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**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
WASHINGTON, DC 20549**

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**FORM 10-Q**

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(Mark One)

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

For the quarterly period ended March 31, 2019

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**  
(State or other jurisdiction of  
incorporation or organization)

**98-1283148**  
(I.R.S. Employer  
Identification No.)

**Block 2 Floor 3, Harcourt Centre,  
Harcourt Street,  
Dublin 2, Ireland**  
(Address of principal executive offices)

**Not applicable**  
(Zip Code)

**(+353) 1 903-8920**  
(Registrant's telephone number, including area code)

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days.

Yes ☒ No ☐

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

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

Large accelerated filer ☐

Accelerated filer ☐

Non-accelerated filer ☒

Smaller reporting company ☒

Emerging growth company ☒

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

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

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

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

As of April 30, 2019, the registrant had 14,369,218 ordinary shares, \$0.01 par value per share, outstanding.

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## SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

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 initiation, timing, progress and results of our preclinical studies and clinical trials, and our research and development programs;
- 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;
- the commercialization of our product candidates, if approved;
- our ability to draw down our second term loan with Silicon Valley Bank;
- 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;
- 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; and
- developments relating to our competitors and our industry.

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.

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.

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

	March 31, 2019	December 31, 2018
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 64,603	\$ 44,551
Short-term investments	4,997	40,000
Prepaid expenses and other current assets	7,188	8,390
Current portion of restricted cash	30	30
Total current assets	76,818	92,971
Property and equipment, net	675	700
Restricted cash, less current portion	90	90
Other assets	11,551	4,110
<b>Total assets</b>	<b>\$ 89,134</b>	<b>\$ 97,871</b>
<b>Liabilities and Shareholders' Equity</b>		
Current liabilities:		
Accounts payable	\$ 6,176	\$ 4,041
Accrued expenses	8,696	7,046
Current portion of long-term debt	2,056	1,019
Income taxes payable	248	113
Other current liabilities	442	—
Total current liabilities	17,618	12,219
Long-term debt, less current portion	12,139	13,079
Other liabilities	7,747	951
Total liabilities	\$ 37,504	\$ 26,249
Commitments and contingencies (Note 12)		
Shareholders' equity:		
Ordinary shares, \$0.01 par value per share: 50,000,000 shares authorized at March 31, 2019 and December 31, 2018; 14,367,441 shares issued at March 31, 2019; 14,352,046 shares issued at December 31, 2018	144	144
Additional paid-in capital	203,859	203,271
Accumulated deficit	(152,373)	(131,793)
Total shareholders' equity	51,630	71,622
<b>Total liabilities and shareholders' equity</b>	<b>\$ 89,134</b>	<b>\$ 97,871</b>

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 March 31,	
	2019	2018
Revenue	\$ 37	\$ 191
Operating expenses:		
Research and development	\$ (17,387 )	\$ (10,879 )
General and administrative	(3,116 )	(1,515 )
Total operating expenses	(20,503 )	(12,394 )
Operating loss	(20,466 )	(12,203 )
Interest (expense) / income, net	(104 )	85
Other income, net	124	61
Total other income	20	146
Loss before income taxes	(20,446 )	(12,057 )
Income tax expense	(134 )	(89 )
Net loss and comprehensive loss	(20,580 )	(12,146 )
Net loss attributable to ordinary shareholders	\$ (20,580 )	\$ (12,146 )
Net loss per share attributable to ordinary shareholders – basic and diluted	\$ (1.44 )	\$ (61.36 )
Weighted average ordinary shares outstanding – basic and diluted	14,290,437	197,949

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)

	<b>Three Months Ended March 31,</b>	
	<b>2019</b>	<b>2018</b>
<b>Cash flows from operating activities:</b>		
Net loss	\$ (20,580 )	\$ (12,146 )
Adjustments to reconcile net loss to cash used in operating activities:		
Depreciation	35	31
Share-based compensation expense	540	149
Gain on short term investments	(88 )	—
Non-cash gain on short term investments	(9 )	(23 )
Interest on short-term investments	(11 )	—
Amortization of SVB loan	98	—
Other	29	—
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	1,193	(793 )
Other assets	(191 )	(52 )
Accounts payable	2,135	422
Accrued expenses	1,662	692
Income taxes	134	82
Other liabilities	—	(2 )
Net cash used in operating activities	(15,053 )	(11,640 )
<b>Cash flows from investing activities:</b>		
Purchases of property and equipment	(10 )	(21 )
Purchases of short-term investments	—	(6,372 )
Proceeds from sale of short-term investments	35,100	15,750
Net cash generated by investing activities	35,090	9,357
<b>Cash flows from financing activities:</b>		
Proceeds from issuance of Series B convertible preferred shares, net of issuance costs	—	32,176
Proceeds from exercise of shares options	49	—
Net cash provided by financing activities	49	32,176
Effect of exchange rates on cash and cash equivalents	(34 )	—
Net increase in cash, cash equivalents and restricted cash	20,052	29,893
Cash, cash equivalents and restricted cash, at beginning of period	44,671	8,485
Cash, cash equivalents and restricted cash, at end of period	<b>\$ 64,723</b>	<b>\$ 38,378</b>
<b>Supplemental Disclosure of Cash Flow Information:</b>		
Income tax paid—U.S.	\$ —	\$ —
Interest paid	\$ 350	\$ —

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

**ITERUM THERAPEUTICS PLC**  
**Notes to Condensed Consolidated Financial Statements**  
(In thousands, except share and per share data)  
(Unaudited)

**1. Basis of Presentation**

Iterum Therapeutics plc (the “Company”) was incorporated under the laws of the state 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 Block 2 Floor 3, Harcourt Centre, Harcourt Street, 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 and only oral and intravenous (IV) branded penem available globally.

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 of ordinary and convertible preferred shares, debt raised under a financing arrangement with Silicon Valley Bank (SVB) and a sub-award from the Trustees of Boston University under the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X) program. The Company has not generated any product revenue. 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 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 significant additional research and development efforts, including preclinical and clinical testing and 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.

On May 15, 2018, the Company’s shareholders approved a consolidation of its ordinary shares and convertible preferred shares at a 1-for-15.71 ratio (the “Reverse Share Split”), effective on that date. Fractional entitlements to ordinary shares and convertible preferred shares arising as a result of the Reverse Share Split were rounded down to the nearest whole number for each holder of ordinary shares and convertible preferred shares. Those fractional entitlements were aggregated and surrendered to the Company for cancellation. Immediately following the Reverse Share Split, the Company redenominated its ordinary shares and convertible preferred shares from \$0.01571 (the nominal value resulting from the Reverse Share Split) per share to \$0.01 per share (the “Renominalisation”). All issued and outstanding ordinary shares, convertible preferred shares, options for ordinary shares, restricted share awards, warrants and per share amounts have been retroactively adjusted to reflect this Reverse Share Split and Renominalisation for all periods presented.

On May 30, 2018, the Company completed an initial public offering (IPO) of its ordinary shares, and issued and sold 6,150,000 ordinary shares at a public offering price of \$13.00 per share, resulting in net proceeds of \$71.8 million after deducting underwriting discounts and commissions and offering costs payable by the Company. On June 26, 2018, the Company issued and sold an additional 200,000 ordinary shares at the IPO price of \$13.00 per share pursuant to the underwriters’ partial exercise of their option to purchase additional ordinary shares, resulting in additional net proceeds of \$2.4 million after deducting underwriting discounts and commissions and offering costs payable by the Company. Aggregate net proceeds from the IPO totaled \$74.2 million after deducting underwriting discounts and commissions and offering costs payable by the Company.

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 the quarterly condensed consolidated financial statements.

The Company has incurred operating losses since inception, including net losses of \$20,580 and \$12,146 for the three months ended March 31, 2019 and 2018, respectively, and a net loss of \$77,056 for the year ended December 31, 2018. The Company had an accumulated deficit of \$152,373 as of March 31, 2019. The Company expects to continue to incur net losses for the foreseeable future and is highly dependent on its ability to find additional sources of funding in the form of debt or equity financing to fund its operations. Management believe that its cash and cash equivalents balance of \$64,603 and short-term investments balance of \$4,997 at March 31, 2019, together with the \$15.0 million potentially available under the secured credit facility with SVB, are sufficient to fund operations for at least one year from the date the condensed consolidated financial statements are issued. In making this assessment management have considered the Company’s available cash resources, future financing options available to the Company, the planned operations of the Company and the ability to adjust its plans if required. The \$15.0 million under the secured credit facility with SVB



**ITERUM THERAPEUTICS PLC**  
**Notes to Condensed Consolidated Financial Statements**  
(In thousands, except share and per share data)  
(Unaudited)

will be available to the Company through October 31, 2019, upon satisfaction of either (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 inability to obtain funding, as and when needed, would have a negative impact on the Company's financial condition and ability to pursue its business strategies. If the Company is unable to obtain funding, the Company could be forced to delay, reduce or eliminate some or all of its research and development programs or commercialization efforts, which could adversely affect its business prospects.

The Company expects to seek additional funding in order to continue to fund its operations through public or private financing of debt or equity or collaboration agreements. Although management intends to pursue plans to obtain additional funding to finance its operations, there is no assurance that the Company will be successful in obtaining sufficient funding on terms acceptable to the Company to fund continuing operations, if at all.

The accompanying condensed consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty. Accordingly, the condensed consolidated financial statements have been prepared on a basis that assumes the Company will continue as a going concern and which contemplates the realization of assets and satisfaction of liabilities and commitments in the ordinary course of business.

**Interim Financial Information**

The condensed consolidated balance sheet at December 31, 2018 was derived from audited financial statements, but does not include all disclosures required by GAAP. The accompanying unaudited condensed consolidated financial statements as of March 31, 2019, 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, 2018, included in the Company's Annual Report on Form 10-K filed with the SEC on March 25, 2019. 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 March 31, 2019, and results of operations for the three months ended March 31, 2019 and 2018, and cash flows for the three months ended March 31, 2019 and 2018 have been made. The results of operations for the three months ended March 31, 2019 are not necessarily indicative of the results of operations that may be expected for the year ending December 31, 2019.

**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 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, 2018.

***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 accrual for research and development expenses, revenue from grant awards, the valuation of restricted ordinary shares and the valuation of share-based compensation awards. 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.

**ITERUM THERAPEUTICS PLC**  
**Notes to Condensed Consolidated Financial Statements**  
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**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 ordinary shares underlying the convertible preferred shares and options, the unvested restricted ordinary shares, restricted share units, performance restricted share units and the warrants have been excluded from the calculation because they would be anti-dilutive.

The following potentially dilutive securities have been excluded from the computation of diluted weighted-average shares outstanding as they would be anti-dilutive:

	Three Months Ended	
	March 31, 2019	March 31, 2018
Options to purchase ordinary shares	1,091,238	248,128
Preferred shares convertible into ordinary shares	—	7,396,313
Unvested restricted ordinary shares	60,250	163,523
Unvested restricted share units	36,924	—
Unvested performance restricted share units	50,000	—
Warrants	19,890	—
<b>Total</b>	<b>1,258,302</b>	<b>7,807,964</b>

**Segment Information**

The Company determines and presents operating segments based on the information that is internally provided to the Chief Executive Officer, Chief Scientific Officer and Chief Financial 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:

Operating expenses	Three Months Ended	
	March 31, 2019	March 31, 2018
Ireland	\$ 17,436	\$ 9,964
U.S.	3,067	2,430
<b>Total</b>	<b>\$ 20,503</b>	<b>\$ 12,394</b>

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

Long lived assets	March 31, 2019	December 31, 2018
Ireland	\$ 9,970	\$ 4,565
U.S.	2,256	245
<b>Total</b>	<b>\$ 12,226</b>	<b>\$ 4,810</b>

**Recently Adopted Accounting Pronouncements**

In February 2016, the Financial Accounting Standards Board (FASB) issued ASU 2016-02, *Leases* (Topic 842) in order to increase transparency and comparability among organizations by recognizing lease assets and lease liabilities on the balance sheet for those leases classified as operating leases under prior GAAP. In July 2018, the FASB issued ASU 2018-11 *Leases* (Topic 842): *Targeted Improvements* which provides the option to adopt the standard retrospectively for each prior period presented, as initially set out in ASU 2016-02, or as of the adoption date with a cumulative-effect adjustment to the opening balance of retained earnings. In March 2019, the FASB issued ASU 2019-03 *Leases* (Topic 842): *Codification Improvements* amending the transition disclosures for Topic 842, in that all companies are exempt from certain interim period transition disclosure requirements.

ASU 2016-02 requires a lessee to recognize a liability to make lease payments (the lease liability) and a right-of-use asset, representing its right to use the underlying asset for the lease term, on the balance sheet. The Company adopted ASU 2016-02 in the

**ITERUM THERAPEUTICS PLC**  
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first quarter of 2019 utilizing the modified retrospective transition method with an effective date as the date of initial application. Consequently, prior period balances and disclosures have not been restated. The adoption of ASU 2016-02 on January 1, 2019 resulted in the recognition of right-of-use assets of \$7.6 million and operating lease liabilities of \$7.8 million, however, the adoption of the standard did not have an impact on the Company's beginning retained earnings, results from operations or cash flows. See Note 7 for further information regarding the impact of the adoption of ASU 2016-02 on the Company's financial statements.

In July 2017, the FASB issued ASU 2017-11, *Earnings Per Share* (Topic 260), *Distinguishing Liabilities from Equity* (Topic 480), *Derivatives and Hedging* (Topic 815), I. Accounting for Certain Financial Instruments with Down Round Features, II. Replacement of the Indefinite Deferral for Mandatorily Redeemable Financial Instruments of Certain Nonpublic Entities and Certain Mandatorily Redeemable Noncontrolling Interests with a Scope Exception.

Part I applies to entities that issue financial instruments such as warrants, convertible debt or convertible preferred shares that contain down-round features. Part II replaces the indefinite deferral for certain mandatorily redeemable noncontrolling interests and mandatorily redeemable financial instruments of nonpublic entities contained within ASC Topic 480 with a scope exception and does not impact the accounting for these mandatorily redeemable instruments. ASU 2017-11 is required to be adopted for annual periods beginning after December 15, 2018, including interim periods within those fiscal years. The adoption of ASU 2017-11 did not have an impact on the 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 March 31, 2019 and December 31, 2018 and indicates the fair value hierarchy of the valuation inputs utilized to determine such fair value.

<b>March 31, 2019</b>				
<b>Assets</b>	<b>Total</b>	<b>Level 1</b>	<b>Level 2</b>	<b>Level 3</b>
Short-term investments	\$ 4,997	\$ 4,997	—	—
Other asset – advance payment to supplier	2,617	—	—	2,617
<b>Total</b>	<b>\$ 7,614</b>	<b>4,997</b>	<b>—</b>	<b>2,617</b>
<b>December 31, 2018</b>				
<b>Assets</b>	<b>Total</b>	<b>Level 1</b>	<b>Level 2</b>	<b>Level 3</b>
Short-term investments	\$ 40,000	40,000	—	—
Other asset – advance payment to supplier	2,649	—	—	2,649
<b>Total</b>	<b>\$ 42,649</b>	<b>40,000</b>	<b>—</b>	<b>2,649</b>

See Note 4 for further details on the short-term investments held. The other asset above relates to advance payments made to a supplier that were recorded at fair value using the discounted cash flow model (DCF) as of March 31, 2019 and December 31, 2018. The fair value measurements of these advance payments were determined based on significant unobservable inputs, including a discount rate of 15% and the expected time to recovery of the payment. Changes to the inputs described above are not expected to have a material impact on the company's financial position and results of operations in any given period. See Note 12—Payments to Supplier, for further details on these advance payments.

The following table presents information about the Company's long-term debt which was carried at amortized cost on the condensed consolidated balance sheet as of March 31, 2019 and December 31, 2018 and indicates the fair value hierarchy of the valuation inputs utilized to determine the approximate fair value.

**ITERUM THERAPEUTICS PLC**  
**Notes to Condensed Consolidated Financial Statements**  
(In thousands, except share and per share data)  
(Unaudited)

<b>March 31, 2019</b>					
<b>Liabilities</b>	<b>Book Value</b>	<b>Approximate Fair Value</b>	<b>Level 1</b>	<b>Level 2</b>	<b>Level 3</b>
Current portion of long-term debt	\$ 2,056	\$ 2,056	—	2,056	—
Long-term debt, less current portion	12,139	11,850	—	11,850	—
<b>Total</b>	<b>\$ 14,195</b>	<b>\$ 13,906</b>	<b>—</b>	<b>13,906</b>	<b>—</b>
<b>December 31, 2018</b>					
<b>Liabilities</b>	<b>Book Value</b>	<b>Approximate Fair Value</b>	<b>Level 1</b>	<b>Level 2</b>	<b>Level 3</b>
Current portion of long-term debt	\$ 1,019	\$ 1,019	—	1,019	—
Long-term debt, less current portion	13,079	13,035	—	13,035	—
<b>Total</b>	<b>\$ 14,098</b>	<b>\$ 14,054</b>	<b>—</b>	<b>14,054</b>	<b>—</b>

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 debt, less current portion was determined based on a DCF analysis using quoted market interest rates, without consideration of transaction costs, which represents a Level 2 basis of fair value measurement. The counterparty to the long-term debt is a major international financial institution.

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.

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 with maturities of more than three months but less than one year at the date of purchase. Short-term investments as of March 31, 2019 have an average maturity of 0.12 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 are 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 March 31, 2019 and December 31, 2018:

<b>March 31, 2019</b>					
				<b>Maturity by period</b>	
<b>Available for sale</b>	<b>Cost Total</b>	<b>Unrealized gains</b>	<b>Unrealized (losses)</b>	<b>Fair Value Total</b>	<b>Less than 1 year</b>
Commercial paper	\$ 4,986	11	—	4,997	4,997
<b>December 31, 2018</b>					
				<b>Maturity by period</b>	
<b>Available for sale</b>	<b>Cost Total</b>	<b>Unrealized gains</b>	<b>Unrealized (losses)</b>	<b>Fair Value Total</b>	<b>Less than 1 year</b>
Commercial paper	\$ 35,745	272	(9)	36,008	36,008
U.S. Treasury and Agency Bonds	3,977	15	—	3,992	3,992
<b>Total</b>	<b>\$ 39,722</b>	<b>287</b>	<b>(9)</b>	<b>40,000</b>	<b>40,000</b>

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**5. Prepaid Expenses and Other Current Assets**

Prepaid expenses and other current assets consist of the following:

	March 31, 2019	December 31, 2018
Prepaid research and development expenses	\$ 5,315	\$ 5,351
Short-term deposits	873	959
Research and development tax credit receivable	395	404
Prepaid insurance	245	438
Interest receivable	151	158
Other prepaid assets	141	921
Value added tax receivable	68	159
Total	\$ 7,188	\$ 8,390

**6. Property and Equipment**

Property and equipment and related accumulated depreciation are as follows:

	March 31, 2019	December 31, 2018
Leasehold improvements	\$ 592	\$ 592
Furniture and fixtures	120	120
Laboratory equipment	81	81
Computer equipment	118	108
	911	901
Less: accumulated depreciation	(236)	(201)
	\$ 675	\$ 700

Depreciation expense was \$35 for the three months ended March 31, 2019 and \$136 for the year ended December 31, 2018.

**7. Leases**

The Company has entered into a number of operating leases, primarily for office space and commercial property. These leases have terms which range from six to 19 years, and generally include one or more options to terminate or renew. The termination options can reduce the lease term for periods ranging from five to 10 years, however the remaining lease terms do not represent these early termination dates as management have concluded that it is reasonably certain that the Company will not exercise these options. The renewal terms can extend the lease term for additional periods ranging from three to five years. These renewal options are represented in the remaining lease term as management have concluded that it is reasonably certain that the Company will exercise the renewal option. 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 expense is recognized on a straight-line basis over the lease term. The Company recognized \$254 of operating lease costs for right-of-use assets during the three months ended March 31, 2019.

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

	<b>Three Months Ended March 31, 2019</b>
Cash paid for operating lease liabilities	\$ 190
Right-of-use assets obtained in exchange for new operating lease obligation(1)	\$ 7,622
Weighted-average remaining lease term	13.2 years
Weighted-average discount rate	7.6%

(1) All operating leases included above were held at January 1, 2019

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"):

	<b>March 31, 2019</b>
Other assets	\$ 7,504
Other current liabilities	\$ 442
Other liabilities	7,117
Total lease liabilities	\$ 7,559

Future lease payments included in the measurement of lease liabilities on the condensed consolidated balance sheet as of March 31, 2019, for the following five fiscal years and thereafter were as follows:

<b>Due in 12 month period ended March 31,</b>	
2020	\$ 982
2021	1,017
2022	1,022
2023	1,033
2024	1,038
Thereafter	6,420
	\$ 11,512
Less imputed interest	(3,953)
Total lease liabilities	\$ 7,559

As of December 31, 2018, future minimum lease payments, as defined under the previous lease accounting guidance of ASC Topic 840, under non-cancelable operating leases for the following five fiscal years and thereafter were as follows:

<b>Due in 12 month period ended December 31,</b>	
2019	\$ 904
2020	1,020
2021	1,030
2022	985
2023	766
Thereafter	2,356
	\$ 7,061

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**8. Accrued Expenses**

Accrued expenses consist of the following:

	March 31, 2019	December 31, 2018
Accrued clinical trial costs	\$ 6,383	\$ 2,849
Accrued manufacturing expenses	859	1,439
Accrued other expenses	843	954
Accrued payroll and bonus expenses	611	1,804
<b>Total</b>	<b>\$ 8,696</b>	<b>\$ 7,046</b>

**9. Shareholders' Equity**

The following tables present a reconciliation of our beginning and ending balances in shareholders' equity for the three months ended March 31, 2019 and 2018:

	Total Shareholders' Equity
Shareholders' equity at January 1, 2019	\$ 71,622
Exercise of share options	48
Share-based compensation expense	540
Net loss	(20,580)
<b>Shareholders' equity at March 31, 2019</b>	<b>\$ 51,630</b>

	Total Shareholders' Equity
Shareholders' equity at January 1, 2018	\$ 39,494
Issuance of Series B convertible preferred shares, net	32,159
Share-based compensation expense	149
Net loss	(12,146)
<b>Shareholders' equity at March 31, 2018</b>	<b>\$ 59,656</b>

**10. 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 223,424 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 is 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 219,605 shares to 443,029 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 our IPO in May 2018. 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, adopted and approved on March 14, 2018, authorized the Company to grant up to 1,018,459 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 will be added back to the ordinary shares available for issuance under the 2018 Plan.

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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 574,081 ordinary shares.

***Restricted Ordinary Shares***

In connection with the Company's formation, 413,110 restricted ordinary shares were issued on October 14, 2015 to the Company's founders at par value. These ordinary shares are subject to various restrictions pursuant to ordinary share purchase agreements between the Company and each founder, including restrictions on transfer and a Company right of repurchase. The restricted ordinary shares were 25% vested as of October 14, 2016 and 1/36th of the remaining restricted ordinary shares vest on a monthly basis thereafter (subject to acceleration of vesting in connection with certain change of control transactions). A change in status occurred on November 18, 2015 when the founders became employees of the Company. The grant date of these shares is now considered to be November 18, 2015 when the fair value was \$3.14 per share.

The Company records share-based compensation expense for the restricted ordinary shares based on the grant date fair value. The Company recorded an expense of \$85 and \$82 for the three months ended March 31, 2019 and 2018, respectively. Total unamortized compensation expense related to restricted ordinary shares was \$175 and \$510 as of March 31, 2019 and March 31, 2018, respectively, expected to be recognized over a weighted average period of 0.54 years and 1.54 years as of March 31, 2019 and March 31, 2018, respectively.

The following table summarizes restricted ordinary shares activity for the three months ended March 31, 2019:

	Number of Shares	Weighted Average Grant Date Fair Value per Share
Unvested at December 31, 2018	86,068	\$ 3.14
Granted	—	
Vested	(25,818)	\$ 3.14
Forfeited	—	
Unvested at March 31, 2019 (unaudited)	60,250	\$ 3.14

***Share Options***

The Company granted 442,500 share options to employees and directors during the three months ended March 31, 2019. The Company awarded 74,152 share options to employees during the three months ended March 31, 2018 under the 2018 Plan. These options were granted and priced upon execution of the underwriting agreement related to the IPO in May 2018. There were 984,913 and 221,553 unvested employee options outstanding as of March 31, 2019 and March 31, 2018, respectively. Total expense recognized related to the employee share options was \$307 and \$67 for the three months ended March 31, 2019 and 2018, respectively. Total unamortized compensation expense related to employee share options was \$4,168 and \$1,132 as of March 31, 2019 and March 31, 2018, respectively, which is expected to be recognized over a remaining average vesting period of 3.30 years and 3.27 years as of March 31, 2019 and March 31, 2018, respectively.

The assumptions that the Company used to determine the grant date fair value of employee and director options granted were as follows, presented on a weighted average basis:

	Three Months Ended March 31,	
	2019	2018
Volatility	69.5% - 70.2%	60%
Expected term in years	6.25	6.25
Dividend rate	0%	0%
Risk-free interest rate	2.44% - 2.57%	1.63%
Share price	\$5.80 - \$6.80	—
Fair value of option on grant date	\$3.74 - \$4.41	—



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The following table summarizes the number of options outstanding and the weighted-average exercise price:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Life in Years	Aggregate Intrinsic Value (in thousands)
Options outstanding December 31, 2018	665,219	\$ 9.31	8.93	395
Granted	442,500	5.82		
Exercised	(15,395)	3.16		
Forfeited	(1,086)	9.44		
Options outstanding March 31, 2019	1,091,238	\$ 7.98	9.27	1,956
Exercisable at March 31, 2019 (unaudited)	106,325	\$ 4.59	8.25	425

***Restricted share units (RSUs)***

No RSUs were awarded to directors during the three months ended March 31, 2019. No RSUs were awarded or outstanding during the three months ended March 31, 2018.

The table below shows the number of RSUs granted covering an equal number of our ordinary shares and the weighted-average grant date fair value of the RSUs granted:

	Number of Shares	Weighted Average Grant Date Fair Value per Share
RSUs outstanding December 31, 2018	36,924	\$ 13.00
Granted	—	
Shares vested	—	
Forfeited	—	
RSUs outstanding March 31, 2019	36,924	\$ 13.00

The fair value of RSUs is determined on the date of grant based on the market price of our ordinary shares on that date. The fair value of RSUs is expensed ratably over the vesting period, which is generally one year for directors. Total expense recognized related to the RSUs was \$119 for the three months ended March 31, 2019. Total unamortized compensation expense related to RSUs was \$72 as of March 31, 2019, which is expected to be recognized over a remaining average vesting period of 0.15 years as of March 31, 2019.

The Company awarded 50,000 RSUs to certain employees during the three months ended March 31, 2019 which are subject to certain performance based vesting conditions (Performance RSUs). No Performance RSUs were awarded or outstanding during the three months ended March 31, 2018.

The table below shows the number of Performance RSUs granted covering an equal number of our ordinary shares and the weighted-average grant date fair value of the Performance RSUs granted:

	Number of Shares	Weighted Average Grant Date Fair Value per Share
Performance RSUs outstanding December 31, 2018	—	
Granted	50,000	\$ 8.21
Shares vested	—	
Forfeited	—	
Performance RSUs outstanding March 31, 2019	50,000	\$ 8.21

The weighted average grant date fair value of restricted share units with a market condition was determined using the Monte Carlo simulation model. The fair value of Performance RSUs is expensed ratably over the vesting period. Total expense recognized related to the Performance RSUs was \$29 for the three months ended March 31, 2019. Total unamortized compensation expense

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related to Performance RSUs was \$381 as of March 31, 2019, which is expected to be recognized over approximately the next 1.56 years as of March 31, 2019.

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

	Three Months Ended March 31,	
	2019	2018
Research and development expense	\$ 163	\$ 71
General and administrative expense	377	78

There was a total of \$4,796 and \$1,642 unamortized share-based compensation expense for restricted ordinary shares, options, restricted share units and performance restricted share units as of March 31, 2019 and March 31, 2018, respectively, which is expected to be recognized over a remaining average vesting period of 2.98 years and 2.32 years as of March 31, 2019 and March 31, 2018, respectively.

## 11. Income Taxes

In accordance with the FASB ASC Topic No. 270 *"Interim Reporting"* and ASC Topic No. 740 *"Income Taxes"* (Topic No. 740) 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 three months ended March 31, 2019 and 2018, the Company recorded an income tax expense of \$134 and \$89, 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 March 31, 2019, and December 31, 2018, the Company has net operating loss carryforwards in Ireland of approximately \$16,183 and \$13,648, 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.

## 12. 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.

As part of the license agreement, 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.

### *Payments to Supplier*

In June 2016, the Company entered into an agreement with a supplier whereby the Company would pay \$2,805 to the supplier to acquire equipment which will be used solely to manufacture product for the Company. In June 2018, the Company entered into a supplemental agreement with this supplier whereby the Company would pay an additional \$2,300 under the same terms as the original agreement. These payments will be offset against the price of the product to be supplied under a future supply agreement. \$1,571 and \$1,604 remained outstanding to the supplier as of March 31, 2019 and December 31, 2018, respectively.

### *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

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the authoritative guidelines that address accounting for contingencies. The Company expenses costs as incurred in relation to such legal proceedings. The Company is not currently involved in any legal matters arising in the normal 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.

### 13. Debt

On April 27, 2018, the Company's 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 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 and the other \$15.0 million is available at the Company's option upon the satisfaction of either of the following conditions which are referred to as the Second Draw Conditions: (i) the achievement of both non-inferiority and superiority primary endpoints from the Company's Phase 3 uUTI clinical trial and reporting satisfactory safety data; or (ii) the achievement of non-inferiority primary endpoints from both of the Company's Phase 3 uUTI and cUTI clinical trials as well as reporting satisfactory safety data, in each case as determined by SVB at its sole discretion. The Company's option to draw the second term loan will terminate upon the earliest to occur of October 31, 2019, the thirtieth day following the occurrence of either of the Second Draw Conditions, or the occurrence of an event of default. A non-utilization fee of 1.50% of the aggregate undrawn principal amount shall apply if the Company satisfies the Second Draw Conditions but chooses not to draw down the second term loan. The principal borrowed under the secured credit facility bears interest 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, which interest is payable monthly in arrears.

The initial draw requires monthly amortization payments commencing November 1, 2019, which will be extended to April 1, 2020 if the second draw is made. All outstanding principal, plus a 4.2% final payment fee, will be due and payable on the earliest to occur of March 1, 2022 (Maturity Date), the acceleration of either term loan or the prepayment of either term loan. The final payment fee of \$0.6 million, which represents 4.2% of the funded loan, is accreted using the effective interest method over the life of the loan as interest expense.

The secured credit facility draws are subject to prepayment fees of 3.00% in the first year, 2.00% in the second year and 1.00% thereafter in the event of prepayment at any time prior to the Maturity Date.

In connection with the initial \$15.0 million draw, the Company issued to SVB and Life Sciences Fund II LLC (LSF) warrants to purchase an aggregate of 19,890 Series B-2 preferred shares (which converted to ordinary shares upon the Company's IPO) at an exercise price of \$18.85 per share. If the Company draws down the second term loan, each of SVB and LSF will be entitled, pursuant to additional share warrants issued to each of them at closing, to purchase such number of additional ordinary shares in an aggregate amount equal to 2.5% of the funded amount, divided by the applicable exercise price. Obligations under the secured credit facility are secured by substantially all of the Company's existing and future assets and the existing and future assets of the Company's subsidiaries, including intellectual property.

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 are being amortized using the effective interest rate method over the term of the loan. The effective annual interest rate of the outstanding debt is approximately 11.4%. For the three months ended March 31, 2019, the Company recognized \$448 of interest expense related to the loan agreement, including \$98 related to the accretion of the debt discounts and deferred financing costs.

Scheduled principal payments on outstanding debt, as of March 31, 2019, are as follows:

Year Ending December 31,	
2019 (remaining)	1,034
2020	6,207
2021	6,207
2022	1,552
2022	<u>\$ 15,000</u>

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**14. Subsequent Events**

There have been no events subsequent to the period end that would require adjustment to, or disclosure in, this Quarterly Report on Form 10-Q.

## 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.*

### Overview

We are a pharmaceutical company dedicated to developing and commercializing sulopenem to be potentially 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  $\beta$ -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 successfully developed sulopenem in an oral tablet formulation, sulopenem etzadroxil-probenecid, which we refer to herein as oral sulopenem. Both sulopenem product candidates 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. We see two distinct opportunities for our sulopenem program: patients at elevated risk for treatment failure in the community setting suffering from uncomplicated urinary tract infections (uUTI) and hospitalized patients suffering from complicated, antibiotic-resistant infections.

During the third quarter of 2018, we initiated all three clinical trials in our Phase 3 development program which includes: a Phase 3 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 are conducting the Phase 3 clinical trials under Special Protocol Assessment (SPA) agreements from the FDA.

On May 30, 2018 we completed an initial public offering, or IPO, of our ordinary shares, and issued and sold 6,150,000 ordinary shares at a public offering price of \$13.00 per share, resulting in net proceeds of \$71.8 million after deducting underwriting discounts and commissions and offering costs payable by us. On June 26, 2018, we issued and sold an additional 200,000 ordinary shares at the IPO price of \$13.00 per share pursuant to the underwriters' partial exercise of their option to purchase additional ordinary shares, resulting in additional net proceeds of \$2.4 million after deducting underwriting discounts and commissions and offering costs payable by us. Aggregate net proceeds from the IPO totalled \$74.2 million after deducting underwriting discounts and commissions and offering costs payable by us.

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 March 31, 2019, we had an accumulated deficit of \$152.4 million. We expect to continue to incur significant expenses for the foreseeable future as we advance our sulopenem program through Phase 3 clinical trials, seek regulatory approval and engage in market preparation and pre-commercialization activities. In addition, if we obtain marketing approval for oral sulopenem and sulopenem, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. We are currently evaluating our commercialization strategy in the United States and other territories. We may also incur expenses in connection with the establishment of additional sources for the manufacture of sulopenem tablets and 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.

As a result, we will require additional capital to fund our operations, to continue to develop our sulopenem program and to execute our strategy. 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, scaleback 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 March 31, 2019, we had cash, cash equivalents and short-term investments of \$69.6 million. We believe that our existing cash, cash equivalents, short-term investments and available borrowings under our credit facility, will enable us to fund our operating expenses and capital expenditure requirements for at least one year from the date this Quarterly Report on Form 10-Q is issued. In making this assessment we have considered our available cash resources, future financing options available to us, our planned operations and our ability to adjust our plans if required. We have based these estimates on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. See the section titled “—Liquidity and Capital Resources.”

## **Components of Our Results of Operations**

### ***Revenue***

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from the sale of oral sulopenem or sulopenem in the near future. If our development efforts for our sulopenem program are successful and result in regulatory approval and/or license agreements with third parties, we may generate revenue in the future from product sales. To date, all of our revenue has been derived from our Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator, or CARB-X, award. We expect that our revenue for the foreseeable future will be derived primarily from payments under government awards that we may enter into in the future. In June 2017, CARB-X awarded us funds of up to \$1.5 million to advance the development of our sulopenem program. We receive funding from CARB-X as we incur qualifying expenses. During the three months ended March 31, 2019 and 2018, we recognized revenue of \$0.0 million and \$0.2 million, respectively, under this award.

### ***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;
- 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;
- 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.

Research and development activities are central to our business model. Product candidates in advanced stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later stage clinical trials. As a result, we expect that our research and development expenses will increase substantially throughout 2019 as we increase personnel costs, including share-based compensation, substantially complete the Phase 3 clinical trials for our sulopenem program, conduct other clinical trials and prepare regulatory filings for oral sulopenem and sulopenem.

The successful development and commercialization of oral sulopenem and 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 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;
- 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. We may obtain unexpected results from our clinical trials. 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. If we experience significant delays in enrollment in any of our ongoing or planned clinical trials, or are required to add additional patients to a study to remain consistent with our original trial design assumptions, we could be required to expend significant additional financial resources and time on the completion of clinical development of that product candidate. For example, we are currently conducting the first of two interim analyses of the blinded enrolled patients in our Phase 3 clinical trial in the uUTI indication and depending on the advice of our independent data monitoring committee who are charged with assessing the pooled and blinded early response rate, we may be required to increase patients in this trial to maintain the original degree of statistical power specified in the trial protocol.

#### *General and Administrative Expenses*

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

We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support the continued development of our sulopenem program. We also anticipate that we will incur increased accounting, audit, legal, regulatory, compliance, director compensation, director and officer insurance costs as well as investor and public relations expenses associated with being a public company. Additionally, if and when we believe regulatory approval of oral sulopenem and sulopenem appears likely, we anticipate an increase in payroll and expenses as a result of our preparation for commercial operations.

#### *Interest (Expense) Income, Net*

Interest (expense) income, net consists of interest paid and amortization of debt costs on our loan from Silicon Valley Bank (SVB), partially offset by interest earned on our cash and cash equivalents, which are generally invested in money market accounts, as well as interest earned on our investments in marketable securities.

#### *Other Income, Net*

Other income, net consists of realized and unrealized gains on our investments in marketable securities, partially offset by realized and unrealized foreign currency gains (losses) incurred in the normal course of business based on movement in the applicable exchange rates.

#### *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. We also accrue for potential interest and penalties related to unrecognized tax benefits in income tax expense.

### Critical Accounting Policies and Significant Judgments and 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 of 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 25, 2019, 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 policies from those described in our Annual Report on Form 10-K filed with the SEC on March 25, 2019, other than the adoption of accounting pronouncements as described in Note 2 to the condensed consolidated financial statements appearing elsewhere in this Quarterly Report on Form 10-Q.

### Results of Operations

#### Comparison of the three months ended March 31, 2019 and 2018

The following table summarizes our operating losses for the three months ended March 31, 2019 and 2018:

	Three Months Ended		
	March 31,		
	2019	2018	Change
Revenue	\$ 37	\$ 191	\$ (154)
Operating expenses:			
Research and development	17,387	10,879	6,508
General and administrative	3,116	1,515	1,601
Total operating expenses	\$ 20,503	\$ 12,394	\$ 8,109
Operating loss	(20,466)	(12,203)	(8,263)

#### Revenue

In June 2017, CARB-X awarded us funds of up to \$1.5 million to advance the development of our sulopenem program. We receive funding from CARB-X as we incur qualifying expenses. During the three months ended March 31, 2019 and 2018, we recognized \$0.0 million and \$0.2 million of revenue, respectively, under this award.



## Research and Development Expenses

	Three Months Ended		
	March 31,		
	2019	2018	Change
CRO and other preclinical and clinical trial related expenses	\$ 13,187	\$ 2,002	\$ 11,185
Chemistry, manufacturing and control (CMC) related expenses	1,384	6,670	(5,286)
Personnel related (including share-based compensation)	2,251	1,971	280
Consulting fees	565	236	329
Total research and development expenses	\$ 17,387	\$ 10,879	\$ 6,508

The increase in CRO and other preclinical and clinical trial related expenses of \$11.2 million was primarily due to costs incurred related to our three Phase 3 clinical trials, as well as an increase in Phase 1 clinical trial activity. CMC related expenses decreased by \$5.3 million primarily as a result of the completion of manufacturing of clinical trial materials for our Phase 3 clinical trials by our primary suppliers. Personnel related costs increased by \$0.3 million as a result of an increase in headcount in our CMC, clinical development and regulatory functions. Personnel related costs for the three months ended March 31, 2019 and 2018 included share-based compensation expense of \$0.2 million and \$0.1 million, respectively. The increase in consulting fees of \$0.3 million was primarily due to the increase in consultants used for clinical trial activity.

## General and Administrative Expenses

	Three Months Ended		
	March 31,		
	2019	2018	Change
Personnel related (including share-based compensation)	\$ 1,411	\$ 906	\$ 505
Professional and consulting fees	1,102	299	803
Facility related and other	603	310	293
Total general and administrative expenses	\$ 3,116	\$ 1,515	\$ 1,601

Personnel-related costs increased by \$0.5 million as a result of an increase in headcount in our general and administrative function. Personnel related costs for the three months ended March 31, 2019 and 2018 included share-based compensation expense of \$0.4 million and \$0.1 million, respectively. Professional and consulting fees increased by \$0.8 million primarily as a result of pre-commercialization activities and increased costs associated with operating as a public company. Facility related and other costs increased by \$0.3 million primarily as a result of increased insurance related costs and higher Board compensation.

## 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 CARB-X. We have funded our operations to date primarily with proceeds from the sale of preferred shares and ordinary shares, debt raised under our financing arrangement with SVB and payments received under the funding arrangement with CARB-X. Through March 31, 2019, we had received cash proceeds of \$195.2 million from sales of our Series A and Series B preferred shares and ordinary shares and \$15.0 million from the first drawdown of our SVB loan. As of March 31, 2019, we had cash, cash equivalents, restricted cash and short-term investments of \$69.7 million.

### 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 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 and the other \$15.0 million is available at our option upon the satisfaction of either of the following conditions which we refer to as the Second Draw Conditions: (i) the achievement of both non-inferiority and superiority primary endpoints from our Phase 3 clinical uUTI trial and reporting satisfactory safety data; or (ii) the achievement of non-inferiority primary endpoints from both our Phase 3 uUTI and cUTI clinical trials as well as reporting satisfactory safety data, in each case as determined by SVB at its sole discretion. Our option to draw the second term loan will terminate upon the earliest to occur of October 31, 2019, the thirtieth day following the occurrence of either of the Second Draw Conditions, or the occurrence of an event of default. A non-utilization fee of 1.50% of the aggregate undrawn principal amount shall apply if we satisfy the Second Draw Conditions but choose not to draw down the second term loan. The principal borrowed under the secured credit facility bears interest 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, which interest is payable monthly in arrears.

The initial draw requires monthly amortization payments commencing November 1, 2019, which will be extended to April 1, 2020 if the second draw is made. All outstanding principal, plus a 4.2% final payment fee, will be due and payable on the earliest to occur of March 1, 2022 (Maturity Date), the acceleration of either term loan or the prepayment of either term loan. The final payment fee of \$0.6 million, which represents 4.2% of the funded loan, is accreted using the effective interest method over the life of the loan as interest expense.

The secured credit facility draws are subject to prepayment fees of 3.00% in the first year, 2.00% in the second year and 1.00% thereafter in the event of prepayment at any time prior to the Maturity Date.

In connection with the initial \$15.0 million draw, we issued to SVB and Life Sciences Fund II LLC (LSF) warrants to purchase an aggregate of 19,890 Series B-2 preferred shares (which converted to ordinary shares upon our IPO) at an exercise price of \$18.85 per share. If we draw down the second term loan, each of SVB and LSF will be entitled, pursuant to additional share warrants issued to each of them at closing, to purchase such number of additional ordinary shares in an aggregate amount equal to 2.5% of the funded amount, divided by the applicable exercise price. Obligations under the secured credit facility are secured by substantially all of our existing and future assets and the existing and future assets of our subsidiaries, including intellectual property.

### **Cash Flows**

The following table summarizes our cash flows for each of the periods presented:

	<b>Three Months Ended March 31,</b>	
	<b>2019</b>	<b>2018</b>
Net cash used in operating activities	\$ (15,053 )	\$ (11,640 )
Net cash provided by investing activities	35,090	9,357
Net cash provided by financing activities	49	32,176
Effect of exchange rates on cash and cash equivalents	(34)	—
Net increase in cash	<u>\$ 20,052</u>	<u>\$ 29,893</u>

### **Operating Activities**

During the three months ended March 31, 2019, operating activities used \$15.1 million of cash, resulting from our net loss of \$20.6 million partially offset by net cash provided by changes in our operating assets and liabilities of \$4.9 million and non-cash charges of \$0.6 million. Net cash provided by changes in our operating assets and liabilities for the three months ended March 31, 2019 consisted primarily of increases in accounts payable and accrued expenses, primarily due to an increase in clinical trial expenses, and a reduction in prepaid expenses and other current assets, largely related to amounts received under the CARB-X award and advance payments to contract manufacturing organizations, partially offset by an increase in other assets.

During the three months ended March 31, 2018, operating activities used \$11.6 million of cash, resulting from our net loss of \$12.1 million partially offset by net cash provided by changes in our operating assets and liabilities of \$0.3 million and non-cash charges of \$0.2 million. Net cash provided by changes in our operating assets and liabilities for the three months ended March 31, 2018 consisted primarily of increases in accrued expenses and accounts payable primarily due to increases in clinical trial expenses and clinical trial supply costs, partially offset by increases in prepaid expenses and other assets primarily related to professional fees associated with the initial public offering.

### **Investing Activities**

During the three months ended March 31, 2019, net cash provided by investing activities of \$35.1 million related to sales of short-term investments. During the three months ended March 31, 2018, net cash provided by investing activities of \$9.4 million was primarily related to sales of short-term investments of \$15.8 million partially offset by purchases of short-term investments of \$6.4 million.

### **Financing Activities**

During the three months ended March 31, 2019, net cash provided by financing activities was \$0.0 million and consisted of net cash proceeds from the exercise of share options. During the three months ended March 31, 2018, net cash provided by financing activities was \$32.2 million, and consisted of cash proceeds from the issuance of Series B-2 preferred shares in February 2018 (which converted to ordinary shares on the closing of our IPO).

### **Funding Requirements**

We expect to continue to incur significant expenses and increasing operating losses as we conduct our ongoing and planned clinical trials of oral sulopenem and sulopenem, seek marketing approval for such product candidates if clinical trials are successful,

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 sulopenem, which include our ongoing and planned Phase 1 clinical trials, which we expect to occur through 2019;
- initiate other studies as part of our sulopenem program, some of which may be required for regulatory approval of our product candidates;
- establish a sales, marketing and distribution infrastructure to commercialize oral sulopenem and sulopenem in the United States if we obtain marketing approval from the U.S. Food and Drug Administration (FDA) and we choose to commercialize directly in the United States;
- establish manufacturing and supply chain capacity sufficient to provide commercial quantities of oral sulopenem and sulopenem, if we obtain marketing approval;
- 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, as well as to support our ongoing transition to a public reporting company; and
- acquire or in-license other product candidates or technologies.

We believe that our existing cash, cash equivalents, short-term investments and available borrowings under our credit facility, will enable us to fund our operating expenses and capital expenditure requirements for at least one year from the date this Quarterly Report on Form 10-Q is issued. In making this assessment we have considered our available cash resources, future financing options available to us, our planned operations and our ability to adjust our plans if required. We have based these estimates on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we expect. We expect that we will require additional capital to file with regulatory agencies and commercialize oral sulopenem and sulopenem, if we receive regulatory approval, and to pursue in-licenses or acquisitions of other product candidates. If we receive regulatory approval for oral sulopenem or sulopenem, we expect to incur significant commercialization expenses related to product manufacturing, sales, marketing and distribution, depending on where we choose to commercialize.

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 ongoing and planned clinical trials of oral sulopenem and sulopenem, including our three Phase 3 clinical trials in our three initial indications;
- 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 have applied for or 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 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 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 our exclusive license

agreement with Pfizer to in-license certain patent rights and know-how related to oral sulopenem and certain know-how related to sulopenem IV (the “Pfizer License”) or other future license agreements;

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

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. 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. Our secured credit facility with SVB imposes 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 and incur additional indebtedness, 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.

#### Contractual Obligations and Commitments

The following table summarizes our contractual obligations as of March 31, 2019, and the effects that such obligations are expected to have on our liquidity and cash flows in future periods:

	Payments due by period				
	Total	Less than 1 year	1 to 3 years	3 to 5 years	More than 5 years
	(In thousands)				
Operating lease commitments (1)	\$ 6,666	\$ 982	\$ 2,039	\$ 1,628	\$ 2,017
Principal loan repayments	15,000	2,586	12,414	—	—
Total	<u>\$ 21,666</u>	<u>\$ 3,568</u>	<u>\$ 14,453</u>	<u>\$ 1,628</u>	<u>\$ 2,017</u>

(1) See note 7 to the condensed consolidated financial statements for further details regarding leases.

Under the Pfizer License, we have agreed to make certain regulatory and sales milestone payments, pay royalties and make a potential one-time payment related to sublicensing income that exceeds a certain threshold. We have not included any contingent payment obligations, such as milestones, royalties, or one-time payments, in the table above as the amount, timing and likelihood of such payments are not known. 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.

In June 2016, we entered into an agreement with a supplier whereby we agreed to pay \$2.8 million to the supplier to acquire equipment, which will be used solely to manufacture product for us. In June 2018, we entered into a supplemental agreement with this supplier whereby we agreed to pay an additional \$2.3 million for additional equipment and dedicated personnel under the same terms of the original agreement. These payments will be offset against the price of the product to be supplied under a future supply agreement. As of March 31, 2019, \$1.6 million remained outstanding to the supplier.

#### 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.

**Off-Balance Sheet Arrangements**

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined in the rules and regulations of the SEC.

**Item 3. Quantitative and Qualitative Disclosures About Market Risk.**

As of March 31, 2019, we had cash, cash equivalents and marketable securities of \$69.6 million, consisting of cash and commercial paper. The primary objectives of our investment activities are to preserve principal, provide liquidity and maximize income without significantly increasing risk. Due to the short-term nature of our portfolio we do not believe an immediate interest rate increase of 100 basis points would have a material effect on the fair market value of our portfolio, and, accordingly, we do not expect our operating results or cash flows to be materially affected by a sudden change in market interest rates.

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 March 31, 2019 and December 31, 2018, 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 three months ended March 31, 2019 and 2018 or the year ended December 31, 2018.

The interest rate on our secured credit facility is sensitive to changes in interest rates. Interest accrues at a per annum rate equal to the greater of (i) 8.31%; or (ii) 3.89% above The Wall Street Journal prime rate. The Wall Street Journal prime rate increased from 4.75% to 5.00% on June 14, 2018, to 5.25% on September 27, 2018 and to 5.50% on December 20, 2018.

**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 March 31, 2019. 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 March 31, 2019, 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 March 31, 2019, 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

From time to time, we may be involved in legal proceedings or be subject to claims arising out of our operations. We are not currently a party to any legal proceedings that in the opinion of our management, would have a material adverse effect on our business.

### 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 and in other documents that we file with the 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 March 31, 2019, we had an accumulated deficit of \$152.4 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 have financed our operations to date primarily through private placements of our preferred shares and, more recently, through our initial public offering of ordinary shares (IPO) in May 2018 and a private placement of our ordinary shares in December 2018, being the subscription for 190,615 ordinary shares by our supplier. In April 2018, we entered into a secured credit facility with Silicon Valley Bank (SVB) and made an initial drawdown of \$15.0 million. We have devoted substantially all of our financial resources and efforts to research and development, including preclinical and clinical development, for our sulopenem program.

We expect to continue to incur significant expenses and increasing operating losses as we conduct our ongoing and planned clinical trials of oral sulopenem and sulopenem, seek marketing approval for such product candidates if clinical trials are successful, 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 sulopenem, which include our ongoing and planned Phase 1 clinical trials, which we expect to occur through 2019;
- initiate other studies as part of our sulopenem program, some of which may be required for regulatory approval of our product candidates;
- establish a sales, marketing and distribution infrastructure to commercialize oral sulopenem and sulopenem in the United States if we obtain marketing approval from the U.S. Food and Drug Administration (FDA) and we choose to commercialize directly in the United States;
- establish manufacturing and supply chain capacity sufficient to provide commercial quantities of oral sulopenem and sulopenem, if we obtain marketing approval;
- 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, as well as to support our ongoing transition to a public reporting company; and
- acquire or in-license other product candidates or technologies.

***We are substantially dependent on the success of our two product candidates, oral sulopenem and sulopenem, and 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, will 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 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:

- enrolling and successfully completing the ongoing Phase 3 clinical trials in our three initial indications;
- applying for and obtaining marketing approval for oral sulopenem and 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 sulopenem, if approved;
- establishing sales, marketing and distribution capabilities to effectively market and sell oral sulopenem and sulopenem, or entering into collaboration arrangements for the commercialization of oral sulopenem and sulopenem where we choose not to commercialize directly ourselves; and
- obtaining market acceptance of oral sulopenem and 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, or if there are any delays in completing our clinical trials, including delays or expense associated with increasing the sample size of any study, 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 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.

***We will require additional capital to fund our operations, and if we fail to obtain financing when needed or on acceptable terms, we may not be able to complete the development and commercialization of our sulopenem program.***

Developing pharmaceutical products is a time-consuming, expensive and uncertain process that takes years to complete. We expect that our expenses will increase substantially as we advance our clinical trials of oral sulopenem and sulopenem, seek marketing approval for such product candidates if clinical trials are successful, and pursue the development of our sulopenem program in additional indications through preclinical and clinical development. If we obtain marketing approval for oral sulopenem, sulopenem or any future product candidate, 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.

Accordingly, 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. 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 believe that our existing cash, cash equivalents, short-term investments, and available borrowings under our credit facility, will enable us to fund our operating expenses and capital expenditure requirements for at least one year from the date this Quarterly Report on Form 10-Q is issued. In making this assessment we have considered our available cash resources, future financing



options available to us, our planned operations and our ability to adjust our plans if required. We have based these estimates on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we expect. We expect that we will require additional capital to file with regulatory agencies and commercialize oral sulopenem and sulopenem, if we receive regulatory approval. If we receive regulatory approval for oral sulopenem or sulopenem, we expect to incur significant commercialization expenses related to product manufacturing, sales, marketing and distribution.

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. 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 ongoing clinical trials of oral sulopenem and sulopenem, including our three Phase 3 clinical trials in our three initial indications;
- 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 have applied for or 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 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 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 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; and
- the extent to which we in-license or acquire other products and technologies.

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

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 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 and the other \$15.0 million is available at our option upon the satisfaction of certain draw requirements (as described in Note 13 to our condensed consolidated financial statements appearing elsewhere in this Quarterly Report on Form 10-Q). Obligations under the secured credit facility are secured by substantially all of our existing and future assets and the existing and future assets of our subsidiaries, including intellectual property. Our secured credit facility imposes operating and other restrictions on us. Such restrictions affect, and in many respects limit or prohibit, our ability to, among other things, dispose of certain assets, pay dividends and incur additional indebtedness. Failure to make payments or comply with these and other terms and covenants under our secured credit facility could result in an event of default, which could lead to an acceleration of amounts due and foreclosure upon and/or sale or other liquidation of all of our and our subsidiaries' assets, including intellectual property. Any of the foregoing would have a material adverse effect on our operations and financial condition. In addition, this indebtedness and the security interests granted to secure it could make it more difficult for us to raise additional capital to fund our operations.

***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 complete a large-scale, pivotal clinical trial, 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 and 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.

***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. In addition, 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.

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. In addition, if we make an additional draw under our secured credit facility, we will be required to issue additional warrants. 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 intend to focus on developing our sulopenem program for the specific indications of uncomplicated urinary tract infections (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.

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 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 as the first and only oral and intravenous (IV) branded penem available globally. Our near-term prospects are substantially dependent on our ability to develop, obtain marketing approval for and successfully commercialize oral sulopenem and sulopenem. The success of our sulopenem program will depend on several factors, including the following:

- successful enrollment in, and completion of, clinical trials, including our three ongoing Phase 3 clinical trials of oral sulopenem and sulopenem;
- 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;
- 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 our license agreement with Pfizer;
- protection of our rights in our intellectual property portfolio;
- launch of commercial sales of oral sulopenem and 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 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 sulopenem;
- the availability, perceived advantages, relative cost and relative efficacy of alternative and competing therapies; and
- an acceptable safety profile of oral sulopenem and 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. If we are unable to develop, receive marketing approval for, or successfully commercialize oral sulopenem and 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 new drug application (NDA) or other respective regulatory filing. It is possible that the FDA may refuse to accept any or all of our planned NDAs for substantive review or may conclude after review of our data that our application is insufficient to obtain regulatory approval for any current or future product candidates. If the FDA does not approve any of our planned NDAs, it may require that we conduct additional costly clinical, non-clinical or manufacturing validation studies before it will reconsider our applications. Depending on the extent of these or any other FDA-required studies, approval of any NDA 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.

Any failure or delay in obtaining regulatory approvals would prevent us from commercializing oral sulopenem and 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 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. We have 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 depends entirely 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.

For example, we present data from clinical trials conducted by Pfizer Japan in the 1990s. The data from those clinical trials is not directly comparable to data from clinical trials that would be conducted today or the data that we anticipate from our Phase 3 program for a variety of reasons, including that protocols were designed for different purposes and as a consequence had different enrollment and efficacy evaluation criteria. For example, while a subjective investigator assessment of outcome is typically included in all cUTI protocols and was performed in the Japanese program, more structured endpoints are required as part of current FDA guidelines for registrational trials. Current FDA guidelines define the primary efficacy outcome based on both clinical and microbiological success, while EMA guidelines recommend microbiologic outcome. The structured endpoint in the Japanese program assessed outcome based on resolution of pyuria and microbiologic outcome. In addition, the pathogens isolated in the course of a clinical trial will vary depending on the types of patients enrolled, the geographic location of the sites that contribute to the study and the year in which the study is performed. While the organisms seen in the Japanese study are similar to those we anticipate in the Phase 3 program, we expect the frequency distribution of these pathogens may be different. Furthermore, adverse event reports can vary by geographic region and we may see a different adverse event rate and different types of events in patients that we study in the Phase 3 program relative to the experience in Japan.

In addition, preclinical and clinical data are often susceptible to varying interpretations and analyses. Although data from Phase 1 and Phase 2 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.

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 ongoing 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 are conducting our Phase 3 clinical trials pursuant to Special Protocol Assessment (SPA) agreements, the FDA or other comparable foreign regulatory authorities may ultimately disagree as to the design or implementation of our Phase 3 clinical trials or other clinical trials;
- 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 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. We cannot assure our shareholders that our three ongoing Phase 3 clinical trials will be completed on schedule, if at all, or that we will not need to restructure our clinical trials. 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. We may not be able to continue or complete our ongoing Phase 3 clinical trials or initiate, continue or complete other clinical trials 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; and
- the risk that patients enrolled in clinical trials will drop out of the clinical trials before completion.

The inclusion and exclusion criteria for our ongoing Phase 3 clinical trials of oral sulopenem and sulopenem may adversely affect our enrollment rates for patients in these 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 sulopenem, or slow down or halt our product development for oral sulopenem and sulopenem.

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 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.

***Success in non-clinical testing and early clinical trials does not ensure that later clinical trials will be successful, and we cannot assure shareholders that any of our ongoing clinical trials or any other 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.***

Our ongoing Phase 3 clinical trials of oral sulopenem and sulopenem are subject to a number of specific risks arising from our clinical program and the design of such clinical trials.

We have not previously completed Phase 3 clinical trials of oral sulopenem or sulopenem in the indications uUTI, cUTI and cIAI, and we have not documented to the satisfaction of regulators that these treatments are effective in treating uUTIs, cUTIs or cIAIs in humans. Although we believe that oral sulopenem and sulopenem have the potential to treat uUTIs, cUTIs, and cIAIs in humans based on the results of prior preclinical studies and clinical trials, the results of these preclinical studies and clinical trials are not necessarily predictive of the results of our ongoing Phase 3 clinical trials, and we cannot guarantee that oral sulopenem and sulopenem will demonstrate the expected efficacy in clinical trial patients. 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 our ongoing Phase 3 clinical trials.

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.

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. There may be unforeseen serious adverse events or side effects that differ from those seen 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. We may see higher rates of adverse events than were reported in the clinical trials Pfizer conducted in Japan.

To date, sulopenem and sulopenem etzadroxil have generally been well tolerated in clinical trials conducted in healthy subjects and patients. 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, 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. 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 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.

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 proves to be inaccurate, then the actual market for oral sulopenem and sulopenem could be smaller than our estimates of the potential market opportunity. If the actual market for oral sulopenem and 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 currently have no commercial organization. If we are unable to establish 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 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 sulopenem receive regulatory approval, we intend to 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 sulopenem through collaboration arrangements. 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.

Factors that may inhibit our efforts to commercialize our products directly include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- our inability to identify the best territories to target based on resistance statistics and prescribers within those territories;

- the inability of a health resources group to obtain access to educate physicians regarding the attributes of our future 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; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

For those countries in which we choose not to commercialize directly ourselves, which may include the United States, 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 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, cephalixin 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 number of oral product candidates in clinical development by third parties that are intended to treat UTIs. Some mid- to late-stage product candidates include ceftibuten clavulanate from Achaogen, Inc., tebipenem pivoxil from Spero Therapeutics, Inc., delafloxacin from Melinta Therapeutics, Inc., pivmecillinam from Utility Therapeutics Limited, ETX0282CPDP (a novel  $\beta$ -lactamase inhibitor combined with cefpodoxime proxetil) from Entasis Therapeutics Holdings Inc. and omadacycline from Paratek Pharmaceuticals, Inc. 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 Allergan plc and Pfizer, Vabomere from Melinta Therapeutics, Inc., Zerbaxa from Merck & Co., Zemdri from Achaogen, Inc. and Xerava from Tetrphase Pharmaceuticals, Inc. There are also a number of IV-administered product candidates in late-stage clinical development that are intended to treat resistant gram-negative infections, including cefiderocol from Shionogi & Co. Ltd., Contempo from Nabriva Therapeutics plc (as successor to Zavante Therapeutics, Inc.) and imipenem-relabactam from Merck & Co.

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 and cIAI and, more recently, for the indications of 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.

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 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 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. For those countries in which we choose not to commercialize directly ourselves, we intend to seek to commercialize oral sulopenem and 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 large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. We are not currently party to any such arrangements but plan to initiate discussions with potential commercial partners.

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.

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.

***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 ongoing 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 commercialization and for any future clinical trials and 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. 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 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 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 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 the conduct of 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.

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 currently do not own any patents and 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. 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. The patent applications that we currently own or may own in the future or in-license may fail to result in issued patents with claims that cover our current and future product candidates in the United States or in other countries. Patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless, and until, a patent issues from such applications, and then only to the extent the issued claims cover the technology.

If any patent applications we may 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, 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 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. For example, under the CARB-X grant funding program, the U.S. Department of Health and Human Services (HHS) awarded us a grant in connection with research to reduce the threat to human health from antimicrobial resistance and we granted the U.S. government a nonexclusive, nontransferable, irrevocable, paid-up license to practice or have practiced for or on behalf of the U.S. government any inventions arising out of our research globally. In addition, under such agreement, if we or our licensees do not use commercially reasonable efforts to exploit or further the development of any intellectual property rights we have generated out of such research within five years of the end date of our research project, Wellcome Trust Limited has the option to take responsibility for the commercialization and exploitation of such intellectual property rights, including by way of sale, assignment and license of such intellectual property rights.

***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). 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 and cIAI and, more recently, for the indications of 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 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 any pending patent applications will not lead to issued patents;
- 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, or USPTO, after that date but before we 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 offices 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 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 have also not yet registered trademarks for any of our product candidates in any jurisdiction. Any trademark applications we may file for our product candidates 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 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, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA objects to any of our proposed proprietary product names, 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 and the EMA.

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 contract research organizations 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, more recently, for the indications of community-acquired bacterial pneumonia, acute bacterial prostatitis, gonococcal urethritis, and pelvic inflammatory disease) which may provide for a more rapid new drug application 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, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may 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 none of our existing product candidates or any product candidates 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 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 are conducting our Phase 3 clinical trials pursuant to SPA agreements, the FDA may still require us to conduct additional non-clinical studies or clinical trials for our product candidates either prior to or post-approval, and it may otherwise object to elements of our clinical development program.

We have not submitted an NDA for any of our product candidates. 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 chemistry, manufacturing and controls 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, although we are conducting our Phase 3 clinical trials pursuant to SPA agreements;
- 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;

- 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.

***Future legislation and/or regulations and policies adopted by the FDA, the EMA or similar regulatory authorities may increase the time and cost required for us to conduct and complete clinical trials of oral sulopenem, sulopenem and other potential product candidates.***

The FDA has established regulations to govern the drug development and approval process, as have foreign regulatory authorities. The policies of the FDA and other regulatory authorities may change and additional laws may be enacted or government regulations may be promulgated that could prevent, limit, delay, or alternatively accelerate regulatory review of our product candidates.

***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. 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.

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  $\beta$ -lactamases (ESBL) resistance. On June 23, 2016, the electorate in the United Kingdom (UK) voted in favor of leaving the European Union (EU), commonly referred to as Brexit. On March 29, 2017, the country formally notified the EU of its intention to withdraw from the EU pursuant to Article 50 of the Lisbon Treaty, commencing a period of two years, for the UK and other EU member states to negotiate the terms of the withdrawal. The EU subsequently extended the withdrawal date to October 31, 2019 although the UK could leave sooner depending on political developments. There has been limited progress so far in the negotiations and continued uncertainty in the UK government which increases the possibility of the UK exiting the EU on or before October 31, 2019 without a formal withdrawal agreement in place and of significant market and economic disruption as a result. Brexit could adversely affect European or worldwide political, regulatory, economic or market conditions and could contribute to instability in global political institutions, regulatory agencies and financial markets. Since a significant proportion of the regulatory framework in the UK is derived from EU directives and regulations, Brexit could materially impact the regulatory regime with respect to the approval of our product candidates in the UK or the EU. Any delay in obtaining, or an inability to obtain, any regulatory approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the UK and/or the EU and restrict our ability to generate revenue.

and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the UK and/or EU for our product candidates, which could significantly and materially harm our business.

***Non-U.S. regulatory authorities may require us to conduct additional clinical trials or non-clinical studies to accommodate submission for the cUTI indication.***

We obtained scientific advice from the EMA for each of the 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 are considering 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 EU.

***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 postmarketing 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.

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.

***If we fail to comply with federal and state healthcare laws, including fraud and abuse and health information privacy and security laws, we could face substantial penalties and our business, results of operations, financial condition and prospects could be adversely affected.***

As a pharmaceutical company, even though we do not provide healthcare services or receive payments directly from or bill directly to Medicare, Medicaid or other third-party payors for our products, certain federal and state healthcare laws and regulations pertaining to fraud and abuse, patients' rights and other healthcare laws and regulations, are applicable to our business. We are subject to healthcare laws and regulations by both the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include:

- the federal Anti-Kickback Statute which prohibits, among other things, any person or entity, from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for either the referral of an individual, or the purchase, lease, furnishing, prescribing, ordering or recommendation of an item, good, facility or service reimbursable by a federally funded healthcare program, such as the Medicare or Medicaid program. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand, and prescribers, purchasers and formulary managers on the other hand. The term "remuneration" has been interpreted broadly and may constrain our marketing practices, educational programs, pricing policies and relationships with healthcare providers or other entities, among other activities;
- the federal civil and criminal false claims laws, including the federal False Claims Act, and false statement laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid or other government payors that are false or fraudulent or making any materially false statement in connection with the delivery or payment for healthcare benefits, items or services. Pharmaceutical manufacturers can be held liable under the federal False Claims Act even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims;
- the Health Insurance Portability and Accountability Act of 1996 (HIPAA), which, among other things, imposes criminal liability for executing or attempting to execute a scheme to defraud any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and creates federal criminal laws that prohibit knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statements or representations, or making or using any false writing or document knowing the same to contain any materially false, fictitious or fraudulent statement or entry in connection with the delivery of, or payment for, benefits, items or services;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (HITECH) and their respective implementing regulations, including the final omnibus rule published on January 25, 2013, mandates, among other things, the adoption of uniform standards for the electronic exchange of information in common healthcare transactions, as well as standards relating to the privacy, security, transmission and breach reporting of individually identifiable health information, upon certain health plans, healthcare clearinghouses and healthcare providers and their respective business associates that perform services for them involving individually identifiable health information, which require the adoption of administrative, physical and technical safeguards to protect such information. Among other things, HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in U.S. federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions;
- the federal physician payment transparency requirements, sometimes referred to as the "Physician Payments Sunshine Act," and its implementing regulations, which imposes annual disclosure requirements to the Centers for Medicare and Medicaid Services (CMS) on certain manufacturers of drugs, biologics, devices and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions), of certain payments or other

transfers of value made to physicians and teaching hospitals, as well as ownership or investment interests held by physicians and their immediate family members;

- state and foreign law equivalents of each of the above federal laws, such as anti-kickback and false claims laws, which may apply to items or services reimbursed by any third-party payor, including commercial insurers, which may impose similar or more prohibitive restrictions;
- state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts;
- state, local and foreign laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, obtain pharmaceutical agent licensure, and/or otherwise restrict payments that may be made to healthcare providers and entities;
- state and local laws that require the registration of pharmaceutical sales representatives; and
- state, local and foreign laws that require drug manufacturers to report information related to payments and other transfers of value to other healthcare providers or entities or marketing expenditures.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement bodies have recently increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. Additionally, the Patient Protection and Affordable Care Act (as amended by the Health Care and Education Reconciliation Act), enacted in 2010 (ACA), among other things, amended the intent requirement of the federal Anti-Kickback Statute and criminal health care fraud statutes, so that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it. In addition, the ACA provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitute a false or fraudulent claim for purposes of the False Claims Act.

Recently, several pharmaceutical and other healthcare companies have been prosecuted under the federal false claims laws for allegedly inflating drug prices they report to pricing services, which in turn are used by the government to set Medicare and Medicaid reimbursement rates, and for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. In addition, certain marketing practices, including off-label promotion, may also violate false claims laws. To the extent that any product we make is sold in a country outside of the United States, we may be subject to similar laws and regulations.

The risks of complying with these laws cannot be entirely eliminated. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Moreover, achieving and sustaining compliance with applicable federal and state privacy, security, fraud and transparency laws is time consuming and costly. If our past or present operations, or those of our distributors are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to sanctions, including civil, criminal and administrative penalties, fines, damages, disgorgement, exclusion from participation in U.S. federal or state health care 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, reputational harm, diminished profits and future earnings, and the curtailment or restructuring of our operations, any of which could materially adversely affect our ability to operate our business and our financial results. Similarly, if healthcare providers, distributors or other entities with whom we do business are found to be out of compliance with applicable laws and regulations, they may be subject to sanctions, which could also have a negative impact on us.

### *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 states levels that seek to reduce healthcare costs. For example, in March 2010 the 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. Among the provisions of the ACA, of greatest importance to the pharmaceutical and biotechnology industry are the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain specified branded prescription drugs and biologic agents apportioned among these entities according to their market share in some government healthcare programs;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for most branded and generic drugs, respectively, and capped the total rebate amount for innovator drugs at 100% of the Average Manufacturer Price (AMP);
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for certain drugs and biologics that are inhaled, infused, instilled, implanted or injected;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (and 70% commencing January 1, 2019) point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- expansion of the entities eligible for discounts under the Public Health program;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- establishment of a Center for Medicare Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending; and
- implementation of the federal physician payment transparency requirements, sometimes referred to as the "Physician Payments Sunshine Act."

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 and will remain in effect through 2024 unless additional congressional action is taken. 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 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, which was signed by the President on December 22, 2017, Congress repealed the "individual mandate". The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, will become effective in 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise. Further, each chamber of the Congress has put forth multiple bills designed to repeal or repeal and replace portions of the ACA. Although none of these measures has been enacted by Congress to date, Congress may consider other legislation to repeal and replace elements of the ACA. The Congress will likely consider other legislation to replace elements of the ACA, during the next congressional session. It is possible that repeal and replacement initiatives, if enacted into law, could ultimately result in fewer individuals having health insurance coverage or in individuals having insurance coverage with less generous benefits. While the timing and scope of any potential future legislation to repeal and replace ACA provisions is highly uncertain in many respects, it is

also possible that some of the ACA provisions that generally are not favorable for the research-based pharmaceutical industry could also be repealed along with ACA coverage expansion provision. We will continue to evaluate the effect that the ACA and its possible repeal and replacement could have on our business.

The Trump administration has also taken executive actions to undermine or delay implementation of the ACA. Since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. One Executive Order directs 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. The second Executive Order terminates the cost-sharing subsidies that reimburse insurers under the ACA. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. In addition, CMS has recently 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. Further, on June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than \$12 billion in ACA risk corridor payments to third-party payors who argued were owed to them. The effects of this gap in reimbursement on third-party payors, the viability of the ACA marketplace, providers, and potentially our business, are not yet known.

In addition, the Centers for Medicare & Medicaid Services, or 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. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

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 inseparable feature of the ACA, and therefore because the mandate was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the ACA are invalid as well. The Trump administration and CMS have both stated that the ruling will have no immediate effect, and on December 30, 2018 the same judge issued an order staying the judgment pending appeal. The Trump Administration has represented to the US Court of Appeals for the Fifth Circuit considering this judgment that it does not oppose the lower court’s ruling. To that end, on May 1, 2019, the Justice Department filed a brief asking the Court to strike down the entirety of the ACA. Oral argument on this case is set for July 2019. It is unclear how this decision and any subsequent appeals and other efforts to repeal and replace the ACA will impact the ACA and our business. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The costs of prescription pharmaceuticals has also been the subject of considerable discussion in the United States, and members of Congress and the Administration have stated that they will address such costs through new legislative and administrative measures. To date, there have been several recent U.S. congressional inquiries and proposed and enacted state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, the Trump administration’s budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. While any proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

Further, there has been heightened governmental scrutiny in the United States of the manner in which manufacturers set prices for their marketed products in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, and reform government



program reimbursement methodologies for drug products. At the federal level, the Trump administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. These new laws and initiatives may result in additional reductions in Medicare and other healthcare funding, as well as 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, all of which could have a material adverse effect on our future customers and accordingly, our financial operations.

Specifically, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. For example, on May 11, 2018, the Trump administration issued a plan to lower drug prices. Under this blueprint for action, the Trump administration indicated that HHS will: take steps to end the gaming of regulatory and patent processes by drug makers to unfairly protect monopolies; advance biosimilars and generics to boost price competition; evaluate the inclusion of prices in drug makers' ads to enhance price competition; speed access to and lower the cost of new drugs by clarifying policies for sharing information between insurers and drug makers; avoid excessive pricing by relying more on value-based pricing by expanding outcome-based payments in Medicare and Medicaid; work to give Part D plan sponsors more negotiation power with drug makers; examine which Medicare Part B drugs could be negotiated for a lower price by Part D plans, and improving the design of the Part B Competitive Acquisition Program; update Medicare's drug-pricing dashboard to increase transparency; prohibit Part D contracts that include "gag rules" that prevent pharmacists from informing patients when they could pay less out-of-pocket by not using insurance; and require that Part D plan members be provided with an annual statement of plan payments, out-of-pocket spending, and drug price increases. More recently, on January 31, 2019, the HHS Office of Inspector General proposed modifications to the federal Anti-Kickback Statute discount safe harbor for the purpose of reducing the cost of drug products to consumers which, among other things, if finalized, will affect discounts paid by manufacturers to Medicare Part D plans, Medicaid managed care organizations and pharmacy benefit managers working with these organizations.

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 authorities 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.

Additionally, on May 30, 2018, the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017 (Right to Try Act) was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase I clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program.

***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.***

Certain countries in which we operate have, or are developing, laws protecting the confidentiality of certain patient health information. EU member states and other jurisdictions have adopted data protection laws and regulations, which impose significant compliance obligations.

For example, the EU General Data Protection Regulation, or GDPR, became enforceable on May 25, 2018 replacing the EU Data Protection Directive. In addition to imposing strict obligations and restrictions on the ability to collect, analyze and transfer personal data, including health data from clinical trials and adverse event reporting (as previously applied under the EU Data Protection Directive), the GDPR introduced new data protection requirements in the EU including expanded disclosures on how personal data is to be used, mandatory data breach notifications, and substantial fines for breaches of the GDPR. It also increased our responsibility and liability in relation to personal data that we process and requires us to put in place additional mechanisms to ensure compliance with the GDPR. This could affect our ability to collect, analyze and transfer personal data, including health data from clinical trials and adverse event reporting, or result in increased costs to ensure compliance.

The GDPR, while directly effective in EU member states, does permit EU member states to introduce their own local laws to give further effect to the GDPR locally and permits local derogations to certain provisions, adding to the complexity of processing personal data in the EU.

We have policies and practices that we believe make us compliant with applicable privacy regulations and are continuously updating these to ensure compliance with the new GDPR and associated guidance on implementation and compliance practices. Nevertheless, any failure to comply with the rules arising from the GDPR and national laws of EU member states, as well as privacy laws in other countries in which we operate, could lead to government enforcement actions and significant sanctions or penalties against us, adversely impact our results of operations and subject us to negative publicity.

***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, and Michael W. Dunne, M.D., our Chief Scientific Officer, as well as the other principal members of our management, scientific and clinical 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 rely 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 expect to grow our organization, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.***

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of clinical development, 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 our limited financial resources and 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 the 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. Our expected growth 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 our expected 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.

***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; and
- failure to comply with Office of Foreign Asset Control rules and regulations and the Foreign Corrupt Practices Act.

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

***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. If we do identify suitable candidates, we may not be able to make such acquisitions on favorable terms, or at all. 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 nondisruptive 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**

*We believe we may 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.*

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

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 for U.S. federal income tax purposes) created or organized in or under the laws of the United States, any state thereof, or the District of Columbia, (3) an estate the income of which is subject to U.S. federal income tax regardless of its 168 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 for U.S. federal income tax purposes.

If we are a PFIC in any taxable year in which a U.S. Holder holds shares, 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 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, 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 adverse 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 our non-U.S. subsidiary 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 PFIC 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, timely mark-to-market election with respect to our ordinary shares, that U.S. Holder will recognize as ordinary income or loss in each 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. U.S. Holders should also be aware that the mark-to-market election generally will not be available with respect to any of our subsidiaries that is a PFIC and that 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.

We currently intend to make available the information necessary to permit a U.S. Holder to make a qualified electing fund, or “QEF election,” under the U.S. federal income tax laws, which may mitigate some of the adverse U.S. federal income tax consequences that could apply to a U.S. Holder. However, we may choose not to provide such information at a future date.

***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, they may have paid more taxes than they 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 and IRS rulings could affect the U.S. federal income tax treatment of us and U.S. Holders of our ordinary shares.

***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 20%) 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. Given the limited trading history of our ordinary shares, 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.*

Since our IPO in May 2018, the trading price of our ordinary shares has fluctuated between a low of \$4.70 and a high of \$13.00 per share. 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. These factors include those discussed elsewhere in this "Risk Factors" section of this document and others, such as:

- results from, and any delays in, our current and future clinical trials, in particular our three ongoing Phase 3 clinical trials related to oral sulopenem and sulopenem;
- announcements of regulatory approval or disapproval of oral sulopenem and sulopenem or future product candidates;
- delays in the commercialization of oral sulopenem and sulopenem or any future product candidates;
- manufacturing and supply issues related to our development programs and commercialization of oral sulopenem and 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 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 or management;
- 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 or sulopenem or future products;
- market conditions in the healthcare market in general, or in the antibiotics segment in particular, including performance of our competitors; and
- general economic conditions in the United States and abroad.

In addition, the stock market in general, or the market for equity securities in our industry or industries related to our industry, may experience extreme volatility unrelated to our operating performance. These broad market fluctuations may adversely affect the trading price or liquidity of our ordinary shares. 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. 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.

*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.

***Our principal shareholders and management own a significant percentage of our ordinary shares and will be able to exert significant control over matters subject to shareholder approval.***

Based on shares outstanding as of April 30, 2019, our executive officers, directors, holders of 5% or more of our ordinary shares and their respective affiliates beneficially own in the aggregate approximately 68.6% of our outstanding ordinary shares. As a result of their share ownership, these holders may have the ability to influence our management and policies and will be able to significantly affect the outcome of matters requiring shareholder approval such as elections of directors, amendments of our organizational documents or approvals of any merger, sale of assets or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our ordinary shares that our shareholders may feel are in their best interest.

***If we raise additional capital in the future, our existing shareholders' level of ownership in our Company could be diluted or require us to relinquish rights.***

Any issuance of securities we may undertake in the future to raise additional capital 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.

Further, if we obtain funds through a debt financing or through the issuance of 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 portion of our outstanding ordinary shares can be traded without restriction at any time. A substantial 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, a portion of our ordinary shares is currently restricted as a result of contractual provisions until November 2019. As such, sales of a substantial number of our ordinary shares in the public market could occur 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.

In addition, ordinary shares that are issuable upon exercise of outstanding options, or reserved for future issuance under our equity incentive plans or issuable upon exercise of outstanding warrants will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules and Rule 144 and Rule 701 under the Securities Act. If 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.

***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.

***As a newly public company, we have incurred and will incur significant additional costs, 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 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 JOBS Act and the rules and regulations of the U.S. Securities and Exchange Commission (the SEC), and the Nasdaq Global 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 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.

The exact implications of the JOBS Act are still subject to interpretations and guidance by the SEC and other regulatory agencies, and we may not be able to take advantage of all of the benefits of the JOBS Act. In addition, investors may find our ordinary shares less attractive if we rely on the exemptions and relief granted by the JOBS Act. 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 Global 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 Global 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 beginning with our second filing of an Annual Report on Form 10-K with the SEC after we become a public company. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants 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.

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. In addition, our ability to pay cash dividends is currently prohibited by the terms of our credit facility with SVB.

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 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 additional 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.

***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, 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, the acquirer and, in certain circumstances, its concert parties would be required (except with the consent of the Irish Takeover Panel) to make an offer for 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. 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 were to increase that person's percentage of the voting rights by 0.05% within a 12 month period. 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 of the concert parties and/or members of our board of directors to acquire more of our securities, including under the terms of any executive incentive arrangements. In the future, we may consult with the Irish Takeover Panel 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 will 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 an ordinary resolution 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 special resolution. Such disapplication can either be generally applicable or be in respect of a particular allotment of shares. Accordingly, our Articles of Association contains, as permitted by Irish company law, provisions authorizing the board to issue new shares, and to disapply statutory preemption rights. 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, which could limit our ability to issue equity and thereby adversely affect the holders of our securities.

## **Item 2. Unregistered Sales of Equity Securities and Use of Proceeds.**

### **Use of Proceeds from Initial Public Offering**

On May 30, 2018, we completed the initial public offering of our ordinary shares pursuant to which we issued and sold 6,150,000 ordinary shares at a price to the public of \$13.00 per share. In addition, on June 26, 2018, we issued and sold an additional 200,000 ordinary shares at the initial public offering price of \$13.00 per share as a result of the partial exercise by the underwriters of their option to purchase additional ordinary shares.

The offer and sale of all of the ordinary shares in our IPO were registered under the Securities Act pursuant to a registration statement on Form S-1 (File No. 333-224582), which was declared effective by the SEC on May 24, 2018.

We received aggregate gross proceeds from our initial public offering of \$82.5 million, or aggregate net proceeds of \$74.2 million after deducting underwriting discounts and commissions of \$5.8 million and offering costs of \$2.5 million. None of the underwriting discounts and commissions or offering expenses were incurred or paid to directors or officers of ours or their associates or to persons owning 10% or more of our ordinary shares or to any of our affiliates.

As of March 31, 2019 we had used approximately \$73.8 million from our IPO proceeds, including clinical milestone payments of \$15 million to Pfizer pursuant to the exclusive license agreement we have entered into with Pfizer, which were paid in 2018. There has been no material change in our planned use of the net proceeds from the IPO as described in our final prospectus filed pursuant to Rule 424(b)(4) under the Securities Act with the SEC on May 25, 2018.

**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
31.1	<a href="#"><u>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.</u></a>	X			
31.2	<a href="#"><u>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.</u></a>	X			
32.1	<a href="#"><u>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.</u></a>	X			
32.2	<a href="#"><u>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.</u></a>	X			
101.INS	XBRL Instance Document	X			
101.SCH	XBRL Taxonomy Extension Schema Document	X			
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document	X			
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document	X			
101.LAB	XBRL Taxonomy Extension Label Linkbase Document	X			
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document	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.

Company Name

Date: May 14, 2019

By: /s/ Corey Fishman  
**Corey Fishman**  
President and Chief Executive Officer

Date: May 14, 2019

By: /s/ Judith Matthews  
**Judith Matthews**  
Chief Financial Officer (Principal Financial Officer)

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)) 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) 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
  - (c) 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.

By: /s/ Corey Fishman  
**Corey Fishman**  
**President and Chief Executive Officer**  
**(Principal Executive Officer)**

**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)) 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) 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
  - (c) 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: May 14, 2019

By: \_\_\_\_\_ /s/ Judith Matthews  
**Judith Matthews**  
**Chief Financial Officer**  
**(Principal Financial and Accounting Officer)**



**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 March 31, 2019, 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: May 14, 2019

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.

- (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.

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.