board") cease for any reason to constitute at least a majority of the members of the Board; provided, however, that if the appointment or election (or nomination for election) of any new Board member was approved or recommended by a majority vote of the members of the Incumbent Board then still in office, such new member shall, for purposes of this Plan, be considered as a member of the Incumbent Board.

For the avoidance of doubt, any one or more of the above events may be effected pursuant to (i) a compromise or arrangement sanctioned by the Irish courts under Section 450 of the 2014 Act or (ii) a scheme, contract or offer which has become binding on all shareholders pursuant to Section 609 of the 2014 Act, or (iii) a bid pursuant to Regulation 23 or 24 of the European Communities (Takeover Bids (Directive 2004/25/EC)) Regulations 2006.

Notwithstanding the foregoing or any other provision of this Plan, (A) the term Change in Control shall not include a sale of assets, merger or other transaction effected exclusively for the purpose of changing the domicile of the Company, and (B) the definition of Change in Control (or any analogous term) in an individual written agreement between the Company or any Affiliate and the Participant shall supersede the foregoing definition with respect to Awards subject to such agreement; provided, however, that if no definition of Change in Control or any analogous term is set forth in such an individual written agreement, the foregoing definition shall apply.

(h)"***Code***" means the U.S. Internal Revenue Code of 1986, as amended, including any applicable regulations and guidance thereunder.

(i)"***Committee***" means a committee of one or more Directors to whom authority has been delegated by the Board in accordance with Section 2(c).

(j)"***Company***" means Iterum Therapeutics Public Limited Company, a public limited company organized under the laws of Ireland.

(k)"***Continuous Service***" means that the Participant's service with the Company or an Affiliate, whether as an Employee or Director is not interrupted or terminated. A change in the capacity in which the Participant renders service to the Company or an Affiliate as an Employee or Director or a change in the Entity for which the Participant renders such service, provided that there is no interruption or termination of the Participant's service with the Company or an Affiliate, will not terminate a Participant's Continuous Service; provided, however, that if the Entity for which a Participant is rendering services ceases to qualify as an Affiliate, as determined by the Board in its sole discretion, such Participant's Continuous Service will be considered to have terminated on the date such Entity ceases to qualify as an Affiliate. To the extent permitted by law, the Board, the chief executive officer of the Company (or an Affiliate, if

applicable) or the Share Plan Administrator, in that party's sole discretion, may determine whether Continuous Service will be considered interrupted in the case of (i) any leave of absence approved by the Company (or an Affiliate, if applicable), including sick leave, military leave or any other personal leave, or (ii) transfers between the Company, an Affiliate, or their successors. Notwithstanding the foregoing, a leave of absence will be treated as Continuous Service for purposes of vesting in a Share Award only to such extent as may be provided in the Company's (or an Affiliate's, if applicable) leave of absence policy, in the written terms of any leave of absence agreement or policy applicable to the Participant, or as otherwise required by law.

(l)"***Corporate Transaction***" means the consummation, in a single transaction or in a series of related transactions, of any one or more of the following events:

(i)a sale or other disposition of all or substantially all, as determined by the Board, in its sole discretion, of the consolidated assets of the Company and its Subsidiaries;

(ii)a sale or other disposition of at least 50% of the outstanding securities of the Company;

(iii)a merger, consolidation or similar transaction following which the Company is not the surviving corporation; or

(iv)a merger, consolidation or similar transaction following which the Company is the surviving corporation but the Ordinary Shares outstanding immediately preceding the merger, consolidation or similar transaction are converted or exchanged by virtue of the merger, consolidation or similar transaction into other property, whether in the form of securities, cash or otherwise.

For the avoidance of doubt, any one or more of the above events may be effected pursuant to (x) a takeover under Irish takeover rules; (y) a compromise or arrangement under Chapter 1 of Part 9 of the 2014 Act or (z) Chapter 2 of Part 9 of the 2014 Act.

(m)"***Director***" means a member of the Board.

(n)"***Disability***" means, with respect to a Participant, the inability of such Participant to engage in any substantial gainful activity by reason of any medically determinable physical or mental impairment that can be expected to result in death or that has lasted or can be expected to last for a continuous period of not less than twelve (12) months as provided in Sections 22(e)(3) and 409A(a)(2)(c)(i) of the Code, and will be determined by the Board on the basis of such medical evidence as the Board deems warranted under the circumstances.

(o)"***Employee***" means any person employed by the Company or an Affiliate.

(p)"***Entity***" means a corporation, partnership, limited liability company or other entity.

(q)"***Exchange Act***" means the U.S. Securities Exchange Act of 1934, as amended, and the rules and regulations promulgated thereunder.

(r)"***Exchange Act Person***" means any natural person, Entity or "group" (within the meaning of Section 13(d) or 14(d) of the Exchange Act), except that "Exchange Act Person" shall not include (i) the Company or any Subsidiary of the Company, (ii) any employee benefit plan of the Company or any Subsidiary of the Company or any trustee or other fiduciary holding securities under an employee benefit plan of the Company or any Subsidiary of the Company, (iii) an underwriter temporarily holding securities pursuant to a registered public offering of such securities, (iv) an Entity Owned, directly or indirectly, by the shareholders of the Company in substantially the same proportions as their Ownership of Ordinary Shares of the Company; or (v) any natural person, Entity or "group" (within the meaning of Section 13(d) or 14(d) of the Exchange Act) that, as of the Effective Date, is the Owner, directly or indirectly, of securities of the Company representing more than 50% of the combined voting power of the Company's then outstanding securities.

(s)"***Fair Market Value***" means, as of any date, the value of the Ordinary Shares determined as follows:

(i)If the Ordinary Shares is listed on any established stock exchange or traded on the Nasdaq Capital Market, the Fair Market Value of a share of Ordinary Shares, unless otherwise determined by the Board, shall be the closing sales price for such Ordinary Shares as quoted on such exchange or market (or the exchange or market with the greatest volume of trading in the Ordinary Shares) on the day of determination, as reported in a source the Board deems reliable.

(ii)Unless otherwise provided by the Board, if there is no closing sales price for the Ordinary Shares on the day of determination, then the Fair Market Value shall be the closing selling price on the last preceding date for which such quotation exists.

(iii)In the absence of such markets for the Ordinary Shares, the Fair Market Value shall be determined by the Board in good faith and in a manner that complies with Section 409A of the Code.

(t)"***Good Reason***" will have the meaning ascribed to such term in any written agreement between the Participant and the Company or a successor corporation defining such term and, in the absence of such agreement, such term means, with respect to a Participant, any of the following actions taken without Cause without Participant's consent:

(i) A material reduction of the Participant's base compensation, other than a reduction that applies generally to all executives;

(i)A material reduction in the Participant's authority, duties or responsibilities, provided, however, that a change in job position (including a change in title) shall not be deemed a "material reduction" unless the Participant's new authority, duties or responsibilities are materially reduced from the prior authority, duties or responsibilities;

(i)failure or refusal of a successor to the Company to materially assume the Company's obligations under the Participant's offer letter and/or employment agreement, if applicable, in the event of a Change in Control; or

(ii)relocation of the Participant's principal place of employment that results in an increase in the Participant's one-way driving distance by more than 50 miles from the Participant's then current principal residence.

In order to resign for Good Reason, the Participant must provide written notice of the event giving rise to Good Reason to the Company within 90 days after the condition arises, allow the Company at least 30 days to cure such condition, and if the Company fails to cure the condition within such period, then Participant's resignation from all positions the Participant then holds with the Company must be effective not later than 90 days after the end of the Company's cure period.

(u)"***Non-Employee Director***" means a Director who either (i) is not a current employee or officer of the Company or an Affiliate, does not receive compensation, either directly or indirectly, from the Company or an Affiliate for services rendered as a consultant or in any capacity other than as a Director (except for an amount as to which disclosure would not be required under Item 404(a) of Regulation S-K promulgated pursuant to the Securities Act ("Regulation S-K")), does not possess an interest in any other transaction for which disclosure would be required under Item 404(a) of Regulation S-K, and is not engaged in a business relationship for which disclosure would be required pursuant to Item 404(b) of Regulation S-K; or (ii) is otherwise considered a "non-employee director" for purposes of Rule 16b-3.

(v)"***Nonstatutory Share Option***" means an option granted pursuant to Section 4 of the Plan that is not intended to qualify as an "incentive share option" within the meaning of Section 422 of the Code.

(w)"***Officer***" means a person who is an officer of the Company within the meaning of Section 16 of the Exchange Act.

(x)"***Option***" means a Nonstatutory Share Option to purchase Ordinary Shares granted pursuant to the Plan.

(y)"***Ordinary Shares***" or "***Shares***" means the Ordinary Shares in the capital of the Company.

(z)"***Other Share Award***" means an award based in whole or in part by reference to the Ordinary Shares which is granted pursuant to the terms and conditions of Section 5(d).

(aa)"***Own***," "***Owned***," "***Owner***," "***Ownership***" A person or Entity shall be deemed to "Own," to have "Owned," to be the "Owner" of, or to have acquired "Ownership" of securities if such person or Entity, directly or indirectly, through any contract, arrangement, understanding, relationship or otherwise, has or shares voting power, which includes the power to vote or to direct the voting, with respect to such securities.

(bb)"***Participant***" means a person to whom an Award is granted pursuant to the Plan or, if applicable, such other person who holds an outstanding Share Award.

(cc)"***Performance Criteria***" means one or more criteria that the Board will select for purposes of establishing the Performance Goals for a Performance Period. The Performance Criteria that will be used to establish such Performance Goals may be based on any one of, or combination of, the following as determined by the Board: (1) earnings (including earnings per share and net earnings); (2) earnings before interest, taxes and depreciation; (3) earnings before interest, taxes, depreciation and amortization; (4) earnings before interest, taxes, depreciation, amortization and legal settlements; (5) earnings before interest, taxes, depreciation, amortization, legal settlements and other income (expense); (6) earnings before interest, taxes, depreciation, amortization, legal settlements, other income (expense) and share-based compensation; (7) earnings before interest, taxes, depreciation, amortization, legal settlements, other income (expense), share-based compensation and changes in deferred revenue; (8) total shareholder return; (9) return on equity or average shareholder's equity; (10) return on assets, investment, or capital employed; (11) share price; (12) margin (including gross margin); (13) income (before or after taxes); (14) operating income; (15) operating income after taxes; (16) pre-tax profit; (17) operating cash flow; (18) sales or revenue targets; (19) increases in revenue or product revenue; (20) expenses and cost reduction goals; (21) improvement in or attainment of working capital levels; (22) economic value added (or an equivalent metric); (23) market share; (24) cash flow; (25) cash flow per share; (26) share price performance; (27) debt reduction; (28) implementation or completion of projects or processes (including, without limitation, clinical trial initiation, clinical trial enrollment, clinical trial results, new and supplemental indications for existing products, regulatory filing submissions, regulatory filing acceptances, regulatory or advisory committee interactions, regulatory approvals, and product supply); (29) shareholders' equity; (30) capital expenditures; (31) debt levels; (32) operating profit or net operating profit; (33) workforce diversity; (34) growth of net income or operating income; (35) billings; (36) bookings; (37) employee retention; (38) initiation of phases of clinical trials and/or studies by specific dates; (39) patient enrollment rates; (40) budget management; (41) submission to, or approval by, a regulatory body (including, but not limited to the U.S. Food and Drug Administration) of an applicable filing or a product candidate; (42) regulatory milestones; (43) progress of internal research or clinical programs; (44) progress of partnered programs; (45) partner satisfaction; (46) timely completion of clinical trials; (47) submission of INDs and NDAs and other regulatory achievements; (48) research progress, including the development of programs; (49) strategic partnerships or transactions (including in-licensing and out-licensing of intellectual property; (50) customer satisfaction; and (51) other measures of performance selected by the Board.

(dd)"***Performance Goals***" means, one or more goals established by the Board for the Performance Period based upon the Performance Criteria. Performance Goals may be based on a Company-wide basis, with respect to one or more business units, divisions, Affiliates, or business segments, and in either absolute terms or relative to the performance of one or more comparable companies or the performance of one or more relevant indices. Unless specified otherwise by the Board (i) in the Award Agreement at the time the Award is granted or (ii) in such other document setting forth the Performance Goals at the time the Performance Goals are established, the Board will appropriately make adjustments in the method of calculating the

attainment of Performance Goals for a Performance Period as follows: (1) to exclude restructuring and/or other nonrecurring charges; (2) to exclude exchange rate effects; (3) to exclude the effects of changes to generally accepted accounting principles; (4) to exclude the effects of any statutory adjustments to corporate tax rates; (5) to exclude the effects of any items that are unusual in nature or occur infrequently as determined under generally accepted accounting principles; (6) to exclude the dilutive effects of acquisitions or joint ventures; (7) to assume that any business divested by the Company achieved performance objectives at targeted levels during the balance of a Performance Period following such divestiture; (8) to exclude the effect of any change in the outstanding ordinary shares of the Company by reason of any share dividend or split, share repurchase, reorganization, recapitalization, merger, consolidation, spin-off, combination or exchange of shares or other similar corporate change, or any distributions to common shareholders other than regular cash dividends; (9) to exclude the effects of share based compensation and the award of bonuses under the Company's bonus plans; (10) to exclude costs incurred in connection with potential acquisitions or divestitures that are required to be expensed under generally accepted accounting principles; (11) to exclude the goodwill and intangible asset impairment charges that are required to be recorded under generally accepted accounting principles; and (12) to exclude the effect of any other unusual, non-recurring gain or loss or other extraordinary item. In addition, the Board retains the discretion to increase, to reduce or to eliminate the compensation or economic benefit due upon attainment of Performance Goals and to define the manner of calculating the Performance Criteria it selects to use for such Performance Period. Partial achievement of the specified criteria may result in the payment or vesting corresponding to the degree of achievement as specified in the Award Agreement.

(ee)"***Performance Period***" means the period of time selected by the Board over which the attainment of one or more Performance Goals will be measured for the purpose of determining a Participant's right to and the payment of a Share Award. Performance Periods may be of varying and overlapping duration, at the sole discretion of the Board.

(ff)"***Performance Share Award***" means a Share Award granted under the terms and conditions of Section 6(c)(i).

(gg)"***Personal Data***" has the same meaning as defined in the Data Protection Acts 1988 and 2003.

(hh)"***Plan***" means this Iterum Therapeutics Public Limited Company 2021 Inducement Equity Incentive Plan.

(ii)"***Restricted Share Award***" means an award of Ordinary Shares which is granted pursuant to the terms and conditions of Section 5(a).

(jj)"***Restricted Share Unit Award***" means a right to receive Ordinary Shares which is granted pursuant to the terms and conditions of Section 5(b).

(kk)"***Rule 16b-3***" means Rule 16b-3 promulgated under the Exchange Act or any successor to Rule 16b-3, as in effect from time to time.

(ll)"***Securities Act***" means the U.S. Securities Act of 1933, as amended.

(mm)"***Share Appreciation Right***" or "***SAR***" means a right to receive the appreciation on Ordinary Shares that is granted pursuant to the terms and conditions of Section 4.

(nn)"***Share Award***" means any right to receive Ordinary Shares granted under the Plan, including a Nonstatutory Share Option, a Restricted Share Award, a Restricted Share Unit Award, a Share Appreciation Right, a Performance Share Award or any Other Share Award.

(oo)"***Share Plan Administrator***" means one or more Officers or Employees designated by the Board pursuant to Section 2(a).

(pp)"***Subsidiary***" means, with respect to the Company, (i) any corporation of which more than 50% of the outstanding capital shares having ordinary voting power to elect a majority of the board of directors of such corporation (irrespective of whether, at the time, shares of any other class or classes of such corporation will have or might have voting power by reason of the happening of any contingency) is at the time, directly or indirectly, Owned by the Company, and (ii) any partnership, limited liability company or other entity in which the Company has a direct or indirect interest (whether in the form of voting or participation in profits or capital contribution) of more than 50%, or, where the context so requires, the definition of "subsidiary" in Irish company law.

Exhibit 31.1

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Corey Fishman, certify that:

1.I have reviewed this Quarterly Report on Form 10-Q of Iterum Therapeutics plc;

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

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

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

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

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

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

(d)Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

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

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

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

Date: November 10, 2022

By: /s/ Corey Fishman
Corey Fishman
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Judith Matthews, certify that:

1.I have reviewed this Quarterly Report on Form 10-Q of Iterum Therapeutics plc;

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

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

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

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

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

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

(d)Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

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

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

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

Date: November 10, 2022

By: /s/ Judith Matthews
Judith Matthews
Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Quarterly Report on Form 10-Q of Iterum Therapeutics plc (the "Company") for the period ended September 30, 2022, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Corey Fishman, President and Chief Executive Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to his knowledge on the date hereof:

(1)The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

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

Date: November 10, 2022

By: /s/ Corey Fishman
Corey Fishman
President and Chief Executive Officer
(Principal Executive Officer)

This certification accompanies the Form 10-Q to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of Iterum Therapeutics plc under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-Q), irrespective of any general incorporation language contained in such filing.

Exhibit 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Quarterly Report on Form 10-Q of Iterum Therapeutics plc (the "Company") for the period ended September 30, 2022 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Judith Matthews, Chief Financial Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to her knowledge on the date hereof:

(1)The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

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

Date: November 10, 2022

By: /s/ Judith Matthews
Judith Matthews
Chief Financial Officer
(Principal Financial and Accounting Officer)

This certification accompanies the Form 10-Q to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of Iterum Therapeutics plc under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-Q), irrespective of any general incorporation language contained in such filing.