As confidentially submitted to the U.S. Securities and Exchange Commission on February 08, 2018
This draft registration statement on Form 20-F/A (Amendment No. 3) has not been publicly filed with the U.S. Securities and Exchange Commission and all information herein remains strictly confidential.

Registration Statement No. 333-

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 20-F/A
Amendment No. 3

ý **REGISTRATION STATEMENT PURSUANT TO SECTION 12(b) OR (g) OF THE SECURITIES EXCHANGE ACT OF 1934**

OR

☐ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 For the fiscal year ended**

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 For the transition period from to**

OR

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

Commission file number:

Tiziana Life Sciences plc

(Exact name of Registrant as specified in its charter and translation of Registrant's name into English)

England and Wales
(Jurisdiction of incorporation or organization)

3rd Floor, 11-12 St James's Square
London SW1 4LB, United Kingdom
(Address of principal executive offices)

Tiziano Lazzaretti
Chief Financial Officer
3rd Floor, 11-12 St James's Square
London SW1 4LB, United Kingdom
+44 20 7495 2379
(Name, Telephone, E-mail and/or Facsimile number and Address of Company Contact Person)

Copies to:
Ed Lukins
Edward Dyson
Cooley (UK) LLP

Dashwood
69 Old Broad Street
London EC2M 1QS
United Kingdom

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

Title of each class	Name of each exchange on which registered
American Depositary Shares, each representing 5 ordinary shares, having a nominal value of £0.03 each	NASDAQ Capital Market
Ordinary shares, nominal value of £0.03 each	

(1) Not for trading, but only in connection with the listing of the American Depositary Shares

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

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

Number of outstanding shares of each of the issuer's classes of capital or common stock as of June 30, 2017: 138,216,920 ordinary shares.

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act.

☐ Yes ý No

If this report is an annual or transition report, indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934.

☐ Yes ☐ No

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

☐ Yes ☐ No

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted 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 and post such files).

☐ Yes ☐ No

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

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

If an emerging growth company that prepares its financial statements in accordance with U.S. GAAP, indicate by checkmark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards† provided pursuant to Section 13(a) of the Exchange Act. ☐

† The term "new or revised financial accounting standard" refers to any update issued by the Financial Accounting Standards Board to its Accounting Standards Codification after April 5, 2012.

Indicate by check mark which basis of accounting the registrant has used to prepare the financial statements included in this filing:

U.S. GAAP ☐	International Financial Reporting Standards as issued by the International Accounting Standards Board ý	Other ☐

If "Other" has been checked in response to the previous question, indicate by check mark which financial statement item the registrant has elected to follow:

☐ Item 17 ☐ Item 18

If this is an annual report, indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act).

☐ Yes ☐ No

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INTRODUCTION

Unless otherwise indicated or the context otherwise requires, all references in this registration statement to the terms “Tiziana,” “Tiziana Life Sciences plc,” “the company,” “we,” “us” and “our” refer to Tiziana Life Sciences plc and its wholly owned subsidiaries, Tiziana Therapeutics Inc., Tiziana Pharma Limited and Longevia Genomics S.r.l.

ABOUT THIS REGISTRATION STATEMENT

Solely for convenience, the trademarks, service marks and trade names in this registration statement may be referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. This registration statement contains additional trademarks, service marks and trade names of others, which are the property of their respective owners. We do not intend to use or display other companies’ trademarks, service marks and trade names to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

In this registration statement, all references to “U.S. dollars” or “US$” or “cents” are to the currency of the United States of America, and all references to “pounds Sterling” or “Sterling” or “GB£” or “£” or “pence” are to the currency of the United Kingdom.

Statements made in this registration statement on Form 20-F concerning the contents of any contract, agreement or other document are summaries of such contracts, agreements or documents and are not complete descriptions of all of their terms. If we filed any of these documents as an exhibit to this registration statement or to any registration statement or annual report that we previously filed, you may read the document itself for a complete description of its terms.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

Certain statements contained in this registration statement, including those in “Item 3.D. Risk Factors,” “Item 4.B. Business Overview” and “Item 5. Operating and Financial Review and Prospects” constitute forward-looking statements that involve substantial risks and uncertainties. In some cases, you can identify forward-looking statements by the words “may,” “might,” “will,” “could,” “would,” “should,” “expect,” “intend,” “plan,” “objective,” “anticipate,” “believe,” “estimate,” “predict,” “potential,” “continue” and “ongoing,” or the negative of these terms, or other comparable terminology intended to identify statements about the future. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. The forward-looking statements and opinions contained in this registration statement are based upon information available to us as of the date of this registration statement and, while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. Forward-looking statements include statements about:

- the development of Milciclib, Foralumab and any of our other product candidates, including statements regarding the timing of initiation, completion and the outcome of clinical studies or trials and related preparatory work, the period during which the results of the trials will become available and our research and development programs;
- our ability to obtain and maintain regulatory approval of our product candidates, including Milciclib and Foralumab, in the indications for which we plan to develop them, and any related restrictions, limitations or warnings in the label of an approved drug or therapy;
- our plans to research, develop, manufacture and commercialize our product candidates;
- the timing of our regulatory filings for our product candidates;
- the size and growth potential of the markets for our product candidates;
- our ability to raise additional capital;
- our commercialization, marketing and manufacturing capabilities and strategy;

- our expectations regarding our ability to obtain and maintain intellectual property protection;
- our ability to attract and retain qualified employees and key personnel;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- our estimates regarding future revenue, expenses and needs for additional financing; and
- regulatory developments in the United States, European Union and foreign countries.

You should refer to the section titled “Risk Factors” for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements in this registration statement will prove to be accurate.

Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

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

MARKET, ECONOMIC AND INDUSTRY DATA

This registration statement contains estimates, projections and other information concerning our industry, our business, and the markets for our product candidates. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties, and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from our own internal estimates and research as well as from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources.

In addition, assumptions and estimates of our and our industry’s future performance are necessarily subject to a high degree of uncertainty and risk due to a variety of factors, including those described in the section titled “Risk Factors.” These and other factors could cause our future performance to differ materially from our assumptions and estimates. See “Special Note Regarding Forward-Looking Statements.”

PRESENTATION OF FINANCIAL INFORMATION; NON-IFRS MEASURES

We maintain our books and records in pounds Sterling, and we prepare our consolidated financial statements in accordance with International Financial Reporting Standards (IFRS) as issued by the International Accounting Standards Board (IASB). Our results have been subsequently converted to U.S. dollars. All references in this registration statement to “$” are to U.S. dollars and all references to “£” are to pounds Sterling. Unless otherwise indicated, certain U.S. dollar amounts contained in this registration statement have been translated into pounds Sterling at the rate in effect at December 30, 2016, the last business day of the year ended December 31, 2016, of £1.00 to $1.2337. These translations should not be considered representations that any such amounts have been, could have been or could be converted into pounds Sterling at that or any other exchange rate as of that or any other date. See “Exchange Rate Information” for more information.

We have made rounding adjustments to some of the figures included in this registration statement. Accordingly, numerical figures shown as totals in some tables may not be an arithmetic aggregation of the figures that preceded them.

EXCHANGE RATE INFORMATION

Fluctuations in the exchange rate between the pound Sterling and the U.S. dollar will affect the U.S. dollar amounts received by potential future owners of our ADSs on conversion of dividends, if any, paid in pounds Sterling on the ordinary shares and will affect the potential future U.S. dollar price of our ADSs on the NASDAQ Capital Market (NASDAQ).

The table below shows the period end, average, high and low exchange rates of U.S. dollars per pound Sterling for the periods shown. Average rates are computed by using the noon buying rate of the Federal Reserve Bank of New York for the U.S. dollar on the last business day of each month during the relevant year indicated or each business day during the relevant month indicated. The rates set forth below are provided solely for your convenience and may differ from the actual rates used in the preparation of our consolidated financial statements included in this registration statement and other financial data appearing in this registration statement.

Year Ended December 31,	Period End	Average Rate for Period	High	Low
		(U.S. dollars per pound Sterling)		
2012	1.6262	1.5853	1.5301	1.6275
2013	1.6574	1.5641	1.4837	1.6574
2014	1.5578	1.6484	1.5517	1.7165
2015	1.4746	1.5284	1.4648	1.5882
2016	1.2337	1.3555	1.2155	1.4800

Month	High	Low
	(U.S. dollars per pound Sterling)	
April 2017	1.2373	1.2952
May 2017	1.2797	1.3036
June 2017	1.2622	1.3007
July 2017	1.2880	1.3079
August 2017	1.3229	1.2796
September 2017	1.3596	1.2957
October 2017	1.3304	1.3063

On October 26, 2017 the exchange rate published by the Federal Reserve Bank of New York was $1.3181 per £1.00.

PART I

ITEM 1: IDENTITY OF DIRECTORS, SENIOR MANAGEMENT AND ADVISERS

A. Directors and Senior Management.

For information on our directors and senior management, see “Item 6A. Directors and Senior Management.”

B. Advisers.

Our principal United States and United Kingdom legal advisers are Cooley LLP, located in the United States at 1114 6th Avenue, New York, NY 10036 and in the United Kingdom at Dashwood, 69 Old Broad Street, London EC2M 1QS, United Kingdom.

C. Auditors.

Mazars LLP has been our auditor since March 2017. For more information on our auditors, see “Item 10.G. Statements by Experts.”

ITEM 2: OFFER STATISTICS AND EXPECTED TIMETABLE

Not applicable.

ITEM 3: KEY INFORMATION

A. Selected Financial Data

The following tables present our selected consolidated financial data as of the dates and for the periods indicated. We derived the selected consolidated statements of operations and comprehensive loss data for the years ended December 31, 2015 and 2016 and the selected consolidated balance sheet data as of December 31, 2015 and 2016, from our audited consolidated financial statements included elsewhere in this registration statement. We prepare our consolidated financial statements in accordance with International Financial Reporting Standards (IFRS), which includes all standards issued by the International Accounting Standards Board (IASB) and related interpretations issued by the IFRS Interpretations Committee. Our historical results are not necessarily indicative of our future results. You should read this data together with our consolidated financial statements and related notes appearing elsewhere in this registration statement and the information in "Item 5. Operating and Financial Review and Prospects."

Our functional currency is the pound Sterling. However, for financial reporting purposes, our financial statements, which are prepared using the functional currency, have been translated into U.S. dollars. Our assets and liabilities are translated at the exchange rates at the balance sheet date, our revenue and expenses are translated at average exchange rates for the period presented and shareholders' equity is translated based on historical exchange rates. Translation adjustments are not included in determining net income (loss) but are included in foreign exchange translation adjustment to other comprehensive loss, a component of shareholders' equity.

Foreign currency transactions in currencies different from the functional currency are translated into the functional currency using the exchange rates prevailing at the dates of the transactions. Foreign exchange differences resulting from the settlement of such transactions and from the translation at period-end exchange rates of monetary assets and liabilities denominated in foreign currencies are recorded in general and administrative expense in the statement of operations and comprehensive loss.

As of December 31, 2015 and 2016, the representative exchange rate was £1.00 = $1.4746 and £1.00 = $1.2337, respectively.

Consolidated Statement of Operations and Comprehensive Loss Data:

	Six months to June 30,	As of December 31,		
	2017	2016	2015	2014
		(In thousand's except share and per share data)		
Operating expenses:				
Research and development	$2,884	$4,007	$9,609	$1,309
General and administrative	1,804	5,872	3,557	4,189
Total operating expenses	4,689	9,879	13,166	5,497
Loss from operations	(4,689)	(9,879)	(13,166)	(5,497)
Other income (expense), net	(5)	(12)	(28)	(86)
Income tax provision	-	121	-	99
Net loss attributable to ordinary shareholders	(4,693)	(9,770)	(13,193)	(5,484)
Other comprehensive loss:				
Foreign currency translation adjustment	(116)	650	3,063	(942)
Total comprehensive loss	(4,809)	(9,120)	(10,130)	(6,426)
Basic and diluted net loss per ordinary share	(0.05)	(0.10)	(0.11)	(0.28)
Weighted-average basic and diluted ordinary shares	(0.05)	(0.10)	(0.11)	(0.28)

Consolidated Balance Sheet Data:

	Six months to June 30,	As of December 31,		
	2017	2016	2015	2014
			(In thousand's)	
Cash and cash equivalents	$2,609	$5,802	$13,128	$3,530
Working capital (1)	$52	$4,054	$12,540	$2,768
Total assets	$3,064	$6,231	$13,640	$3,832
Total shareholders' equity	$79	$4,088	$12,540	$2,768

(1) We define working capital as current assets less current liabilities.

B. Capitalization and Indebtedness

The following table shows our indebtedness (distinguishing between guaranteed, unguaranteed, secured and unsecured indebtedness) as of June 30, 2017 and our capitalization as of June 30, 2017.

	As of June 30, 2017 (in thousands)
Total current debt	
Guaranteed	2,985
Secured	-
Unguaranteed/unsecured	-
Total non-current debt (excluding current portion of non-current debt)	
Guaranteed	-
Secured	-
Unguaranteed/unsecured	-
Shareholders' equity	
Share capital	6,970
Legal reserve	-
Other reserves	(6,891)
Total	79

The following table shows our net indebtedness as of September 30, 2017.

	As of June 30, 2017 (in thousands)
Cash and cash equivalent	2,609
Trading securities	-
Liquidity	2,609
Current financial receivable	-
Current bank debt	-
Current portion of non-current debt	-
Other current financial debt	-
Current financial debt	-
Net current financial indebtedness	-
Net financial indebtedness	-
Non-current bank loans	-
Bonds issued	-
Other non-current loans	-
Non-current financial indebtedness	-
Net financial indebtedness	-

We had no indirect or contingent indebtedness as of June 30, 2017.

There has been no material change in our capitalization and indebtedness as of December 31, 2016 (being the last date in respect of which we have published audited financial information) save that (1) on August 16, 2017 the Company issued 27,645,013 new ordinary shares to convert, with noteholder consent, $16,733,146 (£12,969,219) of convertible loan notes, rendering the Company debt free and adding $16,733,146 (£12,969,219) to our share capital; (2) on November 20, 2017 the Company issued 100,000 new ordinary shares for cash adding $197,715 (£150,000) to our share capital; (3) on November 27, 2017 the Company issued 183,333 new ordinary shares for cash adding $362,477 (£275,000) to our share capital; (4) on December 16, 2017 the Company issued 133,333 new ordinary shares for cash adding $263,620 (£200,000) to our share capital; on January 15, 2018 the Company issued 100,000 new ordinary shares for cash adding $199,500 (£150,000) to our share capital, and 810,201 new ordinary shares to our former noteholders in respect of accrued interest (included in the figure given in respect of (1), above); and on January 19, 2018 the Company issued 66,667 new ordinary shares for cash adding $133,000 (£100,000) to our share capital. Our cash balance as of September 30, 2017 was $1,020,414 and as of that date we had no borrowings.

C. Reasons for the Offer and Use of Proceeds

Not applicable.

D. Risk Factors

You should carefully consider the risks described below, together with all of the other information in this registration statement on Form 20-F. The risks and uncertainties below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we believe to be immaterial may also adversely affect our business. If any of the following risks occur, our business, financial condition and results of operations could be seriously harmed and potential future investors in our ADSs could lose all or part of their investment. Further, if we fail to meet the expectations of the public market in any given period, the potential market price of our ADSs could decline. We operate in a highly competitive environment that involves significant risks and uncertainties, some of which are outside of our control. If any of these risks actually occurs, our business and financial condition could suffer and the potential market price of our ADSs could decline.

Risks Related to the Development of our Product Candidates

If we encounter substantial delays in clinical trials of our product candidates, we may be unable to obtain required regulatory approvals, and therefore will be unable to commercialize our product candidates on a timely basis or at all.

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical trials to demonstrate the safety and utility of the product candidates. Clinical testing is expensive, time-consuming and uncertain as to outcome. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all, as a failure of one or more clinical trials can occur at any stage of testing. Events that may prevent successful or timely completion of clinical development include:

- delays in reaching a consensus with the U.S. Food and Drug Administration (FDA), European Medicines Agency (EMA) or other regulatory authorities on trial design;
- delays in reaching agreement on acceptable terms with prospective contract research organizations (CROs) and clinical trial sites;
- delays in opening clinical trial sites or obtaining required institutional review board or independent ethics committee approval at each clinical trial site;
- delays in recruiting suitable patients to participate in our future clinical trials;
- imposition of a clinical hold by regulatory authorities as a result of a serious adverse event or after an inspection of our clinical trial operations or clinical trial sites;
- failure by us, any CROs we engage or any other third parties to adhere to clinical trial requirements;
- failure to perform in accordance with good clinical practice (GCP), or applicable regulatory guidelines in Europe and other international markets;
- delays in the testing, validation, manufacturing and delivery of our product candidates to the clinical trial sites, including delays by third parties with whom we have contracted to perform certain of those functions;
- delays in having patients complete participation in a clinical trial or return for post-treatment follow-up;
- clinical trial sites or patients dropping out of a clinical trial;
- selection of clinical endpoints that require prolonged periods of clinical observation or analysis of the resulting data;

- occurrence of serious adverse events associated with the product candidate that are viewed to outweigh its potential benefits;
- occurrence of serious adverse events in clinical trials of the same class of agents conducted by other sponsors; and
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols.

Any inability to successfully complete preclinical and clinical development could result in additional costs to us or impair our ability to generate revenues from product sales, regulatory and commercialization milestones and royalties. In addition, if we make manufacturing or formulation changes to our product candidates, we may need to conduct additional studies to bridge our modified product candidates to earlier versions. Clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates and may harm our business, financial condition, results of operations and prospects.

We may fail to demonstrate the safety and therapeutic utility of our product candidates to the satisfaction of applicable regulatory authorities, which would prevent or delay regulatory approval and commercialization.

Before obtaining regulatory approvals for the commercial sale of our product candidates, we must demonstrate through lengthy, complex and expensive preclinical testing and clinical trials that our product candidates are both safe and effective for use in each target indication. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Most product candidates that commence clinical trials are never approved as products. If the results of our registrational trial or future pivotal trials for our other product candidates do not demonstrate therapeutic utility of our product candidates, or if there are safety concerns or serious adverse events associated with our product candidates, we may:

- be delayed in obtaining marketing approval for our product candidates, if 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 safety warnings;
- be subject to additional post-marketing testing requirements;
- be subject to changes in the way the product is administered;
- be required to perform additional clinical trials to support approval or be subject to additional post- marketing testing requirements;
- have regulatory authorities withdraw or suspend their approval of the product or impose restrictions on its distribution in the form of a modified risk evaluation and mitigation strategy (REMS);
- be subject to the addition of labeling statements, such as warnings or contraindications; or
- be sued or experience damage to our reputation.

Success in preclinical studies or clinical trials may not be indicative of results in future clinical trials.

Success in preclinical testing and early clinical trials does not ensure that later clinical trials will generate the same results or otherwise provide adequate data to demonstrate the effectiveness and safety of our product candidate. Frequently, product candidates that have shown promising results in early clinical trials have subsequently suffered significant setbacks in later clinical trials. To date, some of our clinical trials have involved small patient populations and because of the small sample size in such trials, the interim results of these clinical trials may be subject to substantial variability and may not be indicative of either future interim results or final results. In addition, the design of a clinical trial can determine whether its results will support approval of a product and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. Because we have limited experience designing clinical trials, we may be unable to design and execute a clinical trial to support regulatory approval. In addition, there is a high failure rate for drugs and biologic products proceeding through clinical trials. In fact, many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in preclinical testing and earlier-stage clinical trials. Moreover, data obtained from preclinical and clinical activities is subject to varying interpretations, which may delay, limit or prevent regulatory approval. In addition, we may experience regulatory delays or rejections as a result of many factors, including due to changes in regulatory policy during the period of our product candidate development. Any such delays could negatively impact our business, financial condition, results of operations and prospects.

We depend on enrollment of patients in our clinical trials for our product candidates and may find it difficult to enroll patients in our clinical trials, which could delay or prevent us from proceeding with clinical trials of our product candidates and could materially adversely affect our research and development efforts and business, financial condition and results of operations.

Identifying and qualifying patients to participate in clinical trials of our product candidates is critical to our success. The timing of our clinical trials depends on our ability to recruit patients to participate, and to see those patients through the completion of required follow-up periods. If, for any reason, patients are unwilling to enroll in our clinical trials, then the timeline for recruiting patients, conducting studies and obtaining regulatory approvals for our product candidates may be delayed. These delays could result in increased costs, delays in advancing our product candidates, delays in testing the effectiveness of our product candidates or termination of clinical trials altogether.

Our current product candidates are being developed to treat oncology and immune diseases of high unmet medical need. However, we may not be able to initiate or continue clinical trials if we cannot enroll a sufficient number of eligible patients to participate in the clinical trials required by the FDA, EMA or other regulatory authorities. As a result, we may not be able to identify, recruit and enroll a sufficient number of patients, or those with required or desired characteristics, to complete our clinical trials in a timely manner. Patient enrollment can be affected by many factors, including:

- size of the patient population and process for identifying patients;
- eligibility and exclusion criteria for our clinical trials;
- perceived risks and benefits of our product candidates;
- severity of the disease under investigation;
- proximity and availability of clinical trial sites for prospective patients;
- competition with other clinical trials for product candidates competing in the same therapeutic areas as our product candidates;
- ability to obtain and maintain patient consent;
- patient drop-outs prior to completion of clinical trials;
- patient referral practices of physicians; and

- ability to monitor patients adequately during and after treatment.

Our ability to successfully initiate, enroll and complete clinical trials in any foreign country is subject to numerous risks unique to conducting business in foreign countries, including:

- difficulty in establishing or managing relationships with CROs and physicians;
- different standards for the conduct of clinical trials;
- absence in some countries of established groups with sufficient regulatory expertise for review of certain treatment protocols;
- inability to locate qualified local consultants, physicians and partners; and
- the potential burden of complying with a variety of foreign laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatment.

If we have difficulty enrolling a sufficient number of patients or finding additional clinical trial sites to conduct our clinical trials as planned, we may need to delay, limit or terminate ongoing or planned clinical trials, any of which could have an adverse effect on our business, financial condition, results of operations and prospects.

Our product candidates and the process for administering our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit their commercial potential or result in significant negative consequences following any potential marketing approval.

During the conduct of clinical trials, patients report changes in their health, including illnesses, injuries and discomforts, to their study doctor. Often, it is not possible to determine whether the product candidate being studied caused these conditions. Regulatory authorities may draw different conclusions or require additional testing to confirm these determinations. For Milciclib, the most frequent drug-related side effects reported across studies, at all doses tested, were gastrointestinal (GI) adverse events (AEs) (nausea and diarrhoea, followed by less frequent vomiting), neurological effects (mainly tremor, then ataxia, dizziness and dysgeusia), skin disorders and asthenia, fatigue, headache and anorexia. For Foralumab, the most frequent drug-related side effects reported following intravenous administration were infusion related reactions (IRR) including fever, headaches, chills, nausea, vomiting diarrhea and hypotension considered the result of cytokine release also known as cytokine release syndrome (CRS). Other adverse events included reactivation of Epstein-Barr virus (clinically silent); moderate lymphocytopenia, abnormalities in liver function tests. Since most of these changes are related to the infusion route of administration and dosage level, such systemic toxicities are not anticipated when administered orally due to the lack of or minimal absorption of the oral antibody into the systemic circulation.

In addition, it is possible that as we test our product candidates in larger, longer and more extensive clinical programs, or as use of these product candidates becomes more widespread if they receive regulatory approval, illnesses, injuries, discomforts and other adverse events that were observed in earlier trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by patients. Many times, side effects are only detectable after investigational products are tested in large-scale, Phase 3 clinical trials or, in some cases, after they are made available to patients on a commercial scale after approval. If additional clinical experience indicates that our product candidates cause serious or life-threatening side effects, the development of our product candidates may fail or be delayed, or, if the product candidate has received regulatory approval, such approval may be revoked, which would harm our business, prospects, operating results and financial condition.

If in the future we are unable to demonstrate that such adverse events were caused by the administration process or related procedures, the FDA, EMA or other regulatory authorities could order us to cease further development of, or deny approval of, our product candidates for any or all targeted indications. Even if we are able to demonstrate that any serious adverse events are not product-related, such occurrences could affect patient recruitment or the ability of enrolled patients to complete the clinical trial. Moreover, if we elect or are required to delay, suspend or terminate any clinical trial of any of our product candidates, the commercial prospects of such product candidate may be harmed and our ability to generate product revenues from such product candidate may be delayed or eliminated. Any of these occurrences may harm our ability to develop other product candidates, and may harm our business, financial condition and prospects.

Additionally, if we or others later identify undesirable side effects caused by any of our product candidates, several potentially significant negative consequences could result, including:

- regulatory authorities may suspend or withdraw approvals of such product candidate;
- regulatory authorities may require additional warnings on the label;
- we may be required to change the way a product candidate is administered or conduct additional clinical trials;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of our product candidates.

Any contamination in our manufacturing process, shortages of raw materials or failure of any of our key suppliers to deliver necessary components could result in delays in our clinical development or marketing schedules.

Given the nature of biologics and NCE manufacturing, there is a risk of contamination. Any contamination could adversely affect our ability to produce product candidates on schedule and could, therefore, harm our results of operations and cause reputational damage. In addition, some of the raw materials required in our manufacturing process are derived from biologic sources, and are difficult to procure and may be subject to contamination or recall. A material shortage, contamination, recall or restriction on the use of biologically derived substances in the manufacture of our product candidates could adversely impact or disrupt the commercial manufacturing or the production of clinical material, which could adversely affect our development timelines and our business, financial condition, results of operations and prospects.

Risks Related to Our Financial Position and Need For Capital

We have incurred net losses in every year since our inception. We anticipate that we will continue to incur losses for the foreseeable future and may never achieve or maintain profitability.

We are a clinical stage biotechnology company with a limited operating history. Since our inception in May 2013, we have incurred significant net losses. Our net losses were $9.8 million, $13.2 million and $5.5 million for the years ended December 31, 2014, 2015 and 2016, respectively. As of December 31, 2016, we had an accumulated loss of $12.3 million. We have devoted substantially all of our efforts to research and development of our product candidates, including clinical development of our lead product candidates, Foralumab and Milciclib, as well as to building out our management team and infrastructure. We expect that it could be several years, if ever, before we have a commercialized product candidate. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. These net losses will adversely impact our shareholders' equity and net assets and may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase substantially if, and as, we:

- continue research and development of Foralumab, including the initiation of our Phase II trials in non-alcoholic steatohepatitis (NASH) and primary biliary cholangitis (PBC) patients;
- continue our Phase II program for Milciclib as a monotherapy in hepatocellular cancer (HCC) patients and initiate a Phase IIb trial for Milciclib in combination with sorafenib in HCC patients/primary sclerosing cholangitis (PSC);
- initiate clinical trials and preclinical studies for any additional product candidates that we may pursue in the future;
- manufacture our product candidates in accordance with current good manufacturing practices (cGMP) for clinical trials or potential commercial sales;
- invest in the development of our own manufacturing facilities;
- establish a sales, marketing and distribution infrastructure to commercialize any product candidate for which we may obtain marketing approval;
- develop, maintain, expand and protect our intellectual property portfolio;
- identify, assess, and acquire or in-license other product candidates and technologies;
- secure, maintain or obtain freedom to operate for any in-licensed technologies and products;
- address any competing technological and market developments; and
- expand our operations in the United States and Europe.

We may never succeed in any or all of these activities and, even if we do, we may never generate revenues that are significant or large enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. 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.

We may need substantial additional funding to complete the development of our product candidates, which may not be available on acceptable terms, if at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate certain of our product development, research operations or future commercialization efforts, if any.

Our operations have consumed substantial amounts of cash since inception, and we expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development of, initiate further clinical trials of and seek marketing approval for, our product candidates. In addition, if we obtain marketing approval for our product candidates, we expect to incur significant expenses related to product sales, marketing, manufacturing and distribution. Furthermore, we expect to incur additional costs associated with operating as a public company listed on both AIM in the United Kingdom and NASDAQ in the United States. Our future capital requirements will depend on many factors, including:

- the scope, progress, results and costs of laboratory testing, manufacturing, preclinical and clinical development for our current and future product candidates;
- the costs, timing and outcome of regulatory review of our product candidates;
- the extent to which we acquire or in-license and develop other product candidates and technologies;
- our ability to establish and maintain collaborations and license agreements on favorable terms, if at all;

- the costs, timing and outcome of potential future commercialization activities, including manufacturing, marketing, sales and distribution for our product candidates for which we receive marketing approval;
- the costs of developing, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims; and
- the sales price and availability of adequate third-party coverage and reimbursement for our product candidates, if and when approved.

Developing product candidates and conducting preclinical studies and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our product revenues, if any, will be derived from or based on sales of product candidates that may not be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, if at all. To the extent that additional capital is raised through the issuance of equity or equity-linked securities, the issuance of those securities could result in substantial dilution for our current shareholders and the terms of any future issuance may include liquidation or other preferences that adversely affect the rights of our current shareholders. Debt financing, if available, may involve covenants restricting our operations or our ability to incur additional debt. Any debt or additional equity financing that we raise may contain terms that are not favorable to us or our shareholders. If we raise additional funds through collaboration and licensing arrangements with third parties, it may be necessary to relinquish some rights to our technologies or our product candidates, or grant licenses on terms that are not favorable to us. Furthermore, the potential issuance of additional securities in the future, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our ADSs to decline and existing shareholders may not agree with our financing plans or the terms of such financings.

If we are unable to obtain adequate funding on a timely basis, we may be required to significantly curtail, delay or discontinue our research and development programs of our product candidates or any future commercialization efforts, be unable to expand our operations or be unable to otherwise capitalize on our business opportunities, as desired, which could harm our business and potentially cause us to discontinue operations.

Our limited operating history and no history of commercializing pharmaceutical products may make it difficult to evaluate the success of our business to date and to assess the prospects for our future viability.

Since our inception, we have devoted substantially all of our resources to developing Foralumab and Milciclib, and our other product candidates, building our intellectual property portfolio and providing general and administrative support for these operations. Although our research and development efforts to date have resulted in a pipeline of product candidates, we have not yet demonstrated our ability to successfully complete Phase 3 or other pivotal clinical trials, obtain regulatory approvals, or commercialize any of our product candidates. In addition, given our limited operating history, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors in achieving our business objectives.

Additionally, we are not profitable and have incurred losses in each year since our inception, and we expect that our financial condition and operating results may continue to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

Risks Related to Our Reliance on Third Parties

We rely, and expect to continue to rely, on third parties to conduct our preclinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates.

We have relied upon and plan to continue to rely upon third parties, including independent clinical investigators and third-party CROs, to conduct our preclinical studies and clinical trials and to monitor and manage data for our ongoing preclinical and clinical programs. In engaging these third parties, we typically have to, and expect to have to, negotiate budgets and contracts, which may result in delays to our development timelines and increases costs. Additionally, there is a limited number of qualified third-party service providers that specialize or have the expertise required to achieve our business objectives, and so it may be challenging to find alternative investigators or CROs, or do so on commercially reasonable terms. We rely on these parties for execution of our preclinical studies and clinical trials, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our preclinical studies and clinical trials is conducted in accordance with the applicable protocol and legal, regulatory and scientific standards, and our reliance on these third parties does not relieve us of our regulatory responsibilities. We and our third-party contractors and CROs are required to comply with GCP requirements, which are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area and comparable foreign regulatory authorities for all of our product candidates in clinical development. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, principal investigators and clinical trial sites. If we fail to exercise adequate oversight over any of our CROs or if we or any of our CROs fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, EMA or other regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon a regulatory inspection of us or our CROs or other third parties performing services in connection with our clinical trials, such regulatory authority will determine that any of our clinical trials complies with GCP regulations. In addition, our clinical trials must be conducted with product produced under applicable cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

Further, these investigators and CROs are not our employees and we will not be able to control, other than by contract, the amount of resources, including time, which they devote to our product candidates and clinical trials. If independent investigators or CROs fail to devote sufficient resources to the development of our product candidates, or if their performance is substandard, it may delay or compromise the prospects for approval and commercialization of our product candidates. These investigators and CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical studies or other drug development activities, which could affect their performance on our behalf. In addition, the use of third-party service providers requires us to disclose our proprietary information to these parties, which increases the risk that a competitor will discover them or that this information will be misappropriated or disclosed.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, our results of operations and commercial prospects would be harmed, our costs could increase and our ability to generate revenues could be delayed.

Repeating clinical trials or switching or engaging additional CROs involves additional cost and requires our management's time and focus. In addition, there is a natural transition period when a clinical trial has to be repeated or when a new CRO commences work. As a result, delays could occur, which could materially impact our ability to meet our desired clinical development timelines.

Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

We have engaged contract manufacturing organizations, or CMOs, to manufacture Foralumab and Milciclib and to perform quality testing, and because we collaborate with various organizations and academic institutions for the advancement of our platforms, we must, at times, share our proprietary technology and confidential information, including trade secrets, with them. We seek to protect our proprietary technology, in part, by entering into confidentiality agreements and, if applicable, material transfer agreements, collaborative research agreements, consulting agreements or other similar agreements with our collaborators, advisors, employees and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's discovery of our proprietary technology and confidential information or other unauthorized use or disclosure of such technology or information would impair our competitive position and may have an adverse effect on our business, financial condition, results of operations and prospects.

Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of these agreements, independent development or publication of information including our trade secrets by third parties. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business, financial condition, results of operations and prospects.

We utilize, and expect to continue to utilize, third parties to conduct our product manufacturing for the foreseeable future, and these third parties may not perform satisfactorily.

We currently rely on CMOs for the manufacturing of clinical batches and intend to continue to rely on third parties to manufacture our preclinical study and clinical trial product supplies. If our current CMOs, or any future third-party manufacturers, do not successfully carry out their contractual duties, meet expected deadlines or manufacture our product candidates in accordance with regulatory requirements, or if there are disagreements between us and our CMOs or any future third- party manufacturers, we will not be able to complete, or may be delayed in completing, the preclinical studies required to support future IND submissions and the clinical trials required for approval of our product candidates.

In addition to our current CMOs, we may rely on additional third parties to manufacture ingredients of our product candidates in the future and to perform quality testing, and reliance on these third parties entails risks to which we would not be subject if we manufactured the product candidates ourselves, including:

- reduced control for certain aspects of manufacturing activities;
- termination or nonrenewal of manufacturing and service agreements with third parties in a manner or at a time that is costly or damaging to us; and
- disruptions to the operations of our third-party manufacturers and service providers caused by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or service provider.

Any of these events could lead to clinical trial delays or failure to obtain regulatory approval, or impact our ability to successfully commercialize any of our product candidates. Some of these events could be the basis for FDA, EMA or other regulatory authority action, including injunction, recall, seizure or total or partial suspension of product manufacture.

To the extent we rely on a third-party manufacturing facility for commercial supply, that third party will be subject to significant regulatory oversight with respect to manufacturing our product candidates.

The preparation of therapeutics for clinical trials or commercial sale is subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in late-stage clinical trials must be manufactured in accordance with cGMP requirements. These regulations govern manufacturing processes and procedures, including record keeping, and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of outside agents or other contaminants, or to inadvertent changes in the properties or stability of a product candidate that may not be detectable in final product testing. To the extent that we utilize third-party facilities for commercial supply, the third party's facilities and quality systems must pass an inspection for compliance with the applicable regulations as a condition of regulatory approval. In addition, the regulatory authorities may, at any time, audit or inspect the third-party manufacturing facility or the associated quality systems for compliance with the regulations applicable to the activities being conducted. If, for example, these facilities do not pass a plant inspection, the FDA will not approve the applicable NDA or BLA.

We do not directly control the manufacturing of, and are completely dependent on, our CMOs for compliance with cGMP requirements. If our CMOs cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA, EMA or other regulatory authorities, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. In addition, we have no direct control over the ability of our CMOs to maintain adequate quality control, quality assurance and qualified personnel. Furthermore, all of our CMOs are engaged with other companies to supply and/or manufacture materials or products for such companies, which exposes our CMOs to regulatory risks for the production of such materials and products. As a result, failure to meet the regulatory requirements for the production of those materials and products may generally affect the regulatory clearance of our CMOs' facilities. Our failure, or the failure of third parties, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products and product candidates.

Our potential future dependence upon others for the manufacture of our product candidates may adversely affect our future profit margins and our ability to commercialize any products that receive regulatory approval on a timely and competitive basis.

Risks Related to Commercialization of Our Product Candidates

We currently have no marketing and sales force. If we are unable to establish effective sales, marketing and distribution capabilities or enter into agreements with third parties to market, sell and distribute our product candidates that may be approved, we may not be successful in commercializing our product candidates if and when approved, and we may be unable to generate any product revenue.

We currently do not have a marketing or sales team for the marketing, sales and distribution of any of our product candidates. In order to commercialize any of our product candidates that may be approved, we intend to build, on a territory-by-territory basis, marketing, sales, distribution, managerial and other non-technical capabilities or make arrangements with third parties to perform these services. These efforts will require significant capital expenditures, management resources and time, and we face competition in search for qualified personnel or third parties to assist with marketing, sales and distribution of any of our product candidates. We may not be successful in building these capabilities.

There are risks involved with both establishing our own sales, marketing and distribution capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and 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/or distribution capabilities is delayed or does not occur for any reason, we

would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our product candidates on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future product that we may develop;
- the lack of complementary treatments 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.

If we enter into arrangements with third parties to perform sales, marketing and distribution services, our product revenue or the profitability to us from these revenue streams is likely to be lower than if we were to market and sell any product candidates that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market our product candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties and any of them may fail to devote the necessary resources and attention to sell and market our product candidates effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we may not be successful in commercializing our product candidates.

We face significant competition in an environment of rapid technological change and the possibility that our competitors may achieve regulatory approval before us or develop therapies that are more advanced or effective than ours.

The biotechnology and pharmaceutical industries are characterized by rapidly changing technologies, significant competition and a strong emphasis on intellectual property. We face substantial competition from many different sources, including large and specialty pharmaceutical and biotechnology companies, academic research institutions, government agencies and public and private research institutions.

New developments, including the development of other pharmaceutical technologies and methods of treating disease, occur in the pharmaceutical and life sciences industries at a rapid pace. Developments by competitors may render our product candidates obsolete or noncompetitive. We anticipate that we will face intense and increasing competition as new treatments enter the market and advanced technologies become available.

Many of our potential competitors, alone or with their strategic partners, have substantially greater financial, technical and other resources, such as larger research and development, clinical, sales and marketing and manufacturing organizations. These third parties also compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, the development of our products. In addition, mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of competitors. Our commercial opportunity could be reduced or eliminated if competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any product candidate that we may develop. Competitors also may obtain FDA, EMA or other regulatory approval for their products more rapidly or earlier than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, technologies developed by our competitors may render our product candidates uneconomical or obsolete, and we may not be successful in marketing our product candidates against competitors.

In addition, as a result of the expiration or successful challenge of our patent rights, we could face more litigation with respect to the validity and/or scope of patents relating to our competitors' products. The availability of our competitors' products could limit the demand, and the price we are able to charge, for any product candidate that we may develop and commercialize.

The market opportunities for our product candidates may be smaller than we anticipate.

We focus our research and development efforts on treatments for cancer and autoimmune disease. Our understanding of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, is based on estimates. These estimates may prove to be incorrect and new studies may reduce the estimated incidence or prevalence of these diseases. The number of patients in the United States, the European Union and elsewhere may turn out to be lower than expected, may not be otherwise amenable to treatment with our product candidates or patients may become increasingly difficult to identify and access, all of which would adversely affect our business, financial condition, results of operations and prospects.

Further, there are several factors that could contribute to making the actual number of patients who receive our potential products, if and when approved, less than the potentially addressable market. These include, for example, the lack of widespread availability of, and limited reimbursement for, new therapies in many underdeveloped markets.

The future commercial success of our product candidates will depend upon the degree of each product candidates' market acceptance by physicians, patients, third-party payors and others in the medical community.

Our product candidates are at varying stages of development, and we may never have a product that is commercially successful. To date, we have no product authorized for marketing. Due to the inherent risk in the development of pharmaceutical products, we may never successfully complete development and commercialization of any of our product candidates. Even with the requisite approvals from the FDA, EMA and other regulatory authorities internationally, the commercial success of our product candidates will depend, in part, on the acceptance of physicians, patients and third-party payors of our product candidates as medically necessary, cost-effective and safe. Any product that we commercialize may not gain acceptance by physicians, patients, third-party payors and others in the medical community. If these products do not achieve an adequate level of acceptance, we may not generate significant product revenue and may not become profitable. Even if some product candidates achieve market acceptance, the market may not prove to be large enough to allow us to generate significant revenues. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on several factors, including:

- the effectiveness and safety of our product candidates as demonstrated in clinical trials;
- the potential and perceived advantages of our product candidates over alternative treatments;
- the availability and cost of treatment relative to alternative treatments;
- changes in the standard of care for the targeted indications for any product candidate;
- the willingness of physicians to prescribe, and the target patient population to try, new therapies;
- the prevalence and severity of any side effects;
- product labeling or product insert requirements of the FDA, EMA or other regulatory authorities, including any limitations or warnings contained in a product's approved labeling;
- the timing of market introduction of competitive products;
- sales, distribution and marketing support;

- publicity concerning our product candidates or competing products and treatments;
- potential product liability claims;
- any restrictions on the use of our products together with other medications; and
- favorable third-party payor coverage and adequate reimbursement.

Even if a potential product displays favorable clinical properties and safety profile in preclinical studies and clinical trials, market acceptance of the product will not be fully known until after it is launched.

The insurance coverage and reimbursement status of newly approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for our product candidates, if approved, could limit our ability to market those products.

We expect that coverage and adequate reimbursement by government and private payors will be essential for most patients to be able to afford these treatments. Accordingly, sales of our product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or will be reimbursed by government authorities, private health coverage insurers and other third-party payors. Coverage and reimbursement by a third-party payor may depend upon several factors, including the third-party payor's determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

Obtaining coverage and reimbursement for a product from third-party payors is a time-consuming and costly process that could require us to provide to the payor supporting scientific, clinical and cost-effectiveness data. We may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. If coverage and reimbursement are not available, or are available only at limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be adequate to realize a sufficient return on our investment.

There is significant uncertainty related to third-party coverage and reimbursement of newly approved products. In the United States, third-party payors, including government payors such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs and biologics will be covered and reimbursed. The Medicare and Medicaid programs increasingly are used as models for how private payors develop their coverage and reimbursement policies. However, no uniform policy of coverage and reimbursement exists among third-party payors. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. One payor's determination to provide coverage for a product does not assure that other payors will also provide coverage, and adequate reimbursement. It is difficult to predict what the Centers for Medicare and Medicaid Services (CMS) will decide with respect to coverage and reimbursement for fundamentally novel products such as ours, as there is no body of established practices and precedents for these types of products. Moreover, reimbursement agencies in the European Union may be more conservative than the CMS. For example, several cancer drugs have been approved for reimbursement in the United States and have not been approved for reimbursement in certain EU Member States. It is difficult to predict what third-party payors will decide with respect to the coverage and reimbursement for our product candidates.

Also, the containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of drugs have been a focus in this effort. The U.S. government, state legislatures, and foreign governments have shown significant interest in implementing cost-containment programs to limit the growth of government-paid healthcare costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. For example, in the United States, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or the PPACA, contains provisions that may reduce the profitability of products, including, for example, increased rebates for products sold to Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal health care programs. Further, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several recent congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to product pricing, contain the cost of drugs, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products.

Outside the United States, international operations generally are subject to extensive government price controls and other market regulations, and increasing emphasis on cost-containment initiatives in the European Union, Canada and other countries may put pricing pressure on us. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. In general, the prices of medicines under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for medical products, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our product candidates may be reduced compared with the United States and may be insufficient to generate commercially reasonable product revenues.

In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU Member States and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidates to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed.

Moreover, increasing efforts by government and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for new products approved and, as a result, they may not cover or provide adequate payment for our product candidates.

Payors increasingly are considering new metrics as the basis for reimbursement rates, such as average sales price, average manufacturer price and actual acquisition cost. The existing data for reimbursement based on some of these metrics is relatively limited, although certain states have begun to survey acquisition cost data for the purpose of setting Medicaid reimbursement rates, and CMS has begun making pharmacy National Average Drug Acquisition Cost and National Average Retail Price data publicly available on at least a monthly basis. Therefore, it may be difficult to project the impact of these evolving reimbursement metrics on the willingness of payors to cover product candidates that we or our partners are able to commercialize. We expect to experience pricing pressures in connection with the sale of any of our product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become intense. As a result, increasingly high barriers are being erected to the entry of new products such as ours.

Risks Related to Our Intellectual Property

Our rights to develop and commercialize our product candidates are subject to the terms and conditions of licenses granted to us by others. If we fail to comply with our obligations under our existing and any future intellectual property licenses with third parties, we could lose license rights that are important to the business.

We do not currently own any patents; however, we are heavily reliant upon licenses and sublicenses from Nerviano Medical Sciences S.r.l. (Nerviano) and Novimmune SA (Novimmune) to certain patent rights and proprietary technology that are important or necessary to the development of our technology and product candidates, including the patents and know-how relating to manufacture. These and other licenses may not provide exclusive rights to use such intellectual property and technology, or may not provide exclusive rights to use such intellectual property and technology in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and product candidates in the future. As a result, we may not be able to prevent competitors from developing and commercializing competitive products, including in territories covered by our licenses.

In some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties. If our licensors fail to maintain such patents or patent applications, or lose rights to those patents or patent applications, the rights we have licensed may be reduced or eliminated and our right to develop and commercialize any of our product candidates that are the subject of such licensed rights could be adversely affected. In addition to the foregoing, the risks associated with patent rights that we license from third parties will also apply to patent rights we may own in the future.

Licenses to additional third-party technology and materials that may be required for our development programs, including additional technology and materials owned by any of our current licensors, may not be available in the future or may not be available on commercially reasonable terms, or at all, which could have an adverse effect on our business and financial condition.

If we are unable to obtain and maintain patent protection for our current product candidates, any future product candidates we may develop and our technology, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours.

Our success depends, in large part, on our ability to seek, obtain and maintain patent protection in the United States and other countries with respect to our product candidates and to future innovation related to our manufacturing technology. Our licensors have sought and we intend to seek to protect our proprietary position by filing patent applications in the United States, the United Kingdom and elsewhere, related to certain technologies and our product candidates that are important to our business. Our current patent portfolio contains a limited number of patent applications, all of which are in-licensed from third parties and relate to either composition of matter, formulation, method of use or process of manufacturing Foralumab, Milciclib and anti-IL-6r monoclonal antibody (mAb). However, the risks associated with patent rights generally apply to patent rights that we in-license now or in the future, as well as patent rights that we may own in the future. Moreover, the risks apply with respect to patent rights and other intellectual property applicable to our product candidates, as well as to any intellectual property rights that we may acquire in the future related to future product candidates, if any. We have filed a new patent application covering the composition of matter of Foralumab. However, this application is still pending and there is no guarantee that USPTO will grant this application.

The patent prosecution process is expensive, time-consuming and complex, and we may not be able to file, prosecute, maintain, enforce or license all necessary or desirable patent applications at a reasonable cost or in a timely manner.

In some cases, the work of certain academic researchers in the oncology and immunology fields has entered the public domain, which we believe precludes our ability to obtain patent protection for certain inventions relating to such work.

Consequently, we will not be able to assert any such patents to prevent others from using our technology for, and developing and marketing competing products to treat, these indications. 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.

Our existing license agreements impose, and we expect that future license agreements will impose, various due diligence, development and commercialization timelines, insurance, milestone payments, royalties and other obligations on us. See the description in the section titled "Business-Collaboration and License Agreements" herein. If we fail to comply with our obligations under these agreements, or we are subject to a bankruptcy, or, in some cases, under other circumstances, the licensor may have the right to terminate the license, in which event we would not be able to market product candidates covered by the license. In addition, certain of these license agreements are not assignable by us without the consent of the respective licensor, which may have an adverse effect on our ability to engage in certain transactions.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has, in recent years, been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of any patent rights are highly uncertain. Our licensed patent applications may not result in patents being issued which protect our technology or product candidates, effectively prevent others from commercializing competitive technologies and product candidates or otherwise provide any competitive advantage. In fact, patent applications may not issue as patents at all. Even assuming patents issue from patent applications in which we have rights, changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

Other parties have developed technologies that may be related or competitive to our own and such parties may have filed or may file patent applications, or may have received or may receive patents, claiming inventions that may overlap or conflict with those claimed in our own patent applications or issued patents. We may not be aware of all third-party intellectual property rights potentially relating to our current and future product candidates.

Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and in other jurisdictions are typically not published until 18 months after filing, or, in some cases, not at all. Therefore, we cannot know with certainty whether the inventors of our licensed patents and applications were the first to make the inventions claimed in those patents or pending patent applications, or that they were the first to file for patent protection of such inventions. Similarly, should we own any patents or patent applications in the future, we may not be certain that we were the first to file for patent protection for the inventions claimed in such patents or patent applications. As a result, the issuance, scope, validity and commercial value of our patent rights cannot be predicted with any certainty.

The degree of patent protection we require to successfully compete in the marketplace may be unavailable or severely limited in some cases and may not adequately protect our rights or permit us to gain or keep any competitive advantage. We cannot provide any assurances that any of our licensed patents have, or that any of our pending licensed patent applications that mature into issued patents will include, claims with a scope sufficient to protect our product candidates or otherwise provide any competitive advantage. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Furthermore, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Various extensions may be available; however, the life of a patent, and the protection it affords, is limited. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our licensed patent portfolio may not provide us with adequate and continuing patent protection sufficient to exclude others from commercializing products similar to our product candidates, including biosimilar versions of such products. In addition, the intellectual property portfolio licensed to us by Nerviano and Novimmune may be used by them or licensed to third parties, and such third parties may have certain enforcement rights. Thus, patents licensed to us could be put at risk of being invalidated or interpreted narrowly in litigation filed by or against our licensors or another licensee or in administrative proceedings brought by or against our licensors or another licensee in response to such litigation or for other reasons.

Even if we acquire patent protection that we expect should enable us to maintain some competitive advantage, third parties, including competitors, may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. In litigation, a competitor could claim that our patents, if issued, are not valid for a number of reasons. If a court agrees, we would lose our rights to those challenged patents.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability and our licensed patents may be challenged in courts or patent offices in the United States and abroad. For example, we may be subject to a third-party submission of prior art to the U.S. Patent and Trademark Office (USPTO) challenging the validity of one or more claims of our licensed patents. Such submissions may also be made prior to a patent's issuance, precluding the granting of a patent based on one of our pending licensed patent applications. We may become involved in opposition, derivation, reexamination, inter partes review, post-grant review or interference proceedings challenging the patent rights of others from whom we have obtained licenses to such rights. Competitors may claim that they invented the inventions claimed in our licensed issued patents or patent applications prior to the inventors of such patents or applications. A competitor who can establish an earlier filing or invention date may also claim that we are infringing their patents and that we therefore cannot practice our technology as claimed under our licensed patents, if issued. Competitors may also contest our licensed patents, if issued, by showing that the invention was not patent-eligible, was not novel, was obvious or that the patent claims failed any other requirement for patentability.

An adverse determination by former employees or consultants asserting ownership rights to our patents may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar technology and therapeutics, without payment to us, or could limit the duration of the patent protection covering our technology and product candidates. Such challenges may also result in our inability to manufacture or commercialize our product candidates without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Even if they are unchallenged, our licensed patents and pending patent applications, if issued, may not provide us with any meaningful protection or prevent competitors from designing around our patent claims to circumvent our licensed patents by developing similar or alternative technologies or therapeutics in a non-infringing manner. For example, a third party may develop a competitive therapeutic that provides benefits similar to one or more of our product candidates but that uses a different antibody or molecular active ingredient that falls outside the scope of our patent protection. If the patent protection provided by the patents and patent applications we hold or pursue with respect to our product candidates is not sufficiently broad to impede such competition, our ability to successfully commercialize our product candidates could be negatively affected, which would harm our business.

Our intellectual property licenses with third parties may be subject to disagreements over contract interpretation, which could narrow the scope of our rights to the relevant intellectual property or technology or increase our financial or other obligations to our licensors.

We currently depend, and will continue to depend, on our license agreements whereby we obtain rights in certain patents and patent applications owned by them. Further development and commercialization of our current product candidates may, and development of any future product candidates will, require us to enter into additional license or collaboration agreements. The agreements under which we currently license intellectual property or technology from third parties 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 an adverse effect on our business, financial condition, results of operations and prospects.

If any of our licenses or material relationships or any in-licenses upon which our licenses are based are terminated or breached, we may:

- lose our rights to develop and market our product candidates;
- lose patent protection for our product candidates;
- experience significant delays in the development or commercialization of our product candidates;
- not be able to obtain any other licenses on acceptable terms, if at all; or
- incur liability for damages.

In addition, a third party may in the future bring claims that our performance under our license agreements, including our sponsoring of clinical trials, interferes with such third party's rights under its agreement with one of our licensors. If any such claim were successful, it may adversely affect our rights and ability to advance our product candidates as clinical candidates or subject us to liability for monetary damages, any of which would have an adverse effect on our business, financial condition, results of operations and prospects.

These risks apply to any agreements that we may enter into in the future for our current or any future product candidates. If we experience any of the foregoing, it could have a negative impact on our business, financial condition, results or operations and prospects.

If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.

We have entered into license agreements with third parties and may need to obtain additional licenses from one or more of these same third parties or from others to advance our research or allow commercialization of our product candidates. It is possible that we may be unable to obtain additional licenses at a reasonable cost or on reasonable terms, if at all. In that event, we may be required to expend significant time and resources to redesign our product candidates or the methods for manufacturing them 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 our product candidates, which would harm our business. We cannot provide any assurances that third-party patents or other intellectual property rights do not exist which might be enforced against our current product candidates or future product candidates, resulting in either an injunction prohibiting our manufacture or sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties.

In each of our existing license agreements, and we expect in our future agreements, patent prosecution of our licensed technology is controlled solely by the licensor, and we may be required to reimburse the licensor for their costs of patent prosecution. If our licensors fail to obtain and maintain patent or other protection for the proprietary intellectual property we license from them, we could lose our rights to the intellectual property or our exclusivity with respect to those rights, and our competitors could market competing products using the intellectual property. Our license agreements with Nerviano and Novimmune also require us to meet development thresholds to maintain each license, including establishing a set timeline for developing and commercializing product candidates. Disputes may arise regarding intellectual property subject to a licensing agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights pursuant to our collaborative development relationships;

- our diligence obligations under the license agreements and what activities satisfy those diligence obligations;
- the inventorship or 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.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize our product candidates.

We may not be successful in obtaining or maintaining necessary rights to our product candidates through acquisitions and in-licenses.

We currently have certain rights to the intellectual property, through licenses from third parties, to develop our product candidates. Because our programs may require the use of additional proprietary rights held by these or other third parties, the growth of our business likely will depend, in part, on our ability to acquire, in-license or use these proprietary rights. We may be unable to acquire or in-license any compositions, methods of use, processes or other intellectual property rights from third parties that we identify as necessary for our product candidates. The licensing or acquisition of third-party intellectual property rights is a competitive area, and several more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment.

We may collaborate with non-profit and academic institutions to accelerate our preclinical research and development under written agreements with these institutions. These institutions may provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue our program.

If we are unable to successfully obtain rights to required third-party intellectual property or maintain the existing intellectual property rights we have, we may have to abandon development of our product candidates and our business, financial condition, results of operations and prospects could suffer. Moreover, to the extent that we seek to develop other product candidates in the future, we will likely require acquisition or in-license of additional proprietary rights held by third parties.

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

Periodic maintenance fees, renewal fees, annuity fees and various other government fees on patents and/or applications will be due to be paid to the USPTO and various government patent agencies outside of the United States over the lifetime of our licensed patents and/or applications and any patent rights we may own in the future. We rely on our outside counsel or our licensing partners to pay these fees due to non-U.S. patent agencies. The USPTO and various non-U.S. government patent agencies require compliance with several procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply and we are also dependent on our licensors to take the necessary action to comply with these requirements with respect to our licensed intellectual property. In many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, 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. In such an event, potential competitors might be able to enter the market and this circumstance could have an adverse effect on our business.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than those in the United States. In some cases, we may not be able to obtain patent protection for certain licensed technology outside the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States, even in jurisdictions where we do pursue patent protection. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, even in jurisdictions where we do pursue patent protection 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 pursued and obtained patent protection to develop their own products and, further, may export otherwise 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, if pursued and obtained, or marketing of competing products in violation of our proprietary rights generally. Moreover, many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. Many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired and our business and results of operations may be adversely affected.

In addition, proceedings to enforce our patent rights in foreign jurisdictions 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 our 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.

We may not be able to protect our trade secrets in court or at the USPTO.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable or that we elect not to patent, processes for which patents are difficult to enforce and any other elements of our product candidate discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. However, trade secrets can be difficult to protect and some courts inside and outside the United States are less willing or unwilling to protect trade secrets. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors and contractors. However, we may not be able to prevent the unauthorized disclosure or use of our technical know-how or other trade secrets by the parties to these agreements, despite the existence generally of confidentiality agreements and other contractual restrictions.

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. If any of the collaborators, scientific advisors, employees and consultants who are parties to these agreements breach or violate

the terms of any of these agreements, we may not have adequate remedies for any such breach or violation. As a result, we could lose our trade secrets.

We cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary technology and processes. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements and security measures, they may still be breached, and we may not have adequate remedies for any breach.

In addition, our trade secrets may otherwise become known or be independently discovered by competitors. Competitors could purchase our product candidates and attempt to replicate some or all of the competitive advantages we derive from our development efforts, willfully infringe our intellectual property rights, 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, we would have no right to prevent them, or those to whom they communicate such trade secrets, from using that technology or information to compete with us. If our trade secrets are not adequately protected so as to protect our market against competitors' therapeutics, our competitive position could be adversely affected, as could our business.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights.

Our commercial success depends upon our ability and the ability of our future collaborators to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights and intellectual property of third parties. The biotechnology and pharmaceutical industries are characterized by extensive and complex litigation regarding patents and other intellectual property rights. We may in the future become party to, or be threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our product candidates and technology, including interference proceedings, post grant review and inter partes review before the USPTO. Our competitors or other third parties may assert infringement claims against us, alleging that our therapeutics, manufacturing methods, formulations or administration methods are covered by their patents. Given the vast number of patents in our field of technology, we cannot be certain or guarantee that we do not infringe existing patents or that we will not infringe patents that may be granted in the future. Since this area is competitive and of strong interest to pharmaceutical and biotechnology companies, there will likely be additional patent applications filed and additional patents granted in the future, as well as additional research and development programs expected in the future. Furthermore, because patent applications can take many years to issue, may be confidential for 18 months or more after filing and can be revised before issuance, there may be applications now pending which may later result in issued patents that may be infringed by the manufacture, use, sale or importation of our product candidates and we may or may not be aware of such patents. If a patent holder believes the manufacture, use, sale or importation of one of our product candidates infringes its patent, the patent holder may sue us even if we have licensed other patent protection for our technology. Moreover, we may face patent infringement claims from non-practicing entities that have no relevant product revenue and against whom our licensed patent portfolio may therefore have no deterrent effect.

It is also possible that we have failed to identify relevant third-party patents or applications. For example, applications filed before November 29, 2000 and certain applications filed after that date that will not be filed outside the United States may remain confidential until patents issue. Moreover, it is difficult for industry participants, including us, to identify all third-party patent rights that may be relevant to our product candidates and technologies because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. We may fail to identify relevant patents or patent applications or may identify pending patent applications of potential interest but incorrectly predict the likelihood that such patent applications may issue with claims of relevance to our technology. In addition, we may be unaware of one or more issued patents that would be infringed by the manufacture, sale or use of a current or future product candidate, or we may incorrectly conclude that a third-party patent is invalid, unenforceable or not infringed by our activities. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our technologies, our product candidates or the use of our product candidates.

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 or other intellectual property 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, which could adversely affect our ability to commercialize our product candidates. In order to successfully challenge the validity of any such 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 of competent jurisdiction would invalidate the claims of any such U.S. patent. Similarly, there is no assurance that a court of competent jurisdiction would find that product candidates or our technology did not infringe a third-party patent.

Patent and other types of intellectual property litigation can involve complex factual and legal questions, and their outcome is uncertain. If we are found, or believe there is a risk that we may be found, to infringe a third party's valid and enforceable intellectual property rights, we could be required or may choose to obtain a license from such third party to continue developing, manufacturing and marketing our product candidates and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. We could be forced, including by court order, to cease developing, manufacturing and commercializing the infringing technology or product candidate. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right. A finding of infringement could prevent us from manufacturing and commercializing our product candidates or force us to cease some or all of our business operations, which could harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business, financial condition, results of operations and prospects.

Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Litigation or other legal proceedings relating to intellectual property claims, with or without merit, are unpredictable and generally expensive and time-consuming. Competitors may infringe our patents or the patents of our licensing partners, should such patents issue, or we may be required to defend against claims of infringement. To counter infringement or unauthorized use claims or to defend against claims of infringement can be expensive and time consuming. Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. 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. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on us. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities.

We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios.

Accordingly, despite our efforts, we may not be able to prevent third parties from infringing, misappropriating or successfully challenging our intellectual property rights. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a negative impact on our ability to compete in the marketplace.

We may be subject to claims asserting that our employees, consultants or advisors have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting ownership of what we regard as our own intellectual property.

Certain of our employees, consultants or advisors are currently, or were previously, employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors, as well as our academic partners. Although we try to ensure that our employees, consultants and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these individuals or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. An inability to incorporate such technologies or features would harm our business and may prevent us from successfully obtaining necessary regulatory approvals and commercializing our product candidates. In addition, we may lose personnel as a result of such claims, and any such litigation or the threat thereof may adversely affect our ability to hire employees or contract with independent contractors. A loss of key personnel or their work product could hamper or prevent our ability to obtain necessary regulatory approvals and commercialize our product candidates, which would have an adverse effect on our business, results of operations and financial condition. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or 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, conceives or develops intellectual property that we regard as our own. Moreover, even when we obtain agreements assigning intellectual property to us, the assignment of intellectual property rights may not be self-executing or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Furthermore, individuals executing agreements with us may have preexisting or competing obligations to a third party, such as an academic institution, and thus an agreement with us may be ineffective in perfecting ownership of inventions developed by that individual. Disputes about the ownership of intellectual property that we may own may have an adverse effect on our business.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes several significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted and also may affect patent litigation. These also include provisions that switched the United States from a "first-to-invent" system to a "first-to-file" system, allow third-party submission of prior art to the USPTO during patent prosecution and set forth additional procedures to attack the validity of a patent through various post-grant proceedings administered by the USPTO. Under a first-to-file system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to the patent on an invention regardless of whether another inventor had made the invention earlier. The USPTO developed new regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first-to-file provisions, only became effective on March 16, 2013.

Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act 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, all of which could have a negative impact effect on our business, financial condition, results of operations and prospects.

Additionally, the U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of

patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, the combination of new federal legislation, federal court decisions, and guidance from the USPTO has created uncertainty with respect to the value of patents, once obtained. Depending on the decisions by the U.S. Congress, federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or enforce our existing patents and patents we might obtain in the future.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest.

We do not currently have any registered trademarks and we have not filed any trademark applications to date. Any trademark applications in the United States, Europe and in other foreign jurisdictions where we may file may not be allowed or may subsequently be opposed. Once filed and registered, our trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. As a means to enforce our trademark rights and prevent infringement, we may be required to file trademark claims against third parties or initiate trademark opposition proceedings. This can be expensive and time-consuming, particularly for a company of our size. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. 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.

***Intellectual property rights and regulatory exclusivity rights do not necessarily address all potential threats*.**

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to make products that are similar to our product candidates but that are not covered by the claims of the patents that we license or may own in the future;
- we, or our license partners or future collaborators, might not have been the first to make the inventions covered by the issued patent or pending patent applications that we license or may own in the future;
- we, or our license partners or future collaborators, might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our owned or licensed intellectual property rights;
- others may circumvent our regulatory exclusivities, such as by pursuing approval of a competitive product candidate via the traditional approval pathway based on their own clinical data, rather than relying on the abbreviated pathway provided for biosimilar applicants;
- it is possible that our pending licensed patent applications or those that we may own in the future will not lead to issued patents;
- issued patents that we hold rights to now or in the future may be held invalid or unenforceable, including as a result of legal challenges by our competitors;

- others may have access to the same intellectual property rights licensed to us on a non-exclusive basis;
- 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;
- we may not develop additional proprietary technologies that are patentable;
- the patents or other intellectual property rights of others may have an adverse effect on our business; or
- we may choose not to file a patent for certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property.

Should any of these events occur, they could significantly harm our business, financial condition, results of operations and prospects.

Risks Related to Government Regulation

Even if we complete the necessary clinical trials, we cannot predict when, or if, we will obtain regulatory approval to commercialize our product candidates and the approval may be for a more narrow indication than we seek.

We cannot commercialize a product candidate until the appropriate regulatory authorities have reviewed and approved the product candidate. The FDA must review and approve any new pharmaceutical product before it can be marketed and sold in the United States. The FDA regulatory review and approval process, which includes evaluation of preclinical studies and clinical trials of a product candidate and proposed labeling, as well as the evaluation of the manufacturing process and manufacturers' facilities, all of which is lengthy, expensive and uncertain. To obtain approval, we must, among other things, demonstrate with substantial evidence from well-controlled clinical trials that the product candidate is both safe and effective for each indication where approval is sought. Even if our product candidates meet the FDA's safety and effectiveness endpoints in clinical trials, the FDA may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval. The FDA has substantial discretion in the review and approval process and may refuse to file our application for substantive review or may determine after review of our data that our application is insufficient to allow approval of our product candidates. The FDA may require that we conduct additional preclinical studies, clinical trials or manufacturing validation studies and submit that data before it will reconsider our application. Additional delays may result if an FDA Advisory Committee or other regulatory authority recommends non-approval or restrictions on approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory authority policy during the period of product development, clinical trials and the review process.

The FDA, EMA or other regulatory authorities also may approve a product candidate for more limited indications than requested or may impose significant limitations in the form of narrow indications, warnings or an REMS. These regulatory authorities may require precautions or contraindications with respect to conditions of use or may grant approval subject to the performance of costly post-marketing clinical trials. In addition, the FDA, EMA or other regulatory authorities may not approve the labeling claims that are necessary or desirable for the successful commercialization of our product candidates. Any of the foregoing scenarios could harm the commercial prospects for our product candidates and negatively impact our business, financial condition, results of operations and prospects.

Delays in obtaining regulatory approval of our manufacturing process and facility or disruptions in our manufacturing process may delay or disrupt our product development and commercialization efforts.

We do not currently operate manufacturing facilities for clinical or commercial production of our product candidates. Before we can begin to commercially manufacture our product candidates, whether in a third-party facility or in our own facility, if and when established, we must obtain

regulatory approval from the FDA for our manufacturing process and facility. A manufacturing authorization must also be obtained from the appropriate European Union regulatory authorities and from other foreign regulatory authorities, as applicable. In order to obtain approval, we will need to ensure that all of our processes, methods and equipment are compliant with cGMP, and perform extensive audits of vendors, contract laboratories and suppliers. If any of our vendors, contract laboratories or suppliers are found to be non-compliant with cGMP, we may experience delays or disruptions in manufacturing while we work with these third parties to remedy the violation or while we work to identify suitable replacement vendors. The cGMP requirements govern quality control of the manufacturing process and documentation policies and procedures. In complying with cGMP, we will be obligated to expend time, money and effort in production, record keeping and quality control to assure that the product meets applicable specifications and other requirements. If we fail to comply with these requirements, we would be subject to possible regulatory action and may not be permitted to sell any product candidate that we may develop.

If we or our third-party manufacturers fail to comply with applicable cGMP regulations, the FDA, EMA and other regulatory authorities can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new product candidate or suspension or revocation of a pre-existing approval. Such an occurrence may cause our business, financial condition, results of operations and prospects to be harmed.

Additionally, if the supply of our products from our third-party manufacturers to us is interrupted for any reason, including due to regulatory requirements or actions (including recalls), adverse financial developments at or affecting the supplier, failure by the supplier to comply with cGMPs, contamination, business interruptions or labor shortages or disputes, there could be a significant disruption in commercial supply of our products. We do not currently have a backup manufacturer of our product candidate supply for clinical trials or commercial sale. An alternative manufacturer would need to be qualified through a supplement to its regulatory filing, which could result in further delays. The regulatory authorities also may require additional clinical trials if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and could result in a delay in our desired clinical and commercial timelines.

If our competitors are able to obtain orphan drug exclusivity for products that constitute the same drug and treat the same indications as our product candidates, we may not be able to have competing products approved by applicable regulatory authorities for a significant period of time. In addition, even if we obtain orphan drug exclusivity for any of our products, such exclusivity may not protect us from competition.

Regulatory authorities in some jurisdictions, including the United States and the European Union, may designate products for relatively small patient populations as orphan drugs. Under the Orphan Drug Act of 1983, the FDA may designate a product candidate as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as having a patient population of fewer than 200,000 individuals in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. In the European Union, the EMA's Committee for Orphan Medicinal Products grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the European Union. Additionally, orphan designation is granted for products intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the drug or biologic product. In Europe, orphan drug designation entitles a party to a number of incentives, such as protocol assistance and scientific advice specifically for designated orphan medicines, and potential fee reductions depending on the status of the sponsor.

The designation as an orphan product does not guarantee that any regulatory agency will accelerate regulatory review of, or ultimately approve, that product candidate, nor does it limit the ability of any regulatory agency to grant orphan drug designation to product candidates of other companies that treat the same indications as our product candidates prior to our product candidates receiving exclusive marketing approval.

Generally, if a product candidate with an orphan drug designation receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or the EMA from approving another marketing application for a product that constitutes the same drug treating the same indication for that marketing exclusivity period, except in limited circumstances. If another sponsor receives such approval before we do (regardless of our orphan drug designation), we will be precluded from receiving marketing approval for our product for the applicable exclusivity period. The applicable period is seven years in the United States and ten years in the European Union. The exclusivity period in the European Union can be reduced to six years if a product no longer meets the criteria for orphan drug designation or if the product is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be revoked if any regulatory agency determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition.

Even if we obtain orphan drug exclusivity for a product candidate, that exclusivity may not effectively protect the product candidate from competition because different drugs can be approved for the same condition. In the United States, even after an orphan drug is approved, the FDA may subsequently approve another drug for the same condition if the FDA concludes that the latter drug is not the same drug or is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. In the European Union, marketing authorization may be granted to a similar medicinal product for the same orphan indication if:

- the second applicant can establish in its application that its medicinal product, although similar to the orphan medicinal product already authorized, is safer, more effective or otherwise clinically superior;
- the holder of the marketing authorization for the original orphan medicinal product consents to a second orphan medicinal product application; or
- the holder of the marketing authorization for the original orphan medicinal product cannot supply sufficient quantities of orphan medicinal product.

Even if we obtain regulatory approval for a product candidate, our product candidates will remain subject to regulatory oversight.

Even if we obtain regulatory approval for our product candidates, they will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping and submission of safety and other post-market information. Any regulatory approvals that we receive for our product candidates may also be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the quality, safety and clinical effectiveness of the product.

Some of our product candidates are classified as biologics in the United States, and therefore, can only be sold if we obtain a BLA from the FDA. The holder of an approved BLA also must submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process. In addition, the holder of a BLA must comply with the FDA's advertising and promotion requirements, such as those related to the prohibition on promoting products for uses or in patient populations that are not described in the product's approved labeling (known as "off-label use"). Advertising and promotional materials must comply with FDA rules and are subject to FDA review, in addition to other potentially applicable federal and state laws.

In addition, product manufacturers and their facilities are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP requirements and adherence to commitments made in the BLA or foreign marketing application. If we, or a regulatory authority, discover 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 if a regulatory authority disagrees with the promotion, marketing or labeling of that product (in addition to our being obligated as holder of a BLA to monitor and report adverse events and any failure of a product to meet the BLA specifications), a regulatory authority

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

If we fail to comply with applicable regulatory requirements following approval of our product candidates, a regulatory or enforcement authority may:

- issue a warning letter asserting that we are in violation of the law;
- seek an injunction or impose administrative, civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve a pending BLA or comparable foreign marketing application (or any supplements thereto) submitted by us or our strategic partners;
- restrict the marketing or manufacturing of the product;
- seize or detain the product or otherwise require the withdrawal of the product from the market;
- refuse to permit the import or export of the product; or
- refuse to allow us to enter into supply contracts, including government contracts.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and adversely affect our business, financial condition, results of operations and prospects.

In addition, the FDA's policies, and those of the EMA and other regulatory authorities, may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would negatively impact our business, financial condition, results of operations and prospects.

Even if we obtain and maintain approval for our product candidates in a major pharmaceutical market such as the United States, we may never obtain approval for our product candidates in other major markets.

In order to market any products in a country or territory, we must establish and comply with numerous and varying regulatory requirements of such countries or territories regarding safety and effectiveness. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval procedures vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking regulatory approvals in all major markets could result in significant delays, difficulties and costs for us and may require additional preclinical studies or clinical trials, which would be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our product candidates in those countries. For example, in many jurisdictions outside of the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our products would also be subject to approval. Satisfying these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. In addition, our failure to obtain regulatory approval in any country may delay or have negative effects on the process for regulatory approval in other countries. We currently do not have any product candidates approved for sale in any

jurisdiction, whether in the United States, Europe or any other international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be compromised.

We may seek a conditional marketing authorization in Europe for some or all of our current product candidates, but we may not be able to obtain or maintain such designation.

As part of its marketing authorization process, the EMA may grant marketing authorizations for certain categories of medicinal products on the basis of less complete data than is normally required, when doing so may meet unmet medical needs of patients and serve the interest of public health. In such cases, it is possible for the Committee for Medicinal Products for Human Use, or CHMP, to recommend the granting of a marketing authorization, subject to certain specific obligations to be reviewed annually, which is referred to as a conditional marketing authorization.

This may apply to medicinal products for human use that fall under the jurisdiction of the EMA, including those that aim at the treatment, the prevention, or the medical diagnosis of seriously debilitating or life-threatening diseases and those designated as orphan medicinal products.

A conditional marketing authorization may be granted when the CHMP finds that, although comprehensive clinical data referring to the safety and therapeutic utility of the medicinal product have not been supplied, all the following requirements are met:

- the risk-benefit balance of the medicinal product is positive;
- it is likely that the applicant will be in a position to provide the comprehensive clinical data;
- unmet medical needs will be fulfilled; and
- the benefit to public health of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data is still required.

The granting of a conditional marketing authorization is restricted to situations in which only the clinical part of the application is not yet fully complete. Incomplete preclinical or quality data may only be accepted if duly justified and only in the case of a product intended to be used in emergency situations in response to public health threats. Conditional marketing authorizations are valid for one year, on a renewable basis. The holder will be required to complete ongoing trials or to conduct new trials with a view to confirming that the benefit-risk balance is positive. In addition, specific obligations may be imposed in relation to the collection of pharmacovigilance data.

Granting a conditional marketing authorization allows medicines to reach patients with unmet medical needs earlier than might otherwise be the case and will ensure that additional data on a product is generated, submitted, assessed and acted upon.

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

In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, changed the way Medicare covers and pays for pharmaceutical products. The MMA expanded Medicare coverage for outpatient drug purchases by adding a new Medicare Part D program and introduced a new reimbursement methodology based on average sales prices for Medicare Part B physician-administered drugs. In addition, the MMA authorized Medicare Part D prescription drug plans to limit the number of drugs that will be covered in any therapeutic class in

their formularies. The MMA's cost reduction initiatives and other provisions could decrease the coverage and price that we receive for any approved products. While the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from private payors. Similar regulations or reimbursement policies may be enacted in international markets, which could similarly impact our business.

More recently, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or the PPACA, was passed, which substantially changes the way healthcare is financed by both the government and private insurers, and significantly impacts the U.S. pharmaceutical industry. The PPACA, among other things: (i) addresses a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected; (ii) increases the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations; (iii) establishes annual fees and taxes on manufacturers of certain branded prescription drugs; (iv) expands the availability of lower pricing under the 340B drug pricing program by adding new entities to the program; and (v) establishes a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% 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. Additionally, in the United States, the Biologics Price Competition and Innovation Act of 2009 created an abbreviated approval pathway for biologic products that are demonstrated to be "highly similar" (biosimilar) or "interchangeable" with an FDA-approved biologic product. This new pathway could allow competitors to reference data from biologic products already approved after 12 years from the time of approval. This could expose us to potential competition by lower-cost biosimilars even if we commercialize a product candidate faster than our competitors. Moreover, the creation of this abbreviated approval pathway does not preclude or delay a third party from pursuing approval of a competitive product candidate via the traditional approval pathway based on their own clinical trial data.

Additional changes that may affect our business include those governing enrollment in federal healthcare programs, reimbursement changes, rules regarding prescription drug benefits under the health insurance exchanges and fraud and abuse and enforcement. Continued implementation of the PPACA and the passage of additional laws and regulations may result in the expansion of new programs such as Medicare payment for performance initiatives, and may impact existing government healthcare programs, such as by improving the physician quality reporting system and feedback program.

For each state that does not choose to expand its Medicaid program, there likely will be fewer insured patients overall, which could impact the sales, business and financial condition of manufacturers of branded prescription drugs. Where patients receive insurance coverage under any of the new options made available through the PPACA, manufacturers may be required to pay Medicaid rebates on that resulting drug utilization. The U.S. federal government also has announced delays in the implementation of key provisions of the PPACA. The implications of these delays for our and our potential partners' business and financial condition, if any, are not yet clear.

In addition, there have been judicial and congressional challenges to certain aspects of the PPACA, and we expect the current administration and Congress will likely continue to seek legislative and regulatory changes, including repeal and replacement of certain provisions of the PPACA. In January 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the PPACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the PPACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. More recently, the U.S. House of Representatives passed legislation known as the American Health Care Act of 2017, and Senate Republicans have released a draft bill known as the Better Care Reconciliation Act of 2017, each of which would repeal certain aspects of the PPACA if ultimately enacted. The prospects for enactment of these legislative initiatives remain uncertain. Further, Congress also could consider other legislation to replace elements of the PPACA. We cannot know how efforts to repeal and replace the PPACA or any future healthcare reform legislation will impact our business.

We expect that the PPACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products.

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.

We are subject to the U.K. Bribery Act, the U.S. Foreign Corrupt Practices Act and other anti-corruption laws, as well as export control laws, import and customs laws, trade and economic sanctions laws and other laws governing our operations.

Our operations are subject to anti-corruption laws, including the U.K. Bribery Act 2010, or the Bribery Act, the U.S. Foreign Corrupt Practices Act of 1977, as amended, or the FCPA, the U.S. domestic bribery statute contained in 18 §201, the U.S. Travel Act, and other anti-corruption laws that apply in countries where we do business. The Bribery Act, the FCPA and these other laws generally prohibit us and our employees and intermediaries from authorizing, promising, offering, or providing, directly or indirectly, improper or prohibited payments, or anything else of value, to government officials or other persons to obtain or retain business or gain some other business advantage. Under the Bribery Act, we may also be liable for failing to prevent a person associated with us from committing a bribery offense. We and our commercial partners operate in a number of jurisdictions that pose a high risk of potential Bribery Act or FCPA violations, and we participate in collaborations and relationships with third parties whose corrupt or illegal activities could potentially subject us to liability under the Bribery Act, FCPA or local anti-corruption laws, even if we do not explicitly authorize or have actual knowledge of such activities. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in which existing laws might be administered or interpreted.

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

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

Our relationships with customers, physicians and third-party payors will be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, health information privacy and security laws and other healthcare laws and regulations. If we are found in violation of these laws and regulations, we may be required to pay a penalty or be suspended from participation in federal or state healthcare programs, which may adversely affect our business, financial condition and results of operations.

If we obtain FDA approval for our product candidates and begin commercializing them in the United States, our operations will be directly, or indirectly through our prescribers, customers and purchasers, subject to various federal and state fraud and abuse laws and regulations, including, without limitation, the federal Anti-Kickback Statute, the federal civil and criminal laws and Physician Payments Sunshine Act and regulations. These laws will impact, among other things, our proposed

sales, marketing and educational programs. In addition, we may be subject to patient privacy laws by both the federal government and the states in which we conduct our business. The laws that will affect our operations include, but are not limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons or entities 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, in return for either the referral of an individual, or the purchase, leasing, furnishing or arranging for the purchase, lease or order of a good, facility, item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs. 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. The PPACA amended the intent requirement of the federal Anti-Kickback Statute, such that a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it;

- federal civil and criminal false claims 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. The PPACA provides, and recent government cases against pharmaceutical and medical device manufacturers support the view that federal Anti-Kickback Statute violations and certain marketing practices, including off-label promotion, may implicate the False Claims Act;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit, among other things, a person from knowingly and willfully executing a scheme or from making false or fraudulent statements to defraud any healthcare benefit program, regardless of the payor (e.g., public or private);

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their implementing regulations, which impose certain requirements relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization by entities subject to the rule, such as health plans, health care clearinghouses and health care providers, and their respective business associates that perform certain functions or activities that involve the use or disclosure of protected health information on their behalf;

- federal transparency laws, including the federal Physician Payment Sunshine Act, that require certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to report annually to the CMS information related to: (i) payments or other "transfers of value" made to physicians and teaching hospitals and (ii) ownership and investment interests held by physicians and their immediate family members;

- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; and

- state and foreign law equivalents of each of the above federal laws, state and local laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures, and 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.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. 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. It is possible that governmental authorities will conclude that our business practices may not comply with current or

future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant criminal, civil and administrative sanctions including monetary penalties, damages, fines, disgorgement, individual imprisonment, and exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, reputational harm, and we may be required to curtail or restructure our operations, any of which could adversely affect our ability to operate our business and our results of operations.

The risk of our being found in violation of these laws is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations. 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. The shifting compliance environment and the need to build and maintain robust and expandable systems to comply with multiple jurisdictions with different compliance and/or reporting requirements increases the possibility that a healthcare company may run afoul of one or more of the requirements.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur substantial costs.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the generation, handling, use, storage, treatment, manufacture, transportation and disposal of, and exposure to, hazardous materials and wastes, as well as laws and regulations relating to occupational health and safety. We contract with third parties that conduct operations on our behalf that involve the use of hazardous and flammable materials, including chemicals and biologic materials. Our contractors also produce and dispose of hazardous waste products. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our contractors’ use of hazardous materials, we could be held liable for any resulting damages and any liability could exceed our resources, and our clinical trials or regulatory approvals could be suspended. We also could incur significant costs associated with civil or criminal fines and penalties. Our third-party contractors may not carry specific biological or hazardous waste insurance coverage, and their property, casualty and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination.

Although we maintain workers' compensation insurance for certain costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials or other work-related injuries, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for toxic tort claims that may be asserted against us in connection with our storage or disposal of biologic, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations, which have tended to become more stringent over time. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions or liabilities, which could adversely affect our business, financial condition, results of operations and prospects.

Risks Related to our Business Operations

We may not be successful in our efforts to identify or discover additional product candidates and may fail to capitalize on programs or product candidates that may be a greater commercial opportunity or for which there is a greater likelihood of success.

The success of our business depends upon our ability to identify, develop and commercialize product candidates. Research programs to identify new product candidates require substantial technical, financial and human resources. Although a substantial amount of our efforts will focus on the continued preclinical and clinical testing and potential approval of our product candidates, a key element of our long-term growth strategy is to develop and market additional products and product

candidates. However, we may fail to identify other potential product candidates for clinical development for several reasons. For example, our research may be unsuccessful in identifying potential product candidates or our potential product candidates may be shown to have harmful side effects, may be commercially impracticable to manufacture or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval.

Additionally, because we have limited resources, we may forego or delay pursuit of opportunities with certain programs or product candidates or for indications that later prove to have greater commercial potential. Our spending on current and future research and development programs may not yield any commercially viable products. If we do not accurately evaluate the commercial potential for a particular product candidate, we may relinquish valuable rights to that product candidate through strategic collaboration, licensing or other arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate. Alternatively, we may allocate internal resources to a product candidate in a therapeutic area in which it would have been more advantageous to enter into a partnering arrangement.

Our long-term growth strategy to develop and market additional products and product candidates is heavily dependent on precise, accurate and reliable scientific data to identify, select and develop promising pharmaceutical product candidates and products. Our business decisions may therefore be adversely influenced by improper or fraudulent scientific data sourced from third parties. Any irregularities in the scientific data used by us to determine our focus in research and development of product candidates and products could have a material adverse effect on our business, prospects, financial condition and results of operations.

If any of these events occur, we may be forced to abandon our development efforts with respect to a particular product candidate or fail to develop a potentially successful product candidate, which could have a negative impact on our business, financial condition, results of operations and prospects.

Our future success depends on our ability to retain key employees, consultants and advisors and to recruit, retain and motivate qualified personnel.

Our ability to compete in the highly competitive biotechnology and pharmaceutical industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. While we have entered into employment agreements with each of our executive officers, any of them could leave our employment at any time. We currently do not have "key person" insurance on any of our employees. The loss of the services of one or more of our current employees might impede the achievement of our research, development and commercialization objectives.

Recruiting and retaining other qualified employees, consultants and advisors for our business, including scientific and technical personnel, also will be critical to our success. We may not be able to attract and retain personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies and academic institutions for individuals with similar skill sets. In addition, failure to succeed in preclinical studies or clinical trials or applications for marketing approval may make it more challenging to recruit and retain qualified personnel. The inability to recruit, or loss of services of certain executives, key employees, consultants or advisors, may impede the progress of our research, development and commercialization objectives and have an adverse effect on our business, financial condition, results of operations and prospects.

***If we are unable to manage expected growth in the scale and complexity of our operations, our performance may suffer*.**

At September 30, 2017, we had 5 full-time employees, who were engaged in research and development activities. If we are successful in executing our business strategy, we will need to expand our managerial, operational, financial and other systems and resources to manage our operations, continue our research and development activities and, in the longer term, build a commercial infrastructure to support commercialization of any of our product candidates that are approved for sale. Future growth would impose significant added responsibilities on members of management and, to a potentially significant extent, divert our management and business development resources away from their current uses. It is likely that our management, finance, development personnel, systems and facilities currently in place may not be adequate to support this

future growth. Our need to effectively manage our operations, growth and any future product candidates requires that we continue to develop more robust business processes and improve our systems and procedures in each of these areas, to attract and retain sufficient numbers of talented employees and to expand the group of contractors we use.

We may be unable to successfully implement these tasks on a larger scale and, accordingly, may not achieve our research, development and growth goals.

Our employees, principal investigators, consultants and commercial partners may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading, which could have a material adverse impact on our business.

We are exposed to the risk of fraud or other misconduct by our employees, principal investigators, consultants and commercial partners. Misconduct by these parties could include intentional failures to: comply with FDA or EMA regulations or the regulations applicable in other jurisdictions, provide accurate information to the FDA, EMA and other regulatory authorities, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Such misconduct also could involve the improper use of information obtained in the course of clinical trials or interactions with the FDA, EMA or other regulatory authorities, which could result in regulatory sanctions and cause serious harm to our reputation. Additional, we are subject to the risk that a person could allege fraud or other misconduct, even in none occurred. We have adopted a code of conduct applicable to all of our employees, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent these activities may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from government investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, financial condition, results of operations and prospects, including the imposition of significant criminal, civil and administrative sanctions, such as monetary penalties, damages, fines, disgorgement, individual imprisonment, and exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, reputational harm, and we may be required to curtail or restructure our operations.

Product liability lawsuits against us could cause us to incur substantial liabilities and could limit commercialization of any product candidate that we may develop.

We face an inherent risk of product liability exposure related to the testing of our current and future product candidates in clinical trials and may face an even greater risk if we commercialize any product candidate that we may develop. For example, we may be sued if our current or future product candidates cause or are perceived to cause injury or are found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidate that we may develop;
- loss of revenue;
- substantial monetary awards to trial participants or patients;
- significant time and costs to defend the related litigation;

- withdrawal of clinical trial participants;
- the inability to commercialize any product candidates that we may develop; or
- injury to our reputation and significant negative media attention.

Although we maintain product liability insurance coverage, such insurance may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase our insurance coverage each time we commence a clinical trial and if we successfully commercialize any product candidate. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

The United Kingdom's vote in favor of withdrawing from the European Union may have a negative effect on global economic conditions, financial markets and our business, which could reduce the potential value of our ADSs and make it more difficult to do business in Europe.

In June 2016, a majority of the eligible members of the electorate in the United Kingdom voted to withdraw from the European Union in a national referendum (commonly referred to as Brexit). The withdrawal of the United Kingdom from the European Union will take effect either on the effective date of the withdrawal agreement or, in the absence of agreement, two years after the United Kingdom provides a notice of withdrawal pursuant to Article 50 of the EU Treaty, unless the European Council, in agreement with the United Kingdom, unanimously decides to extend this period. On March 29, 2017, the U.K. Prime Minister formally delivered the notice of withdrawal. It appears likely that this withdrawal will involve a process of lengthy negotiations between the United Kingdom and EU Member States to determine the future terms of the United Kingdom's relationship with the European Union.

These developments, or the perception that any of them could occur, have had and may continue to have a significant adverse effect on global economic conditions and the stability of global financial markets, and could significantly reduce global market liquidity and restrict the ability of key market participants to operate in certain financial markets. In particular, it could also lead to a period of considerable uncertainty in relation to the U.K. financial and banking markets, as well as on the regulatory process in Europe. As a result of this uncertainty, global financial markets could experience significant volatility, which could adversely affect the potential value of our ADSs. Asset valuations, currency exchange rates and credit ratings may also be subject to increased market volatility. Lack of clarity about future U.K. laws and regulations as the United Kingdom determines which European Union rules and regulations to replace or replicate in the event of a withdrawal, including financial laws and regulations, tax and free trade agreements, intellectual property rights, supply chain logistics, environmental, health and safety laws and regulations, immigration laws and employment laws, could decrease foreign direct investment in the United Kingdom, increase costs, depress economic activity and restrict our access to capital. If the United Kingdom and the European Union are unable to negotiate acceptable withdrawal terms or if other EU Member States pursue withdrawal, barrier-free access between the United Kingdom and other EU Member States or among the European Economic Area overall could be diminished or eliminated.

We may also face new regulatory costs and challenges that could have an adverse effect on our operations. Depending on the terms of Brexit, the United Kingdom could lose the benefits of global trade agreements negotiated by the European Union on behalf of its members, which may result in increased trade barriers that could make our doing business in Europe more difficult. In addition, currency exchange rates in the pound Sterling and the euro with respect to each other and the U.S. dollar have already been adversely affected by Brexit. Furthermore, at present, there are no indications of the effect Brexit will have on the pathway to obtaining marketing approval for any of our product candidates in the United Kingdom, or what, if any, role the EMA may have in the approval process.

Exchange rate fluctuations may materially affect our results of operations and financial condition.

Owing to the international scope of our operations, fluctuations in exchange rates, particularly between the pound Sterling and the U.S. dollar, may adversely affect us. Although we are based in the United Kingdom, we may source research and development, manufacturing, consulting and other services from the United States and the European Union. Further, potential future revenue may be derived from abroad, particularly from the United States. As a result, our business and the potential value of our ADSs may be affected by fluctuations in foreign exchange rates not only between the pound Sterling and the U.S. dollar, but also the euro, which may have a significant impact on our results of operations and cash flows from period to period. Currently, we do not have any exchange rate hedging arrangements in place.

Our internal computer systems, or those of our collaborators or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

Our internal computer systems and those of our current and any future collaborators and other contractors or consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such material system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position could be harmed and the further development and commercialization of our product candidates could be delayed.

Risks Related to the Ownership of Our Securities

We do not know whether an active, liquid and orderly trading market will develop for our ADSs or what the market price of our ADSs will be. As a result, it may be difficult for shareholders to sell their ADSs.

Our stock is currently traded on AIM, a submarket of the London Stock Exchange. And while we intend to apply to list our ADSs on the NASDAQ Capital Market through a direct listing, there will not be any active market for our ADSs on NASDAQ following the completion of our direct listing. We are not conducting an offering of ADSs to the public in connection with our direct listing. If we were to conduct an offering of our ADSs in the future, there is no way of knowing whether an active, liquid and orderly trading market will develop for our ADSs, or what the market price of our ADSs would be.

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

We are incorporated under English law. The rights of holders of ordinary shares and, therefore, certain of the rights of any potential future holders of ADSs, are governed by English law, including the provisions of the U.K. Companies Act 2006, or the Companies Act, and by our Articles of Association. These rights differ in certain respects from the rights of shareholders in typical U.S. corporations. See "Description of Share Capital and Articles of Association-Differences in Corporate Law" in this report for a description of the principal differences between the provisions of the Companies Act applicable to us and, for example, the Delaware General Corporation Law relating to stockholders' rights and protections.

If we engage in future acquisitions or strategic partnerships, this may increase our capital requirements, dilute our AIM shareholders, cause us to incur debt or assume contingent liabilities and subject us to other risks.

We intend to continue to evaluate various acquisitions and strategic partnerships, including licensing or acquiring complementary drugs, intellectual property rights, technologies or businesses. Any potential acquisition or strategic partnership may entail numerous risks, including:

- increased operating expenses and cash requirements;
- the assumption of additional indebtedness or contingent liabilities;
- assimilation of operations, intellectual property and drugs of an acquired company, including difficulties associated with integrating new personnel;
- the diversion of our management's attention from our existing drug programs and initiatives in pursuing such a strategic partnership, merger or acquisition;
- retention of key employees, the loss of key personnel and uncertainties in our ability to maintain key business relationships;
- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing drugs or drug candidates and regulatory approvals; and
- our inability to generate revenue from acquired technology and/or drugs sufficient to meet our objectives in undertaking the acquisition or even to offset the associated acquisition and maintenance costs.

***As a foreign private issuer, we are exempt from a number of rules under the U.S. securities laws and are permitted to file less information with the SEC than U.S. public companies*.**

We are a "foreign private issuer," as defined in the SEC rules and regulations and, consequently, we are not subject to all of the disclosure requirements applicable to companies organized within the United States. For example, we are exempt from certain rules under the U.S. Securities Exchange Act of 1934, as amended, or the Exchange Act, that regulate disclosure obligations and procedural requirements related to the solicitation of proxies, consents or authorizations applicable to a security registered under the Exchange Act. In addition, our officers and directors are exempt from the reporting and "short-swing" profit recovery provisions of Section 16 of the Exchange Act and related rules with respect to their purchases and sales of our securities. Moreover, we are not required to file periodic reports and financial statements with the SEC as frequently or as promptly as U.S. public companies. Accordingly, there may be less publicly available information concerning our company than there is for U.S. public companies.

As a foreign private issuer, we will file an annual report on Form 20-F within four months of the close of each fiscal year ended December 31 and reports on Form 6-K relating to certain material events promptly after we publicly announce these events. However, because of the above exemptions for foreign private issuers, our shareholders will not be afforded the same protections or information generally available to investors holding shares in public companies organized in the United States.

While we are a foreign private issuer, we are not subject to certain NASDAQ corporate governance rules applicable to U.S. listed companies.

We are entitled to rely on a provision in NASDAQ's corporate governance rules that allows us to follow English corporate law and the Companies Act with regard to certain aspects of corporate governance. This allows us to follow certain corporate governance practices that differ in significant respects from the corporate governance requirements applicable to U.S. companies listed on NASDAQ.

For example, we are exempt from NASDAQ regulations that require a listed U.S. company to (i) have a majority of the board of directors consist of independent directors, (ii) require non-

management directors to meet on a regular basis without management present and (iii) promptly disclose any waivers of the code for directors or executive officers that should address certain specified items.

In accordance with our NASDAQ listing, our audit committee is required to comply with the provisions of Section 301 of the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, and Rule 10A-3 of the Exchange Act, both of which are also applicable to NASDAQ-listed U.S. companies. Because we are a foreign private issuer, however, our audit committee is not subject to additional NASDAQ requirements applicable to listed U.S. companies, including an affirmative determination that all members of the audit committee are "independent," using more stringent criteria than those applicable to us as a foreign private issuer. Furthermore, NASDAQ's corporate governance rules require listed U.S. companies to, among other things, seek shareholder approval for the implementation of certain equity compensation plans and issuances of ordinary shares, which we are not required to follow as a foreign private issuer.

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

As a foreign private issuer, we are not required to comply with all of the periodic disclosure and current reporting requirements of the Exchange Act applicable to U.S. domestic issuers. We may no longer be a foreign private issuer as early as June 30, 2018 (the end of our second fiscal quarter in the fiscal year following this direct listing), which would require us to comply with all of the periodic disclosure and current reporting requirements of the Exchange Act applicable to U.S. domestic issuers as of January 1, 2019. In order to maintain our current status as a foreign private issuer, either (a) a majority of our ADSs must be either directly or indirectly owned of record by non-residents of the United States or (b)(i) a majority of our executive officers or directors cannot be U.S. citizens or residents, (ii) more than 50% of our assets must be located outside the United States and (iii) our business must be administered principally outside the United States. If we lose our status as a foreign private issuer, we would be required to comply with the Exchange Act reporting and other requirements applicable to U.S. domestic issuers, which are more detailed and extensive than the requirements for foreign private issuers. We may also be required to make changes in our corporate governance practices in accordance with various SEC and NASDAQ rules. The regulatory and compliance costs to us under U.S. securities laws if we are required to comply with the reporting requirements applicable to a U.S. domestic issuer may be significantly higher than the cost we would incur as a foreign private issuer. As a result, we expect that a loss of foreign private issuer status would increase our legal and financial compliance costs and is likely to make some activities highly time consuming and costly. We also expect that if we were required to comply with the rules and regulations applicable to U.S. domestic issuers, it would make it more difficult and expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced coverage or incur substantially higher costs to obtain coverage. These rules and regulations could also make it more difficult for us to attract and retain qualified members of our board of directors.

We are an emerging growth company within the meaning of the Securities Act and will take advantage of certain reduced reporting requirements.

We are an "emerging growth company," or EGC, as defined in the Jumpstart Our Business Start-ups Act of 2012, or the JOBS Act. For as long as we continue to be an EGC, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, or Section 404, exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. As an EGC, we are required to report only two years of financial results and selected financial data compared to three and five years, respectively, for comparable data reported by other public companies. We may take advantage of these exemptions until we are no longer an EGC. We could be an EGC for up to five years, although circumstances could cause us to lose that status earlier, including if the aggregate market value of our ADSs held by non-affiliates exceeds $700 million as of any June 30 (the end of our second fiscal quarter) before that time, in which case we would no longer be an EGC as of the following December 31 (our fiscal year-end). We cannot predict if investors will find our ADSs less attractive because we may rely on these exemptions. If some investors find our ADSs less attractive as a result, there may

be a less active trading market for our ADSs and the price of our ADSs may be more volatile in the event that we decide to make an offering of our ADSs following this direct listing.

If we fail to establish and maintain proper internal controls, our ability to produce accurate financial statements or comply with applicable regulations could be impaired.

Section 404(a) of the Sarbanes-Oxley Act, or Section 404(a), requires that beginning with our second annual report following our initial public offering, management assess and report annually on the effectiveness of our internal control over financial reporting and identify any material weaknesses in our internal control over financial reporting. Although Section 404(b) of the Sarbanes-Oxley Act, or Section 404(b), requires our independent registered public accounting firm to issue an annual report that addresses the effectiveness of our internal control over financial reporting, we have opted to rely on the exemptions provided in the JOBS Act, and consequently will not be required to comply with SEC rules that implement Section 404(b) until such time as we are no longer an EGC.

We expect our first Section 404(a) assessment will take place for our annual report for the fiscal year ending December 31, 2018. The presence of material weaknesses could result in financial statement errors which, in turn, could lead to errors in our financial reports, delays in our financial reporting, which could require us to restate our operating results or our auditors may be required to issue a qualified audit report. We might not identify one or more material weaknesses in our internal controls in connection with evaluating our compliance with Section 404(a). In order to maintain and improve the effectiveness of our disclosure controls and procedures and internal control over financial reporting, we will need to expend significant resources and provide significant management oversight.

Implementing any appropriate changes to our internal control may require specific compliance training of our directors and employees, entail substantial costs in order to modify our existing accounting systems, take a significant period of time to complete and divert management's attention from other business concerns. These changes may not, however, be effective in maintaining the adequacy of our internal control.

If either we are unable to conclude that we have effective internal control over financial reporting or, at the appropriate time, our independent auditors are unwilling or unable to provide us with an unqualified report on the effectiveness of our internal control over financial reporting as required by Section 404(b), then in the event we have decided to make an offering of our ADSs following this direct listing, investors may lose confidence in our operating results, the price of our ADSs could decline and we may be subject to litigation or regulatory enforcement actions. In addition, if we are unable to meet the requirements of Section 404, we may not be able to remain listed on NASDAQ.

We will incur significant increased costs as a result of operating as a company that publicly listed on NASDAQ in the United States, and our management will be required to devote substantial time to new compliance initiatives.

As a U.S. public company, and particularly after we no longer qualify as an EGC, we will incur significant legal, accounting and other expenses that we did not incur previously. The Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of NASDAQ and other applicable securities rules and regulations impose various requirements on non-U.S. reporting public companies, including the establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our senior management and other personnel will need to devote a substantial amount of time to these compliance initiatives.

Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance, which in turn could make it more difficult for us to attract and retain qualified senior management personnel or members for our board of directors.

However, these rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

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

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

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

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

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

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

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

Holder (as defined below under "Material Income Tax Considerations-Material U.S. Federal Income Tax Considerations for U.S. Holders") holds our shares, the U.S. Holder may be subject to adverse tax consequences regardless of whether we continue to qualify as a PFIC, including ineligibility for any preferred tax rates on capital gains or on actual or deemed dividends, interest charges on certain taxes treated as deferred, and additional reporting requirements.

We believe that we were a PFIC for our taxable year ended December 31, 2016, but cannot provide any assurances regarding our PFIC status for any past, current or future taxable years. The determination of whether we are a PFIC is a fact-intensive determination made on an annual basis applying principles and methodologies which in some circumstances are unclear and subject to varying interpretation. In particular, the characterization of our assets as active or passive may depend in part on our current and intended future business plans, which are subject to change. In addition, for our current and future taxable years, the total value of our assets for PFIC testing purposes may be determined in part by reference to the market price of our ordinary shares or ADSs from time to time, which may fluctuate considerably. Under the income test, our status as a PFIC depends on the composition of our income which will depend on the transactions we enter into in the future and our corporate structure. The composition of our income and assets is also affected by how, and how quickly, we spend the cash we raise in any offering.

In certain circumstances, a U.S. Holder of shares in a PFIC may alleviate some of the adverse tax consequences described above by making a "qualified electing fund," or QEF, election to include in income its pro rata share of the corporation's income on a current basis. However, a U.S. Holder may make a QEF election with respect to our ordinary shares or ADSs only if we agree to furnish such U.S. Holder annually with a PFIC annual information statement as specified in the applicable U.S. Treasury Regulations. We currently do not intend to prepare or provide the information that would enable U.S. Holders to make a QEF election if we are treated as a PFIC for any taxable year, and prospective investors should assume that a QEF election will not be available.

For further discussion of the PFIC rules and the adverse U.S. federal income tax consequences in the event we are classified as a PFIC, see the section of this report entitled "Material Income Tax Considerations-Material U.S. Federal Income Considerations For U.S. Holders."

We may be unable to use net operating loss and tax credit carryforwards and certain built-in losses to reduce future tax payments or benefit from favorable U.K. tax legislation.

As a U.K. resident trading entity, we are subject to U.K. corporate taxation. Due to the nature of our business, we have generated losses since inception. As of December 31, 2016, we had cumulative carryforward tax losses of $12.4 million. Subject to any relevant restrictions, we expect these to be available to carry forward and offset against future operating profits. As a company that carries out extensive research and development activities, we benefit from the U.K. research and development tax credit regime for small and medium-sized companies, whereby we are able to surrender the trading losses that arise from our qualifying research and development activities for a payable tax credit of up to 33.35% of eligible research and development expenditures. Qualifying expenditures largely comprise employment costs for research staff, consumables and certain internal overhead costs incurred as part of research projects. Certain subcontracted qualifying research expenditures are eligible for a cash rebate of up to 21.67%. The majority of our pipeline research, clinical trials management and manufacturing development activities are eligible for inclusion within these tax credit cash rebate claims. We may not be able to continue to claim payable research and development tax credits in the future as we become a public company because we may no longer qualify as a small or medium-sized company.

We may benefit in the future from the United Kingdom's "patent box" regime, which allows certain profits attributable to revenues from patented products to be taxed at an effective rate of 10%. We are the exclusive licensee or owner of several patent applications which, if issued, would cover our product candidates, and accordingly, future upfront fees, milestone fees, product revenues and royalties could be taxed at this tax rate. When taken in combination with the enhanced relief available on our research and development expenditures, we expect a long-term lower rate of corporation tax to apply to us. If, however, there are unexpected adverse changes to the U.K. research and development tax credit regime or the “patent box” regime, or for any reason we are unable to qualify for such advantageous tax legislation, or we are unable to use net operating loss and tax credit

carryforwards and certain built-in losses to reduce future tax payments then our business, results of operations and financial condition may be adversely affected.

ITEM 4: INFORMATION ON THE COMPANY

A. History and Development of the Company

We were originally incorporated under the laws of England and Wales on February 11, 1998, with the goal of leveraging the expertise of our management team as well as Napoleone Ferrara, M.D., Arun Sanyal, M.D., Howard Weiner, M.D. and Kevan Herold, M.D., and to acquire and exploit certain intellectual property in biotechnology. We subsequently changed our name to Tiziana Life Sciences plc in May 2014 as a result of the acquisition of Tiziana Pharma Limited in April 2014.

Our registered office is located at 3rd Floor, 11-12 St James's Square, London SW1Y 4LB and our telephone number is +44 20 7495 2379. Our website address is www.tizianalifesciences.com. The reference to our website is an inactive textual reference only and the information contained in, or that can be accessed through, our website is not a part of this registration statement.

B. Business Overview

Overview

We are a biotechnology company that is focused on the discovery and development of novel molecules and related diagnostics to treat high unmet medical needs in oncology and immunology. Our lead product candidate in immunology is Foralumab (TZLS-401), which is the only fully human monoclonal anti-CD3 mAb in clinical development. Monoclonal antibodies represent a single pure antibody produced by single clones and are a rapidly growing class of human therapeutics for treating cancers and autoimmune diseases. Generation of antibodies against human proteins in animals, leads to strong, immune responses limiting their effectiveness and potentially leading to severe side effects. A process known as "humanization" removes most of the animal components of the antibody thereby lowering the immune response from the human immune system. The entire omission of other animal material, as in fully human antibodies, is the optimal goal to avoid incompatibility with the human immune system. Our lead product candidate in oncology is Milciclib (TZLS-201), which is an orally bioavailable, small molecule broad spectrum inhibitor of cyclin-dependent kinases (CDKs) and Src family kinases. Cyclin dependent kinases are a highly conserved family of enzymes that phosphorylate a specific group of proteins that are involved in regulating the cell cycle. The cell cycle is a series of events that takes place in cells leading to division and duplication of its DNA to produce two daughter cells. Src family kinases are non-receptor tyrosine kinase proteins encoded by the Src gene also involved in regulating cell growth and potential transformation of normal cells to cancer cells. We also have a drug discovery pipeline of small molecule new chemical entities (NCEs) and biologics. We employ a lean and virtual research and development model using highly experienced teams of experts for each business function to maximize value accretion by focusing resources on the drug discovery and development processes. Our mission is to design and deliver next generation therapeutics and diagnostics for oncology and immune diseases of high unmet medical need by combining deep understanding of disease biology with clinical development expertise.

We are developing Foralumab, which we in-licensed the intellectual property from Novimmune SA (Novimmune) in December 2014, as a potential treatment for non-alcoholic steatohepatitis (NASH) PBC/PSC. We believe that oral administration of Foralumab has the potential to reduce inflammation while minimizing the toxicity and related side effects of existing treatments for inflammatory diseases such as NASH, PBC and other autoimmune and inflammatory diseases. To date, Foralumab has been studied in a total of three Phase I and Phase II clinical trials in 68 patients. In these trials, Foralumab was observed to be well-tolerated and produced immunologic effects consistent with potential clinical benefit. We expect to initiate two Phase II trials for Foralumab in H1 2018, one in patients with NASH and one in patients with PBC/PSC.

We are developing Milciclib, which we in-licensed the intellectual property from Nerviano Medical Sciences S.r.l. (Nerviano) in January 2015, as a potential treatment for hepatocellular carcinoma (HCC). A unique feature of Milciclib is its ability to reduce levels of microRNAs, miR-221 and miR-222. MicroRNAs are small RNA molecules that play a significant role in the regulation of gene expression. miR-221 and miR-222 are believed to be linked to the development of blood supply in cancer tumors. Levels of these microRNAs are consistently elevated in HCC patients ("upregulation") and may contribute towards resistance to treatment with sorafenib, a multikinase inhibitor (a drug which may inhibit the cellular division and proliferation associated with certain cancers) often prescribed to HCC patients. To date, Milciclib has been studied in a total of seven completed and ongoing Phase I and Phase II clinical trials in approximately 285 patients. In these trials, Milciclib was well-tolerated with minimal adverse events. We initiated a Phase IIa trial for Milciclib as a monotherapy in patients with HCC in the fourth quarter of 2017 and expect to initiate a Phase IIb trial for Milciclib in combination with sorafenib (a multikinase inhibitor drug, also known under its brand name Nexavar®, used to treat some types of kidney, liver and thyroid cancers) in patients with HCC in H1 2018.

Our Competitive Strengths

Our mission is to design and deliver next generation therapeutics and diagnostics for oncology and immune diseases of high unmet medical need by combining deep understanding of disease

biology with clinical development expertise. We believe the following strengths will allow us to continue to pursue this mission:

- ***Advanced, innovative pipeline***. We have an advanced pipeline of innovative and proprietary drug candidates, including antibodies and small molecules, to address high unmet medical needs in the inflammation, autoimmune and oncology markets with significant commercial potential.

- ***Proprietary technology***. Our proprietary technology enables the development of alternative routes of administration of antibodies, including oral delivery. We believe oral delivery will alleviate the significant time and cost burden associated with other routes of administration, including intravenous delivery.

- ***Broad and engaged network of experts.*** Our strong relationships with key opinion leaders contribute to our clinical development efforts and position us well to support our products, if approved. Napoleone Ferrara, M.D., Arun Sanyal, M.D., Kevan Herold, M.D. and Howard Weiner, M.D. are among the thought leaders on our scientific advisory committee.

- ***Specialized expertise and focus on oncology and inflammation***. Our management team, including Dr Kunwar Shailubhai, Jules Jacob, Dr Priya Eddy, Dr Vaseem Palejwala], and Betty Chu, has significant experience translating technologies from bench to market, and managing the global administration of clinical trials.

- ***Strong intellectual property and know-how***. We believe our proprietary intellectual property portfolio, in-licensed from Nerviano Medical Sciences and Novimmune, provides us with a substantial competitive advantage for the commercial development of small molecule new chemical entities and biologics, as well as expanded possibilities for new development programs in the future. We have retained the worldwide development and commercialization rights to all of our product candidates.

- ***Lean research and development model, designed to maximize value***. We employ a lean and virtual research and development (R&D) model using highly experienced teams of experts for each business function to maximize value accretion by focusing resources on the drug discovery and development processes.

Our Strategy

Our goal is to become a leading biotechnology company focused on developing and delivering best-in-class and potentially life-altering therapies and related diagnostics in both oncology and immunology. The key elements of our strategy to achieve this goal are to:

- Advance the clinical development of orally administered Foralumab, (TZLS-401) for the treatment of NASH and PBC/PSC using a novel and proprietary oral formulation by initiating Phase I/II trials in the first half of 2018.

- Continue to advance the clinical development and obtain regulatory approval for our lead product candidate, Milciclib (TZLS-201), as a monotherapy in HCC and as a combination therapy for the treatment of refractory solid tumours (being cancers which are non-responsive or become resistant to treatment) and HCC by enrolling the ongoing Phase IIa trial as a monotherapy and a planned Phase IIb trial in combination with sorafenib.

- Continue to leverage relationships with key opinion leaders to promote clinical trial success and enhance future commercialization.

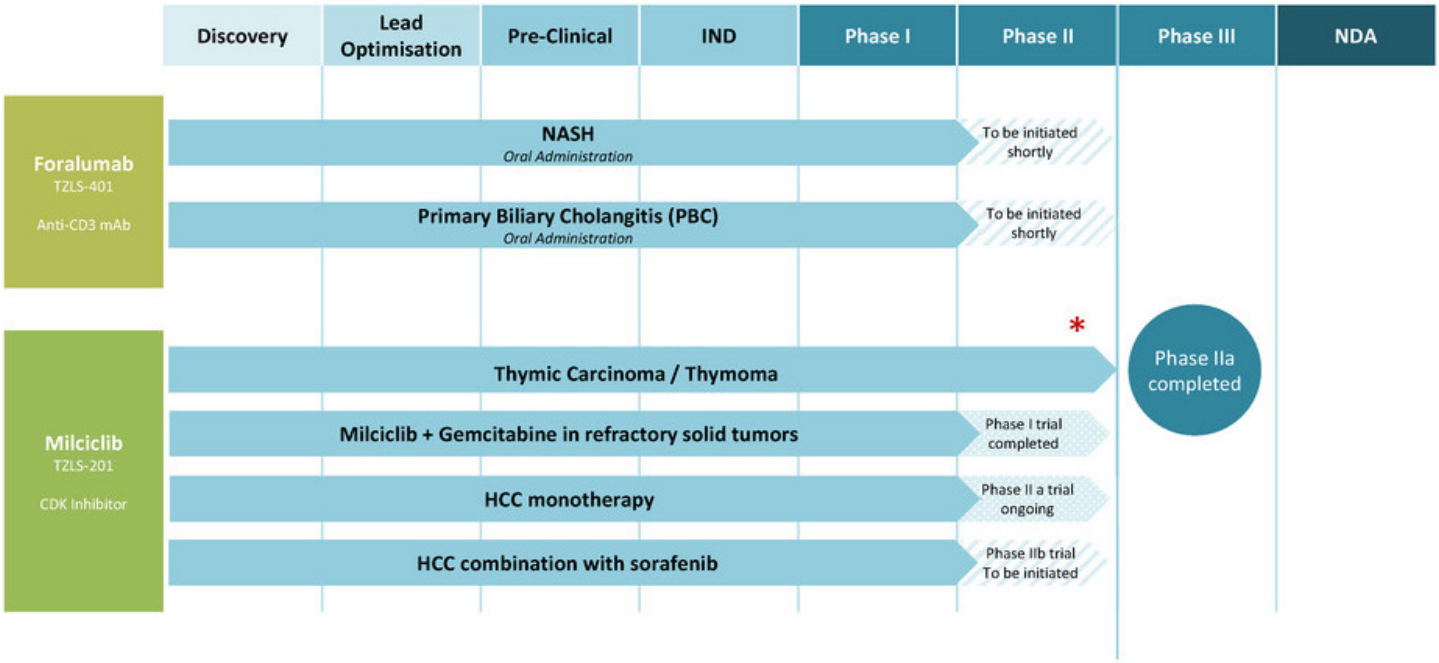
- Continue preclinical studies and non-clinical development of our product candidate, TZLS-0501, an anti-IL6R mAb (a biological monoclonal antibody which may control the proteins involved in cell signaling relevant to many inflammatory diseases and cancers), for treatment of inflammatory and oncology indications.

- Opportunistically identify and acquire or in-license complimentary product and technology candidates.

- Seek orphan drug, fast track or breakthrough designation for our product candidates where warranted.

Our Product Candidates

Our product candidate pipeline is set forth below:



* We will seek guidance from regulatory authorities for next steps.

Foralumab (TZLS-401 formerly known as NI-0401)

Foralumab (TZLS-401) is the only fully human monoclonal anti-CD3 mAb in clinical development, in contrast to the previous non-human or humanized anti-CD3 mAbs. Foralumab targets the CD3 epsilon (CD3ε) receptor, which is a recognized approach for modulating T-Cell response and achieving immunosuppression. We believe Foralumab could have broad application to other autoimmune and inflammatory diseases, such NASH, PBC, multiple sclerosis, type-1 diabetes (T1D), inflammatory bowel disease (IBD), psoriasis and rheumatoid arthritis, where modulation of a T-cell response is desirable. In July 2017, we announced publication of a research article in a prestigious journal, Clinical Immunology, entitled: “Oral treatment with Foralumab, a fully human anti-CD3 mAb, prevents skin xenograft rejection in humanized mice”. This is the first-ever published report demonstrating the potential of oral therapy with Foralumab for inflammatory diseases such as NASH. We are initially investigating Foralumab for the treatment of NASH and PBC/PSC and expect to initiate two Phase II trials for Foralumab, one in each of these indications, in 1H of 2018.

Non-alcoholic steatohepatitis (NASH)

Non-alcoholic fatty liver disease comprises a spectrum of progressive liver diseases, which currently affects approximately one-third of the western world. It is associated with liver-related morbidity and mortality and with increased risk of cardiovascular disease, type 2 diabetes mellitus (T2DM), hyperlipidemia (acquired or genetic disorders resulting in elevated levels of lipids circulating in the blood) and abdominal obesity. NASH, one of the manifestations of fatty infiltration in the liver, leads to inflammation and fat and fibrous tissue buildup in the liver, and elevated liver enzymes levels, and can lead to liver cirrhosis, end-stage liver disease and primary liver cancer, or HCC (as shown in the graphic on page 49 under “—Milciclib—Hepatocellular Cancer (HCC).” NASH is predicted to become the leading cause of liver transplantation in the USA by 2020. Both genetic predisposition and environmental factors have been implicated in its onset, and inflammation and associated fibrogenesis contribute to its perpetuation.

Chronic inflammatory processes involve an imbalance in pro- versus anti-inflammatory cytokines (small proteins which are secreted by certain cells of the immune system and have an effect on other cells), altered insulin responses due to inflammation and fat and fibrous tissue buildup. Therapeutic avenues must provide for multifactorial effects, with focus on reduced insulin resistance and inflammatory processes. Mild inflammation imparts a hepatoprotective effect (preventing damage to the liver), while excessive inflammation triggers hepatocyte damage (damage to cell membranes and tissue death) and irreversible liver damage, fibrosis and carcinogenesis. Such detrimental effects are associated with overexpression of inflammatory genes and increased activity of Kupffer cells, natural killer T cells, hepatic stellate cells, sinusoidal endothelial cells, dendritic cells, monocytes and lymphocytes, which secrete a range of proinflammatory factors, including cytokines, chemokines, lipid messengers and reactive oxygen species.

While several drugs, such as pioglitazone (Actos®), have proven effective in improving NASH-related features, side effects, including weight gain, adipose tissue insulin resistance, increased risk of bone fracture in women, congestive heart failure, heightened risk of bladder cancer, increased mortality, risk of hemorrhage stroke, prostate cancer in men over 50 years of age, pruritus and increased low-density lipoprotein (LDL) cholesterol have been measured following their chronic use.

Primary Biliary Cholangitis (PBC)

PBC is an autoimmune cholestatic chronic liver disease, with risk of life-threatening complications, accounting for 8% of liver transplantations. The disease is characterized by T cell-mediated attack of small intralobular bile duct epithelial cells, resulting in cholestasis, which can progress to cirrhosis and liver failure. PBC shows a distinct female predominance, with over 90% of patients being women, typically over the age of 40. Similarly, primary sclerosing cholangitis (PSC) is a chronic liver disease, thought to be rooted in an autoimmune process. The condition is characterized by a progressive course of cholestasis, alongside inflammation and fibrous tissue buildup in the bile ducts, which can culminate in cirrhosis and end-stage liver disease. PSC shows a 2:1 male predominance, is the fourth-leading indication for liver transplantation among adults, and is associated with a mean overall survival rate of 10 years from diagnosis. Both genetic predisposition and

environmental factors have been implicated in the onset of these diseases, while inflammation and associated fibrogenesis contribute to their perpetuation.

Currently, ursodeoxycholic acid-based treatment is the first and single line of therapy available, and primarily treats disease symptoms, with limited evidence of prevention or slowing of PSC progression. Pruritus is the most commonly treated symptom of both diseases, whereas, no effective therapies are available to combat fatigue, another commonly reported symptom.

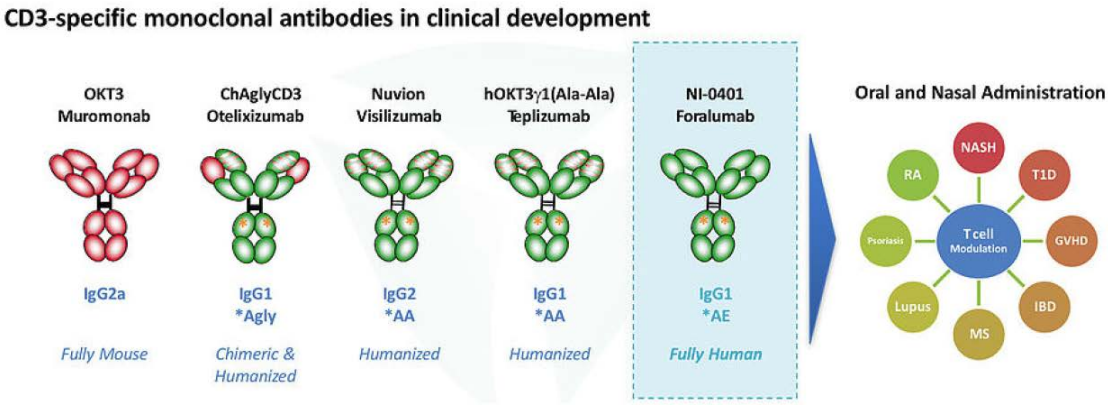
Autoimmune and Inflammatory Diseases

Autoimmune diseases are primarily due to a malfunction when the immune system attacks certain cells in the body as foreign invaders. This can result in irreparable damage to critical organs and tissues eventually resulting in autoimmune diseases.

In humans, CD3-epsilon is encoded by the CD3ε gene on Chromosome 11. The CD3ε molecule, along with four other membrane-bound polypeptides (CD3-gamma, -delta, -zeta, and -eta) form the CD3 complex, which is associated with the T-cell receptor (TCR). Upon antigen bindings, the CD3 complex sends signals through the cell membrane to the cytoplasm inside the T-cell. This leads to activation of the T-cell that rapidly divides to produce new T-cells sensitized to fight the particular antigen to which the TCR was exposed. While T-cell activation is critical for the human immune system to properly fight bacterial, viral or parasitic infections, abnormal T-cell induction can cause and worsen numerous human diseases, including T-cell lymphoma and leukemia, human malignancies, autoimmune disorders, cardiovascular disease and transplant rejection.

Our Solution

Foralumab is the only fully human monoclonal anti-CD3 mAb in clinical development. Since the discovery of the hybridoma technology a method to generate large quantities of a single (monoclonal) antibody, the production and manufacture of mAb's has become widely available showing promise in several autoimmune and inflammatory disease clinical trials and therapeutic utility in animal models. The first murine anti-CD3 mAb (IgG2a) was developed and approved by the FDA in 1985 under the name of muromonab, OKT3, (Ortho Kung T3; Orthoclone®) to treat allograft rejection in kidney, liver and heart transplantation by exerting its potent immunosuppressive effects, mainly due to depletion of T cells in tissues and thereby preventing rejection of the allografts. Subsequently, OKT3 was administered in clinical trials to patients with multiple sclerosis, T1D, IBD and rheumatoid arthritis. Although showing promise to alleviate the disease process, the mAb being of murine origin and extremely immunogenic in humans, was associated with a wide range of side effects that included the typical cytokine release or flu-like syndrome, limiting its clinical development. The side effect profile of OKT3 is a consequence of T-cell activation resulting in the release of numerous cytokines into the systemic circulation. These shortcomings of the murine OKT3 led to the development of a new generation of anti CD3 mAb's using genetic engineering of the mAb structure, as depicted below.



Foralumab dosed intravenously has been observed to alter T-cell function via antigenic modulation, that is, removal of the CD3/TCR complex from the T-cell surface. Modulation has two therapeutic benefits:

- It transiently renders the T-cells incapable of recognizing an antigen and thus unable to orchestrate an immune response such as an allograft rejection; and

- It has a favorable long-term effect on generation and maintenance of regulatory T-cells, a specialized subset of T-cells that promote immunological tolerance.

In comparison with the two other anti-CD3 mAbs evaluated in patients with T1D (otelixizumab and teplizumab respectively), Foralumab was less mitogenic (capable of causing cell division), therefore allowing re-treatment, and to have a better risk/benefit profile. As such, Foralumab was previously developed by Novimmune as an intravenous formulation for the treatment of autoimmune indications: Crohn's disease and in renal allograft recipients.

Further, recent data from studies conducted in the laboratories of our Scientific Advisory Committee members, of Prof. Howard Weiner of Harvard University and Prof. Kevan Herold of Yale University, suggest that oral administration of Foralumab has the potential for therapeutic utility while minimizing toxicity associated with intravenous administration, such as cytokine release syndrome. Importantly, recent clinical studies conducted by Prof. Yaron Ilan with oral administration of anti-CD3 (OKT3; murine mAb) in hepatitis C virus infected patients (non-respondents) and in NASH patients suggested that the treatment was well-tolerated and produced immunologic effects consistent with potential clinical benefits.

In addition, increasing appreciation for the gut-liver cross-talk and of its role in the initiation of NASH-associated inflammation and fibrogenesis has led to the understanding that systemic inflammatory processes can be alleviated by modulating the gut immune system, without inducing generalized immunosuppression. This has been achieved in multiple approaches, including oral administration of fatty liver-derived proteins, anti-CD3 antibodies, tumor necrosis factor fusion protein, anti-lipopolysaccharide antibodies, glucosylceramide, delayed-release mercaptopurine and soy-derived extracts. Several of these compounds were shown to be effective in patients with NASH.

More recent animal studies conducted separately by Prof. Howard Weiner and Prof. Kevan Herold (members of our Scientific Advisory Committee) strongly demonstrated therapeutic utility of orally administered Foralumab for immune-inflammatory diseases. Our strategy is to build on these findings to develop orally administered Foralumab for the treatment of NASH, PBC/PSC and other liver diseases. We believe Foralumab may also be combined with our other product candidate, TZLS-501, a fully human anti-IL-6R mAb, for the treatment of rheumatoid arthritis and other diseases.

Clinical Development Plan

Proposed Phase I Clinical Trial for Foralumab in Healthy Volunteers

The proposed Phase I clinical trial for Foralumab in healthy volunteers is a single center single arm study in which low dose (2.5 mg/dose) Foralumab will be orally dosed for 5 consecutive days followed by safety monitoring for 10 days. If safe, a high dose of 5 mg/dose will be administered orally further for 5 consecutive days followed by 10 days of safety monitoring. If data indicates that the drug is safe, Phase IIa trials will be initiated. The primary endpoint of this study is safety and tolerability of Foralumab in humans.

Proposed Phase IIa Clinical Trial for Foralumab for the Treatment of NASH and Type 2 Diabetes (T2D)

The proposed Phase IIa clinical trial for Foralumab is a randomized, placebo-controlled, four-arm, double-blind study. Subjects (48) will be randomized (1:1:1:1) to receive either a once daily oral placebo or Foralumab dose of 0.5 mg, 2.5 mg or 5.0 mg for 30 consecutive days. Subjects will record adverse events and daily administration of study medication in a subject diary. This will serve as a measure of compliance and record of safety and tolerability. Subjects will be followed up for 30 days following completion of treatment. Study visits performed on Days 14, 30 and 60 of the study, will monitor metabolic parameters (body mass index (BMI) and waist circumference), serum lipid profiles, immunological markers (C-reactive protein (CRP) and an array of cytokines), hepatic enzymes and functions (13C-methacetin breath test (MBT)) and liver steatosis/fibrosis, which will be compared to baseline levels (Day 1).

The safety and tolerability of the treatment regimen is the primary endpoint and will be determined by monitoring vital signs, laboratory values, adverse events and physical findings throughout the study. In addition, efficacy will be established upon either reduced Day 30 serum alanine aminotransferase (ALT) levels, reduced hemoglobin A1c (HbA1c) or improved homeostasis model assessment (HOMA) or HOMA of insulin resistance (HOMA-IR) scores as compared to baseline (Day 1).

Proposed Phase IIa Clinical Trial for Foralumab for the Treatment of PBC/PSC

The proposed Phase IIa clinical trial for Foralumab in 20 PBC/PSC patients is a single-center, single-arm study. Subjects will receive a daily oral dose of 2.5 and 5.0 mg Foralumab for 90 consecutive days. Subjects will record adverse events and daily administration of study medication in a subject diary. This will serve as a measure of compliance and record of safety and tolerability. Subjects will be followed up for 30 days following completion of treatment. Study visits performed on Days 30, 60 and 90 of the study, will assess the safety and tolerability of the treatment regimen by monitoring vital signs, laboratory values, adverse events and physical findings. In addition, serum lipid profiles, immunological markers (c-reactive protein (CRP) and an array of cytokines), which will be compared to baseline levels (Day 1). Therapeutic utility will be established upon either reduced Day 90 serum alanine aminotransferase (ALT) levels, alkaline phosphatase (ALP), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT) or bilirubin levels, or changes in CRP levels as compared to baseline (Day 1). Quality of life will be assessed by scoring changes in pruritus, pain and fatigue severity, using standard questionnaires. Survival probability will be determined by assessing patient Mayo Risk Score (a widely used statistical model, designed to estimate probability of survival over a period of time based on certain key data determined from a liver biopsy).

The primary endpoints will be the assessment of safety and tolerability of the test article Foralumab regimen in subjects with either PBC or PSC. The secondary endpoints will be to (a) assess any clinically significant effect of the oral Foralumab regimen in improving serum ALT, ALP, GGT, AST, CRP, bilirubin and cytokine levels and (b) to assess any clinically significant effect of the oral Foralumab regimen in improving patient quality of life measures and survival probability. Safety and tolerability of the anti-CD3, Foralumab will be determined by AEs, vital signs, physical examination and routine safety laboratory measures.

Clinical Data

Intravenous Foralumab has been studied in a total of three Phase I and Phase II clinical trials in 68 patients conducted by Novimmune. In a Phase IIa trial conducted by Novimmune, patients with Crohn's disease and renal allograft rejection in kidney transplants demonstrated Foralumab's immunomodulatory activity in humans. Although clinical data were encouraging, we have decided not to pursue evaluation of intravenous Foralumab in Crohn's Disease because we believe the market for this disease is saturated by other FDA approved drugs. Further, while intravenous administration of antibodies has been widely used, side effects from the intravenous administration still are prevalent as well as patient compliant issues come into play.

Two of Novimmune's clinical trials were in patients with Crohn's disease and the third clinical trial was conducted in patients undergoing kidney transplantation and suffering with renal allograft rejection. Sixty-eight subjects with active Crohn's disease and 11 subjects with acute cellular renal allograft rejection were treated with Foralumab. The route of administration of Foralumab in these studies was via intravenous administration.

In these trials, it was observed that:

- The short-term safety profile of Foralumab was very similar to those reported with other anti CD3 antibodies and no new emerging concerns have been identified.
- Total daily doses of up to 1mg (~ 500 μg/m^2) per patient were generally well tolerated without corticosteroid premedication. The most common adverse events following exposure to Foralumab were infusion related reactions (IRRs), which occurred in all patients treated with the compound. In the majority of cases, these symptoms were mild (66%) in intensity and were reported following the first two infusions of the 5-infusion treatment course. The number of affected patients and the severity of symptoms tended to increase with increasing dose level.

- A clear reduction of cytokine release and its associated IRRs were observed with steroid pre-medication. All patients who received pre-medication with steroids had mild or no IRRs, and cytokine release was reduced. Only one patient who did not receive steroid pre-medication had significant levels of cytokine release, in particularly IL-6.
- Usage of steroid pre-medication allows the administration of higher doses.
- Both the magnitude and duration of CD3 modulation increased in a dose related manner.
- No anti-drug antibodies were detected.

Preclinical Data

Oral anti-CD3 antibodies, as opposed to the narrow therapeutic window of its intravenous counterpart, have been shown to impact the gut immune system and mesenteric lymph nodes, thereby promoting regulatory T cells (Treg) activity, without inducing immunosuppression. The treatment alleviated experimental autoimmune encephalitis and T1D mellitus, which was associated with Treg induction. Orally and nasally administered anti-CD3 suppressed autoantibody production in a mouse lupus model. Oral anti-CD3 yielded reduced pancreatic hyperplasia, hepatic fat accumulation and muscle inflammation in a leptin-deficient model of NASH and diabetes.

Pharmacology Summary (In Vitro Studies)

The key conclusions arising from the non-clinical studies of Foralumab by Novimmune are:

- Foralumab is a specific anti-CD3 epsilon mAb, as it binds to human T-cells and the recombinant human CD3 epsilon chain, and can be displaced by another specific anti-CD3 epsilon mAb, muromonab CD3.
- When bound to its target, Foralumab triggers calcium flux into the cell and modulates the CD3/TCR complex causing its' transient removal from the cell surface.
- The combination of the two-point mutations introduced into the Fc portion (the constant region of the antibody that has limited structural variability and is responsible for adverse side effects) of Foralumab, resulting in the abrogation of the binding to Fc gamma receptors (FcγRs) and C1q, consequently eliminates T-cell proliferation and the release of numerous cytokines including tumor necrosis factor (TNF) and interferon gamma (IFNγ) *in vitro*.
- Foralumab does not cross react with CD3 molecules expressed by T-cells of other species including baboon, *Rhesus* monkey, *Cynomolgus* monkey, rabbit, dog, rat and mouse. As a consequence, options for the most relevant species selection for pharmacology and toxicology assessment of Foralumab are limited. Novimmune addressed this limitation by studying LCD3 transgenic mice. This transgenic mouse line expresses the human as well as the mouse CD3 epsilon chain on the surface of their T-cells.
- Using a transgenic line of mice expressing both human and mouse CD3 molecules (1:1 ratio) at the surface of T-cell (LCD3*),* following a single intravenous injection, Foralumab dose dependently:
    - Modifies human CD3 epsilon expression; that is, more than 80% of the cell surface protein was removed within 24 hours when given at a saturating dose. This modulation was transient as receptor expression levels returned to baseline values within 7 days of dosing;
    - Caused a reduction of 70-80% in the number of circulating T-cells when given at a saturating dose. The maximal effect was observed at hour 6 post dose. Cell counts returned to baseline levels within 3.5 days;
    - Demonstrated a half-life of 1.4 and 1.7 days for doses of 5 and 200 µg per mouse, respectively. This seemingly short half-life is similar to that observed in vivo for other anti-CD3 mAbs and reflects internalization of Foralumab by the human CD3 molecule on the T-cells of these transgenic mice. It was therefore expected that Foralumab will be internalized by human T-cells in patients and consequently have a half-life comparable to other therapeutic anti-CD3 mAbs.

Milciclib (TZLS-201)

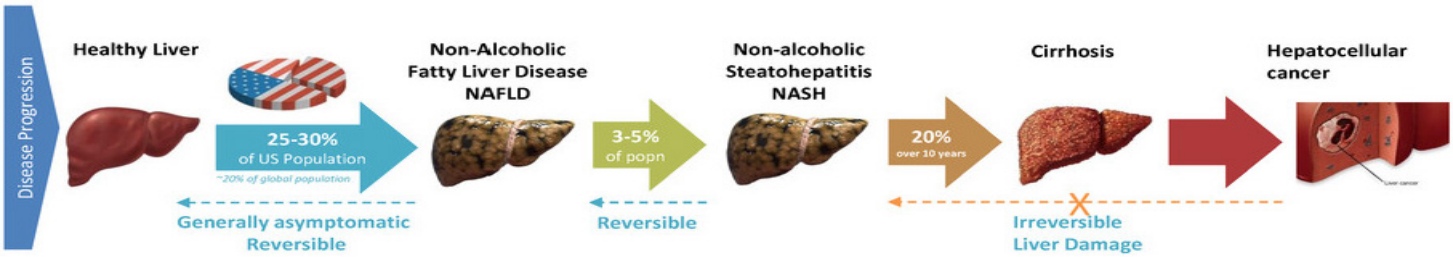
Milciclib (TZLS-201) is an orally bioavailable, small molecule broad spectrum inhibitor of Cyclin Dependent Kinases (CDKs): 1, 2, 4, 5 and 7 and Src family kinases. Cyclin dependent kinases are a family of highly conserved enzymes that are involved in regulating the cell cycle, which is a series of events that takes place in cells leading to division and duplication of its DNA to produce two daughter cells. Src family kinases regulate cell growth and potential transformation of normal cells to cancer cells. A unique feature of Milciclib is its ability to reduce microRNAs, miR-221 and miR-222, that silence gene expression. miR-221 and miR-222 promote the formation of blood vessels (angiogenesis) that are important for spread of cancer cells (metastasis). Levels of these microRNAs are consistently increased in HCC patients and may contribute towards resistance to treatment with sorafenib. As a result we are investigating Milciclib both as a monotherapy and plan a combination treatment with sorafenib. To date, Milciclib has been studied in a total of seven completed and ongoing Phase I and Phase II clinical trials in approximately 285 patients. In these trials, Milciclib was observed to be well-tolerated and showed initial signals of anti-tumor action. We initiated a Phase IIa trial (CDK-125a-010) for Milciclib as a single therapy in patients with HCC in the first half of 2017 and expect to initiate a Phase IIb trial (TZLS (201)-125a-011) for Milciclib in combination with sorafenib (the standard of care for treatment of HCC) in patients with HCC in 1H 2018.

Hepatocellular Cancer (HCC)

We are initially developing Milciclib for the treatment of HCC. HCC, or liver cancer, is the fifth most common cancer in men and the eighth most common cancer in women in the United States. Liver cancer incidence and death rates are steadily rising. As of 2012, rates of new liver cancer cases went up 38% from 2003 to 2012 according to the CDC ((https://www.cdc.gov/cancer/liver/index.htm).

Most HCC patients present with advanced disease and do not benefit from transplantation, surgical resection, or locoregional therapies, and there is only one chemotherapeutic agent, sorafenib approved in the United States and EU for advanced HCC patients.

The primary risk factor for HCC is hepatic cirrhosis, with an estimated 78% of HCC cases and 57% of cases of liver cirrhosis caused by chronic infection with hepatitis B virus (HBV) or hepatitis C virus (HCV). Recently, the combination of insulin resistance, hypertension, dyslipidemia and obesity, termed “metabolic syndrome,” has also been recognized as a cause of nonalcoholic fatty liver disease (NAFLD), cirrhosis and HCC. The following graphic represents the progression from a healthy liver to NAFLD, NASH and HCC.



Generally, cancer is primarily due to deficiencies in cell cycle control, eventually resulting in transformation of normal cells to rapidly growing cancer cells. Therapeutic intervention to control cell cycle has long been anticipated as effective cancer therapies. CDKs are a family of enzymes first discovered as regulators of the cell cycle. CDKs have been found to be overexpressed in a variety of human diseases with abnormal cell growth such as cancers, viral infections, neurodegenerative disorders and other proliferative diseases. We believe that modulating CDK activity with targeted therapies is an attractive strategy to reinforce cell cycle control and decrease the rate of abnormal proliferation of cancer cells. The first FDA approval in March 2015 of a CDK inhibitor for palbociclib, and more recently in 2017, ribociclib, for a type of breast cancer, has led to great interest in the development of this class of drugs as oncology therapeutics.

Our Solution

Milciclib is an oral, broad-spectrum inhibitor of cyclin dependent kinases (CDKs), as well as several other protein kinases responsible for controlling cell growth and replication. Milciclib has an unusual kinase inhibitory profile making it active against other receptors such as, tyrosine kinase, Src family and splicing kinases, which play a role in cell growth and transformation from normal to cancerous cell types.

In tumor cells exposed to Milciclib, a block in G1 phase (first phase of the growth cycle where the cell synthesizes messenger RNA and proteins before cell division) of the cell cycle was observed, supporting the postulated mechanism of action of the compound as determined in biochemical assays. Additionally, Milciclib was able to modulate the phosphorylation of the Retinoblastoma protein, a substrate of the CKD/cyclin complex as well as to reduce phosphorylation status of proteins of the TRKa signaling pathway in cells expressing the tyrosine kinase receptor. These results supported that Milciclib was active against several families of protein kinases that actively controlled cell growth and transformation from normal to cancerous cell types. This is important because many chemotherapeutic agents are effective at only a single point in the cell cycle, allowing cells to “escape” the biochemical blockage through alternative biochemical pathways.

Significant anti-tumor activity was observed in all tested preclinical animal models with different oral treatment schedules of Milciclib. Cancerous cell types were transplanted into immunosuppressed animals and the number and volume of cancerous lesions were evaluated by magnetic resonance imaging (MRI) after oral administration of milcicilib at different dose levels and dose schedules compared to untreated, control animals. In various human xenograft and transgenic models (prostate cancer, lung adenocarcinoma and hepatocarcinoma), consistent tumor growth inhibition, up to 91%, (evaluated by measuring the number and volume of tumors for treated animals versus control animals) was observed - with repeat daily treatment at tolerated doses. Similar results were obtained in a mammary carcinoma model (stasis and partial remission in 58% and 25% of the primary tumors, respectively) with repeat daily dosing.

Clinical Development Plan

Phase IIa Clinical Trial (CDKO-125a-010) for Milciclib as a Monotherapy for the Treatment of HCC

In January 2017, we initiated a single-arm, multicenter, Phase IIa clinical trial (CDK-125a-010) for Milciclib in adult patients with unresectable or metastatic HCC and good liver function. The trial is studying the tolerability and safety of Milciclib in these adult patients. We have enrolled approximately 10 patients at sites in Italy and Greece. Eligible patients are receiving Milciclib orally, 100 mg/day for four consecutive days a week (four days on followed by three days off) for a total of 12 weeks. The dose will be reduced to 80 mg/day on subsequent cycles if more than two of the first six treated patients exhibit poor tolerability.

The primary endpoint for the study is the overall safety profile, evaluated based on laboratory findings and adverse events emerging during the trial. The occurrence of adverse events and laboratory tests will be performed weekly during treatment. All the enrolled patients who receive at least one drug administration will be evaluated for safety. An interim evaluation of the safety and tolerability was undertaken as soon as the 10th patient had completed the first cycle of treatment a second interim evaluation will be conducted when 10 patients have completed their first cycle of treatment. Enrollment of additional patients was allowed after a positive safety evaluation of the first 10 patients by an independent data monitoring committee (IDMC). On December 8, 2017 we announced the results of the first interim review by the independent data monitor committee (the “IDMC”) fund that treatment with Milciclib was safe and well-tolerated with no drug-related series adverse events. The IDMC recommended continuing with the trial. Secondary endpoints include Objective Tumor Response Rate, based on the modified RECIST (mRECIST), a set of criteria developed to assess tumor response in HCC. In this study, objective response by RECIST will also be evaluated as supportive analysis, along with several secondary parameters. The decrease in

alpha-fetoprotein (AFP) as compared to baseline in patients with high AFP at baseline will also be considered, based on reports suggesting a better outcome for patients who achieve an AFP response. As an exploratory endpoint, the expression of micro-RNAs and their possible association with Milciclib treatment will be investigated.

- On November 23, 2017 we announced that Milciclib met its primary endpoints in two phase II clinical trials in patients with thymic carcinoma and thymoma. The treatment regimen with Milciclib (150 mg/day; 7 days On/7 days Off) was safe and well tolerated in these patients with continuing expose of up to 5 years. In both clinical trials it was demonstrated that treatment with Milciclib met progression free survival as the primary endpoint and overall survival as a secondary endpoint. (Progression free survival or PFS is defined as the time measured from first day of treatment to the date at which disease “progresses” or the date on which the patient dies from any cause. Overall Survival or OS is defined as the length of time measured from first day of treatment to patient death from any cause).

Phase IIb Clinical Trial (TZLS (201)-125a-011) for Milciclib as a Combination Therapy with Sorafenib for the Treatment of HCC

In 1H of 2018, we intend to initiate a randomized, multicenter study to explore tolerability, safety and antitumor activity, of Milciclib in combination with sorafenib, administered as first-line systemic therapy in adult patients with recurrent, unresectable or metastatic HCC and good liver function.

Clinical Data

Milciclib has been studied in a total of seven completed and ongoing Phase I and Phase II clinical trials in approximately 285 patients. Milciclib was observed to be well tolerated by patients with thymoma in Phase I and Phase II clinical trials.

Phase I Development

Milciclib has been investigated in each of the below, open-label, multi-center, non-randomized, dose-escalation Phase I clinical trials.

Trial	Patient Population	Treatment Schedule / Dosing	Key Findings
CDKO-125a-001	Advanced/metastatic solid tumors 37 patients	1st Schedule: Orally, once daily for 7 consecutive days every 14 days in a 2-week cycle at escalating doses of 50, 100, 150, 200 and 300 mg 2nd Schedule: Orally, once daily for 4 consecutive days a week for 3 weeks in a 4-week cycle at escalating doses of 150, 180 and 200 mg	*Pharmacokinetics:* Comparable plasma pharmacokinetic parameters between the two schedules were observed. The exposure to Milciclib increased with the dose and there was a 3-fold accumulation in the daily systemic exposure after repeated dosing, in good agreement with expectations on the basis of the half-life of the compound (24-43 h). *Clinical observations:* No objective responses were achieved on 1st schedule; Disease stabilizations, defined as cancer disease that is neither increasing or decreasing in extent or severity, was observed in 6 of 14 evaluable patients (42.9%). A partial response was achieved in 2 out of 14 evaluable patients (14.3%) on 2nd schedule; Disease stabilization (no change in extent or severity of disease state) was reported in 3 patients (21.4%), all treated at 180 mg/day dose level (DL), including a stabilization lasting 31 weeks in a patient with pancreatic cancer and stable disease (SD) lasting 29 weeks in a patient with carcinoid.

CDKO-125a-002	Recurrent malignant glioma 28 patients (Phase I) 34 patients (Phase II)	Escalating oral doses of 18, 36, 54 and 72 mg/m2 once a day for 14 consecutive days followed by 7 days of rest in a 3-week cycle 54 mg/m2 (RP2D)	*Pharmacokinetics:* Results indicated that the pharmacokinetics of Milciclib was dose-independent in the dose range 18 – 72 mg/m^2 Systemic exposure values of Milciclib maleate accumulated by a factor of 3 *Clinical observations:* Phase I: No evidence of clinical effect was observed in all the 28 treated patients. However 5 patients seemed to have benefitted from therapy with stable disease (SD) observed (no change in extent or severity of cancer). Phase II: One out of 34 patients achieved the primary endpoint. Progression free survival at 6 months or PFS-6 rate was 2.9%. No complete response (CR, disappearance of all signs of cancer in response to treatment) or partial response (PR decrease in tumor size or extent of cancer in the body) were reported. 4 patients showed SD as best overall response (11.8%). Prolonged SD (≥ 6 months) was observed in one patient whose SD lasted for 24.9 months. *Safety:* 34 patients were enrolled and treated: 29 patients of non-EIAEDs (EIAED is defined as Enzyme Inducing Anti-Epileptic Drugs) population and 5 of EIAEDs population. The primary clinical endpoint was not met. Only one patient (non-EIAEDs) achieved the study primary endpoint out of 34 treated patients. PFS-6 rate evaluated in the treated patients was 2.9% (95% CI, 0.07-15.33). No CR or PR was reported; 4 patients in the treated patients showed SD as best overall response on treatment (11.8%). Prolonged SDs (≥6 months) was observed in one patient whose SD lasted for 24.9 months. Median overall survival in treated patients was 7.03 months (95% CI, 5.72-10.58). The exploration of the role play by potential prognostic factors, such as performance status KPS (≥90 vs. <90), age (<40 vs. ≥40) and interval between initial diagnosis and current recurrence ((≥52 weeks vs. <52 weeks) indicated a better survival outcome for patients whose interval between initial diagnosis and current recurrence was (≥52 weeks. Given the non-comparative nature of the study, it cannot be said whether the treatment played any role in this result. The influence of other factors cannot be excluded but was not apparent in the current sample

CDKO-125a-003	Advanced/metastatic solid tumors 30 patients	1st Schedule: Orally, once daily for 21 consecutive days followed by 7 days of rest in a 4-week cycle at escalating doses of 16 and 24 mg/m^2 2nd Schedule: Orally, once daily for 14 consecutive days followed by 7 days of rest in a 3-week cycle at escalating doses of 24, 48, 54 and 72 mg/m^2	*Pharmacokinetics:* No differences in the pharmacokinetics were observed between the two schedules after both single and repeated dosing The systemic exposure to Milciclib (amount of milcicilib available systemically in the patient) increased with dose in terms of both Cmax (maximum concentration of Milciclib in plasma) and daily AUC (Area Under the Plasma Drug Concentration vs Time Curve, a measure of drug bioavailability) without deviations from dose-proportionality (plasma concentration changes in a linear relationship to amount of drug dosed). After repeated administrations, Milciclib Cmax and AUC accumulated by a factor of 2-4, independent of the dose-level *Clinical observations:* No objective (measurable) responses were achieved. Stable Disease (SDs) were reported in 5 out of 16 evaluable patients (31.3%), starting from the dose of 48 mg/m2/day. One clinically significant disease stabilization maintained for 12 cycles (10.5 months) at 48 mg/m2/day, was achieved in a parotid gland patient.
CDKO-125a-004	Advanced/metastatic solid tumors 16 patients	Orally administered at 45, 60 and 80 mg/m^2 once daily for 7 days on / 7 days off (Days 1 to 7 and 15 to 21) in a 4-week cycle in combination with fixed dose of IV gemcitabine (1000 mg/m^2/day) on Days 1, 8, 15 over 30 minutes every 4 weeks	*Pharmacokinetics:* Pharmacokinetic parameters (Cmax, AUC) of Milciclib after Milciclib maleate/ gemcitabine combination were consistent with those previously observed after Milciclib maleate administration as single agent, suggesting no influence of gemcitabine on the pharmacokinetics of the compound *Clinical observations:* One PR in 14 evaluable patients (7.1%) and one SD in 10 patients (71.4%). Clinically significant disease stabilizations lasting ^{3} 6 months were recorded in 4 cases (28.6%) in thyroid, prostatic, pancreatic carcinoma and peritoneal mesothelioma, in 2 of them lasting 13.4 months (peritoneal mesothelioma) and 14.3 months (prostate cancer). The PR and 3 of the 4 long lasting disease stabilizations were obtained at the recommended Phase II dose (RP2D) of 80 mg/m2/day plus 1000 mg/m2/day gemcitabine, supporting development of combination therapies with Milciclib in advanced cancer patients.

Phase II Development

Trial	Patient Population	Treatment Schedule / Dosing	Key Findings
CDKO-125a-005	Malignant pleural mesothelioma 38 patients	150 mg/day orally administered for 7 consecutive days every 14 days in 2-week cycles	*Pharmacokinetics:* Plasma levels of Milciclib were comparable to those previously obtained in the Phase I study CDK0-125a-001 at the same dosage and with the same schedule, confirming the reliability of the pharmacokinetic profile of the compound *Clinical observations:* No objective responses were reported; prolonged SDs were observed in 2 patients, lasting 8.9 months and 8.7 months, respectively.
CDKO-125a-006 Trial cutoff: 1/9/2017	Malignant B3 thymoma / thymic carcinoma approximately 72 patients		*Clinical Observations:* Treatment with milciclib met the primary endpoint of progression free survival at 3 months (PFS-3). 56 of 72 treated patients had median PFS of 5.78 months with upper and lower 95% confidence limits of 3.48 months and 7.89 months, respectively. The secondary endpoint, Overall Survival (OS), was also met in this trial. 36 of 72 patients (50%) had median OS of 24.44 months with upper and lower 95% confidence limits of 22.05 and 54.55 months, respectively. Five patients from this study are continuing treatment with milciclib.
CDKO-125a-007 Trial cutoff: 1/9/2017	Malignant B3 thymoma / thymic carcinoma approximately 30 patients		*Clinical Observations:* Treatment with milciclib met the primary endpoint of PFS-3. 18 of 30 patients had median PFS of 5.65 months with upper and lower 95% confidence limits of 3.94 months and 17.45 months, respectively. The secondary endpoint, OS, was met in this trial. 18 of 30 treated patients (54.5%) had OS of 48 months. Upper and lower 95% confidence limits could not be calculated because the median survival probability was not reached

Source: Milciclib Investigators Brochure version 13

Safety

Overall, Milciclib has indicated a similar pattern of toxicity across studies. Consistent with preclinical findings, the safety profile of the compound in humans is characterized by a dose-limiting neurological toxicity and, to a lesser extent, by gastrointestinal (GI) toxicity. Asthenia (weakness) and fatigue have also been observed, as well as effects on liver, especially with prolonged schedules of administration. Mild/moderate tremors are a common finding, reported also at recommended Phase II Doses (RP2Ds) (only one case of grade 3), whereas ataxia (loss of muscle control and balance) was observed primarily during the first dose-escalation study (one case of grade 3 ataxia occurred also at the RP2D in the combination study CDKO-125a-004 and one in CDKO-125a-006 trial). Both tremor and ataxia were generally reversible in all cases in up to 7-9 days, upon drug discontinuation or dose reduction in some cases. Grade 1-2 dizziness was also reported, with only one grade 3 occurrence, overall. Mild dysgeusia (disorder of sense of taste) is another event that was reported across studies, as well as headache and anorexia (loss of appetite). Grade 3 myasthenia (muscle weakness) was also reported in two patients. Nausea and/or vomiting and/or diarrhea were mostly of grade 1-2 in severity and were manageable with appropriate therapy. Diarrhea was occasionally severe, leading to dehydration in several instances. Skin disorders were also reported across studies; the events were mainly of grade 1-2 in severity except for one case of grade 3 rash maculopapular and one case grade 3 of erythema multiforme. Hematological toxicity was mainly represented by lymphocytes (white blood cells) decrease and, to a lesser extent by all the other hematological parameters. Severe thrombocytopenia (decrease in number of platelets in blood) was sporadically observed, especially at the highest doses tested and in combination with gemcitabine. Effects on liver were dose-dependent and mainly represented by transient transaminase elevation (with bilirubin slightly less affected). ALT/AST (liver enzymes measured to monitor liver damage) elevations were usually mild using the 7 days on /7 days off schedule (even if prolonged transaminases (liver enzymes) were occasionally observed). The more prolonged administrations were associated with a more frequent and pronounced effect on liver function tests. Asymptomatic grade 3-4 lipase (a pancreatic enzyme that breaks down fats, measured to monitor pancreatic function) elevations were sometimes reported, without clinical manifestation. No important effects on renal function were noted.

Monitoring of visual function was performed through visual acuity, funduscopy (ophthalmic examination of the back of the eye) and, in a subset of studies, ERG examinations. Overall, no clinically relevant abnormalities for these parameters emerged during treatment across studies, except for ERG worsening, compared to baseline, observed in three patients, who for this reason discontinued study treatment as per protocol, and one case of retinal detachment reported as a serious event in one patient (CDKO-125a-006 trial) and assessed as probably related to Milciclib maleate.

Our interim review in trial CDKD-125A-010, as noted above, found Milciclib to be safe and well-tolerated with no drug-related serious adverse events in 6 patients with unresectable or metastatic HCC who had concluded a first cycle of treatment with Milciclib.

Phase II Data in Thymoma and Thymic Carcinoma

Thymomas and thymic carcinomas are tumors that originate in epithelial cells of the thymus gland. Generally, thymoma does not spread beyond the thymus, while thymic carcinoma, represents an aggressive cancer that metastasizes rapidly and poses treatment challenges. Both cancers are rare, and it is estimated that together they account for ~400 cases per year in the US, or about 1.5 persons per million diagnosed with thymoma/thymic carcinoma. Patients more often present with advanced disease, with a 5-year survival of 30% to 50%. Standard primary treatment for patients with these types of tumors is surgical resection. Depending on tumor stage, treatment options include the use of radiation therapy and chemotherapy with or without surgery. First line of chemotherapy treatment is the combination of cisplatin, doxorubicin and cyclophosphamide for thymoma. For thymic carcinoma the first line of treatment is the combination of paclitaxel and carboplatin.

Milciclib met its primary endpoints in two phase II clinical trials in patients with thymic carcinoma and thymoma. Clinical trials, CDKO-125A-006 (72 patients) and CDKO-125A-007 (30 patients) in patients with thymic carcinoma and thymoma, respectively, were conducted in the USA, France and Italy. Monotherapy treatment regimen with milciclib (150mg/day; 7days On/7days Off) was safe and well-tolerated. Seven patients (5 patients in the CDKO-125A-006 study and 2 patients in the CDKO-125A-007) have been continuing treatment with milciclib for more than 2 years with excellent safety profile. Among these, 2 patients have been treated with milciclib for approximately 5 years, demonstrating safety of the drug for long term treatment.

In trial CDKO-125A-006, 56 of 72 treated patients had median PFS of 5.78 months with upper and lower 95% confidence limits of 3.48 and 7.89 months, respectively. In trial CDKO-125A-007, 18 of 30 treated patients had median “PFS” of 5.65 months with upper and lower 95% confidence limits of 3.94 and 17.45 months, respectively. These results exceed the acceptance criterion of “clinically interesting” (median PFS> 10.2 weeks) established for monotherapy with pemetrexed. The overall survival (OS) secondary endpoint was also met in both trials. In trial CDKO-125A-006, 36 of 72 (50%) treated patients had median OS of 24.44 months with upper and lower 95% confidence limits of 22.05 and 53.55 months, respectively. In trial CDKO-125A-007, 18 of 30 patients had an OS (54.5%) of 48 months. As a median was not reached, the 95% confidence limits could not be calculated.

Both clinical studies demonstrated that treatment with milciclib met Progress Free Survival (PFS) as the primary endpoint and Overall Survival (OS) as a secondary endpoint.

Preclinical Data

The pharmacokinetics of Milciclib were investigated in mouse, rat, dog and monkey models after single intravenous and oral administration of the compound. Since the compound is intended for the oral administration route, the pharmacokinetics were further characterized after single and repeated oral administrations. These preclinical studies were performed with Milciclib formulated as maleate or mono/di/tri-hydrochloride salt. Following intravenous administration, Milciclib was characterized by a moderate clearance in mice, rats and monkeys and a high clearance in dogs. The volume of distribution was higher than the total body water in all tested species, suggesting an extensive tissue distribution. Following oral administration to rats and monkeys, Milciclib crossed the blood-brain barrier and distributed in the brain. In all species, Milciclib plasma levels increased largely in direct proportion with the dose.

Preclinical toxicology studies conducted with Milciclib have shown that the hemolymphopoietic (HLP) system, the GI tract and the male reproductive organs are the major target organs considered related to the pharmacological activity of the compound in all species. The effects on the HLP system and GI tract were reversible after drug withdrawal. Reversibility could not be demonstrated in the male reproductive organs at the end of the 2-3-week recovery period because of the longtime of maturation of the seminiferous epithelium. Additional toxicities, that are considered not related to the mechanism of action of the compound, were CNS, ocular and renal toxicities. In addition, hemorrhages in different organs were observed in dogs and monkeys. Clinical signs of CNS toxicity were observed at high doses given as single or repeated administrations in all species.

Our Preclinical Programs

Anti-IL6R Fully Human mAb TZLS-501 (formerly known as NI-1201)

TZLS-501 is a fully human mAb targeting the interleukin-6 receptor (IL-6R). Tiziana Life Sciences licensed the intellectual property from Novimmune in January 2017. This fully human mAb has a unique mechanism of action, binding to both the membrane-bound and soluble forms of the IL-6R and depleting circulating levels of the IL-6 in the blood. An excessive production of IL-6 is regarded as a key driver of chronic inflammation, associated with autoimmune diseases such as multiple myeloma, oncology indications and rheumatoid arthritis, and we believe that TZLS-501 may have potential therapeutic value for these indications.

In preclinical studies, TZLS-501 demonstrated the potential for overcoming the limitations of other IL-6 pathway drugs. Compared to tocilizumab and sarilumab, TZLS-501 has been observed to have a higher affinity for the soluble IL-6 receptor from antibody binding studies conducted in cell culture. TZLS-501 also demonstrated the potential to block or reduce IL-6 signaling in mouse models of inflammation. The soluble form of IL-6 has been implicated to have a larger role in disease progression compared to the receptor bound form (Kallen, K.J. (2002). “The role of transsignalling via the agonistic soluble IL-6 receptor in human diseases”. Biochimica et Biophysica Acta. 1592 (3): 323–343.).

StemPrintER™

StemPrintER is a multi-gene signature assay intended for use in patients diagnosed with estrogen-receptor positive ER+/HER2 negative breast cancers. We believe this in-vitro prognostic test will be used in conjunction with clinical evaluation to identify those patients at increased risk for early and/or late metastasis. StemPrintER is designed to help physicians distinguish ER+/HER2 negative patients:

- with an elevated risk of early recurrence (<5 years) who could benefit from chemotherapy in addition to hormonal therapy
- with a high risk of late recurrence who could benefit from prolonged endocrine treatment up to 10 years
- with a low risk of early recurrence who might be spared chemotherapy or be eligible for less aggressive treatments

Our diagnostic has a unique biological basis, being based on the detection of cancer stem cell markers, uses a reliable platform (qRT-PCR, FFPE), and has been evaluated in an initial retrospective validation study using a consecutive cohort of approximately 2400 patients with breast cancer. The development team is preparing for a retrospective validation study using an independent cohort and has conducted a pre-submission meeting with the FDA.

Manufacturing

We believe our current CMOs will be able to fully meet our current clinical trial needs and anticipated future commercial demand for Foralumab and Milciclib in a cost-effective manner, removing the risk typically associated with clinical to commercial scale-up.

A large-scale cGMP manufacturing of Foralumab drug substance has been accomplished and we have produced sufficient purified material for completing all clinical studies up to Phase 3. This material was produced by Lonza using a proprietary cell culture technology. The Foralumab material is highly stable when stored at -80^{O}C for several years. A novel and proprietary formulation suitable for oral administration of Foralumab has been successfully developed. We are currently producing formulated drug product for clinical studies under cGMP condition.

We have also accomplished cGMP manufacturing of Milciclib at pilot scale. The chemical scheme for manufacturing is simple with reproducible yields. This method has been used for producing drug substance to supply the ongoing clinical studies. The chemical process is very cost-effective and can be scaled-up for much larger scale needed for commercialization.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly changing technologies, significant competition and a strong emphasis on intellectual property. We face substantial competition from many different sources, including large and specialty pharmaceutical and biotechnology companies, academic research institutions, government agencies and public and private research institutions.

We are aware of a number of companies focused on developing therapies in various indications. Any advances made by a competitor may be used to develop therapies that could compete against any of our product candidates.

For our specific product candidates, the main competitors include:

- Sorafenib is currently the standard of use therapy for HCC but the drug exhibits severe toxicities and patients often develop resistance to the treatment with sorafenib. As a result, there is an immediate need for improvement in treatment for HCC.

- Foralumab is currently the only fully human anti-CD3 mAb in clinical development for treatment of NASH and PBC/PSC. Ocalvia is the only FDA approved drug for treatment of PBC. Although a number of pharmaceutical companies are engaged in development of therapies for NASH but Foralumab is the only mAb currently in development as oral immunotherapy treatment for NASH.

Many of our potential competitors, alone or with their strategic partners, have substantially greater financial, technical and other resources than we do, such as larger research and development, clinical, marketing and manufacturing organizations. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of competitors. Our commercial opportunity could be reduced or eliminated if competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, technologies developed by our competitors may render our potential product candidates uneconomical or obsolete, and we may not be successful in marketing our product candidates against competitors.

Intellectual Property

We strive to protect and enhance the proprietary technologies, inventions and improvements that we believe are important to our business, including seeking, maintaining and defending patent rights, whether developed internally or licensed from third parties. Our policy is to seek to protect our proprietary position by, among other methods, pursuing and obtaining patent protection in the United States and in jurisdictions outside of the United States related to our proprietary technology, inventions, improvements, platforms and our product candidates that are important to the development and implementation of our business.

As of September 30, 2017, our intellectual property portfolio was made up as follows.

Family	Subject	Priority	Status	Expires	Jurisdiction
Foramulab TZLS-401 Licensed from Novimmune	Composition of matter	2004	Issued	2025	US, Europe, Australia, Eurasia, HK, India, Israel, Japan, Korea, Singapore, South Africa, South America
	Methods of use	2004	Issued	2025	US
	Composition and methods	2004	Pending	2025	US
	Methods of use	2004	Issued	2025	US, Australia, Canada, China, Europe, Eurasia, Hong Kong, Israel, Japan, Mexico, Singapore, South Africa
	Methods of use (combination therapies)	2011	Pending	2032	PCT treaty countries
	Methods of use (in combination with anti Il-6R and TNF antagonists)	2010	Pending	2031	PCT treaty countries
	Methods of use (in combination with anti Il-6R)	2011	Pending	2032	PCT treaty countries
	Formulation, dosages, dosing regimens and methods of use	2016	Pending	2036	US
Milciclib TZLS-201 Licensed from Nerviano Medical Sciences	Composition of matter, methods of use, process of manufacturing	2003	Issued	2024	US, Europe, Eurasia, Africa, Algeria, Antigua & Barbuda, Argentina, Australia, Barbados, Bosnia & Herzegovina, Brazil, Canada, Colombia, Costa Rica, Croatia, Cuba, Ecuador, Egypt, Georgia, Iceland, India, Indonesia, Israel, Japan, Korea, Kosovo, Malaysia, Mexico, Mongolia, Montenegro, New Zealand, Nicaragua, Norway, Pakistan, Philippines, Serbia, Singapore, South Africa, Sri Lanka, Taiwan, Thailand, Trinidad & Tobago, Tunisia, Ukraine, Uzbekistan, Venezuela, Vietnam
	Methods of use (multiple indications)	2008; 2009	Issued	2029; 2030	US, EU, China, Hong Kong, Japan
	Methods of use (combination therapies with cytotoxics)	2008; 2009	Issued	2029; 2030	US, EU, China, Hong Kong, Japan
	Compositions of related entities, formulations and methods of treatment	2009	Issued	2030	US, EU, China, Hong Kong, Japan
	Methods of use (combination therapies with therapeutic antibodies)	2006	Issued	2027	US, EU, China, Hong Kong, Japan
Anti-IL6R TZLS-501 Licensed from Novimmune	Methods of use	2009	Issued	2029	US, Austria, Australia, Belgium, China, Denmark, France, Germany, Ireland, Italy, Luxembourg, Mexico, Netherlands, Spain, Sweden, Switzerland and UK

NTD: According to our records, the application covering combination therapies with a therapeutic antibody (PCT/EP2007/051020) has a priority date of 2006, and was filed in 2007.

We have rights to a patent family that discloses the Milciclib compound, methods of using the compound, and processes for making the compound under license from Nerviano Medical Services (which is further described below). This patent family includes five granted U.S. patents, one granted European patent, and one granted Eurasian patent. This patent family also includes granted patents in Africa (African Intellectual Property Organization, African Regional Intellectual Property Organization), Algeria, Argentina, Australia, Bosnia & Herzegovina, Canada, Colombia, Costa Rica, Croatia, Cuba, Ecuador, Georgia, Iceland, India, Indonesia, Israel, Japan, Korea, Kosovo, Malaysia, Mexico, Mongolia, Montenegro, New Zealand, Nicaragua, Norway, Pakistan, Philippines, Serbia, Singapore, South Africa, Sri Lanka, Taiwan, Tunisia, Ukraine, Uzbekistan, and Vietnam. Several applications are pending in the U.S. and other countries in this family. The patents in this family will expire in April, 2024, excluding any patent term adjustment in the U.S. and patent term extensions available in the U.S. and several other jurisdictions, such as Europe.

We also have rights to a second patent family covers related entities, such as salts and crystal forms, of Milciclib, and methods of using the salts and crystal forms. This patent family comprises one granted U.S. patent and one granted patent in each of China, Japan, and Hong Kong. One application is pending (allowed) in this family in Europe. The patents in this family will expire in April, 2030, excluding any patent term adjustment in the U.S. and patent term extensions available in the U.S. and several other jurisdictions, such as Europe.

In addition, we have rights to five patent families cover methods of using Milciclib in the treatment of multiple indications. These patent families comprise five granted U.S. patents, and granted patents in Europe, China, Hong Kong, and Japan, and one pending patent application in Europe. The patents in these families will expire between February, 2027 and March, 2030, excluding any patent term adjustment in the U.S. and patent term extensions available in the U.S. and several other jurisdictions, such as Europe.

Among the above five patent families, two families also cover combination therapies of Milciclib with cytotoxic agents. These families comprise two granted U.S. patents, and granted patents in Europe, China, Hong Kong, and Japan. The patents in these families will expire between November,

2029 and March, 2030, excluding any patent term adjustment in the U.S. and patent term extensions available in the U.S. and several other jurisdictions, such as Europe.

One family of the above five patent families also covers combination therapies of Milciclib with therapeutic antibodies. This patent family includes one granted U.S. patent, and granted patents in Europe, China, Hong Kong, and Japan. The patents in this family will expire in February, 2027, excluding any patent term adjustment in the U.S. and patent term extensions available in the U.S. and several other jurisdictions, such as Europe.

Individual patents extend for varying periods depending on the date of filing of the patent application or the date of patent issuance and the legal term of patents in the countries in which they are obtained. Generally, patents issued for regularly filed applications in the United States are granted a term of 20 years from the earliest effective non-provisional filing date. In addition, in certain instances, a patent term can be extended to recapture a portion of the U.S. Patent and Trademark Office, or the USPTO, delay in issuing the patent as well as a portion of the term effectively lost as a result of the FDA regulatory review period. However, as to the FDA component, the restoration period cannot be longer than five years and the total patent term including the restoration period must not exceed 14 years following FDA approval. The duration of foreign patents varies in accordance with provisions of applicable local law, but typically is also 20 years from the earliest effective filing date. However, the actual protection afforded by a patent varies on a product by product basis, from country to country and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent.

Furthermore, we rely upon trade secrets and know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part, using confidentiality agreements with our collaborators, employees and consultants and invention assignment agreements with our employees. We also have confidentiality agreements or invention assignment agreements with our collaborators and selected consultants. These agreements are designed to protect our proprietary information and, in the case of the invention assignment agreements, to grant us ownership of technologies that are developed through a relationship with a third party. These agreements may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our collaborators, employees and consultants use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

Our commercial success will also depend in part on not infringing upon the proprietary rights of third parties. It is uncertain whether the issuance of any third-party patent would require us to alter our development or commercial strategies, or our product candidates or processes, obtain licenses or cease certain activities. Our breach of any license agreements or failure to obtain a license to proprietary rights that we may require to develop or commercialize our future product candidates may have an adverse impact on us. If third parties have prepared and filed patent applications prior to March 16, 2013 in the United States that also claim technology to which we have rights, we may have to participate in interference proceedings in the USPTO, to determine priority of invention. For more information, see “Risk Factors—Risks Related to Our Intellectual Property.”

Collaborations and License Agreements

Nerviano Agreement

In January 2015, we entered into a license agreement with Nerviano (the Nerviano Agreement), pursuant to which we obtained a worldwide, exclusive license to patents owned or controlled by Nerviano (the Nerviano License) to develop and commercialize products and services incorporating Milciclib as an active ingredient, and any product or service controlled or owned by Nerviano that is used to diagnose or assess responsiveness to Milciclib therapy or dosage. The Nerviano License confers the right on us grant sub-licenses, and otherwise to employ third party manufacturers and distributors to produce and sell licensed products and services.

Each party to the Nerviano Agreement agreed to a development plan (the Nerviano Development Plan) approved by a joint development committee (JDC). The JDC is comprised of at least two members of each party, meets at least twice a year and endeavors to make decisions by consensus,

save that where there is a disagreement with respect to any aspect of the licensed products or services we shall have a deciding vote.

Under the Nerviano Development Plan, we (or, as the case may be, our sub-licensee(s)) are obliged to use commercially reasonable efforts to develop and commercialize a licensed product or service in at least one therapeutic indication that arises out of the Nerviano Development Plan, and Nerviano is obliged to use commercially reasonable efforts to manufacture such product(s) or service(s). Pursuant to the Nerviano Development Plan, we have sole responsibility for costs for further clinical development and Nerviano is obliged to perform phase II studies of licensed products and services, save that the amounts to be invoiced by Nerviano to us for phase II studies shall be commercially reasonable and not be greater than a low-double-digit percentage in excess than amounts estimated to be invoiced by another reputable clinical research organization.

During the term of the Nerviano Development Plan (the Nerviano Exclusivity Period), we and our affiliates may not, directly or indirectly, develop, make, use, sell, offer for sale or import any small molecule compound or other biological or chemical molecule other than Milciclib that directly binds to, with an affinity indicated by an IC50 of 100nM or less, and modulates the following specified pharmacological targets hit by Milciclib: Cdk-2, Cdc-4 and Cdc6.

Upon entry into the Nerviano Agreement, we paid an upfront, non-refundable initial license fee of $3,500,000 to Nerviano. We issued 4,233,616 of ordinary shares in the capital of the Company, fully paid with a nominal value of three pence each (the Consideration Shares) to Nerviano at an issue price of 50.5 pence (equivalent to an aggregate value of £2,137,976.08).

Nerviano granted us an option (the Nerviano Option) to purchase all the Consideration Shares for a de minimis aggregate consideration exercisable on written notice at any time after the earlier of:

(i) an unsuccessful phase II trial for hepatocellular carcinoma or breast cancer with a licensed product or service and the concomitant decision of the Company, our affiliates or sub-licensees to discontinue development of a licensed product or service;

(ii) the fifth anniversary of the Nerviano Agreement, provided that if on such date a phase II trial has commenced by not been completed our ability to exercise the Nerviano Option shall be delayed until the outcome of the phase II trial has become clear; or

(iii) our abandonment of any licensed product or service for bona fide scientific reasons.

The Nerviano Option shall not be exercisable after any of the following events (each, a Release Event), occurs:

(i) a successful completion of a phase II trial for hepatocellular carcinoma or breast cancer with a licensed product or service, where such successful conclusion renders the licensed product or service eligible for entry into a phase III trial with no further clinical study,

(ii) our abandonment of the development of, or failure to exercise commercially reasonable efforts develop any, licensed product or service, save for where we have bona fide scientific reasons, or

(iii) the valid exercise of the Nerviano Option by the Company.

Prior to a Release Event, Nerviano has agreed to not transfer, dispose of, or grant options or other rights over directly or indirectly any interests in the Consideration Shares nor to derive any financial benefit from the Shares, but is entitled to exercise all voting rights arising from the Consideration Shares.

Following a Release Event, Nerviano has agreed to a 12 month lock up (the Nerviano Lock Up), in respect of the Consideration Shares, subject to customary exceptions, including the prior written consent of the Company and our nominated adviser from time to time (which consent may be approved, provided or provided subject to conditions as each may determine in its absolute discretion), acceptance of takeover bids, share buy-backs by the Company, or where required by law.

Following the lapse of the term of the Nerviano Lock Up, Nerviano has agreed to not directly or indirectly, transfer, sell, mortgage, charge or otherwise dispose of more than 10% of the Consideration Shares (i.e. 423,362 ordinary shares) per calendar month, and to utilize the Company's broker from time to time to execute those transactions in respect of the legal and or beneficial ownership or any other interest in the Consideration Shares so as to ensure an orderly market.

We are obligated to pay Nerviano the following additional amounts in respect of the first licensed product or service which achieves the stated development milestones:

(a) $100,000 upon initiation, first patient dosed (FPD), of the first phase III registration trial in thymic carcinoma.

(b) $4,000,000 upon FPD of the first phase III registration trial in hepatocellular carcinoma.

(c) $6,000,000 upon FPD of the first phase III registration trial in breast cancer.

(d) Upon the first new drug application (NDA) equivalent in: thymic carcinoma, $900,000; hepatocellular carcinoma, $9,000,000; breast cancer, $15,000,000.

We are obliged to pay Nerviano a low-single-digit percentage royalty fee of the annual net sales of licensed products or services, subject to certain royalty off-sets on a country-by-country basis and, subject to certain exclusions, a low-double-digit percentage of sub-licensing revenues from the sale of licensed products or services for the life of the licensed patents.

During the Nerviano Exclusivity Period, we have the right to terminate activities and funding to Nerviano after 24 months from the beginning of the Nerviano Exclusivity Period but not prior thereto. If we exercise our termination right, we are obliged to transfer to Nerviano all relevant data, licensed products and services and an exclusive license pertaining to the licensed product or services, and Nerviano shall pay us a low-single-digit percentage royalty on annual net sales of licensed products and services, subject to certain exceptions.

Following the expiry of the Nerviano Exclusivity Period, we may terminate the Nerviano Agreement at any time on 90 days' written notice, and either party may terminate the Nerviano Agreement for material breach by the other party of any material obligation or condition of the Nerviano Agreement by written notice, subject to a 45 day cure period for a payment breach, and a 120 day cure period for any other breach.

Absent early termination, the Nerviano Agreement shall remain in force until the later of, in all countries in which licensed products and services are marketed pursuant to the Nerviano Agreement, (a) the expiration of the last claim in an issued, unexpired patent within the licensed patents, subject to certain exceptions, which covers the sale of such licensed products or services, or (b) five years from the date of first commercial sale of such licensed product or service in such country.

Novimmune CD3 Agreement

In December 2014, we entered into a license and sublicense agreement with Novimmune (the Novimmune CD3 Agreement), pursuant to which we obtained a worldwide, exclusive licenses to certain patents owned or controlled by Novimmune (the Novimmune CD3 License), together with a sublicense to certain patent licenses from Bristol-Myers Squib Company (BMS) (the BMS CD3 Sublicense), and any associated know-how, biologic materials, clinical data or other technology relating to CD3 receptor monoclonal antibodies and their use in order to research, develop and commercialize products and services. The Novimmune CD3 License and BMS CD3 Sublicense both confer the right to us to grant sublicenses, and otherwise to employ third party manufacturers and distributors to produce and sell licensed products and services, respectively.

Pursuant to the Novimmune CD3 Agreement, Novimmune granted the BMS CD3 Sub-License to us. Novimmune effected such grant pursuant to a research and commercialization agreement between Novimmune and BMS dated September 2004 (the BMS R&C Agreement) and the agreement for the exclusive commercial license for the CD3 licensed product (NI-0401) between Novimmune and BMS dated February 2005.

Under the Novimmune CD3 Agreement, we have full control and authority over the research, development and commercialization of licensed products and services, and are required to exercise commercially reasonable efforts to commercialize such licensed products and services at all times.

Upon our entry into the Novimmune CD3 Agreement we paid an upfront fee of $750,000 to Novimmune (to be on paid by Novimmune to BMS pursuant to the terms of the BMS R&C Agreement), and a further upfront fee of $500,000 to Novimmune. We are required to pay Novimmune installments of $250,000 on each of the 14 month, 26 month and 38 month anniversaries of the date of the Novimmune CD3 Agreement. For the term of the Novimmune Agreement, we are obligated to pay to Novimmune a royalty of a low-single-digit percentage on net sales of licensed products and services, together with any amounts owed to BMS incurred pursuant to the BMS CD3 Sub-License.

We may terminate the Novimmune CD3 Agreement at any time on 90 days' written notice, and either party may terminate the Novimmune CD3 Agreement by written notice for a payment breach or any other breach, subject to 45 day and 120 day cure periods, respectively. Absent early termination, the Novimmune CD3 Agreement will continue until the later of, in all countries in which licensed products are marketed pursuant to the Novimmune CD3 Agreement, (a) the expiration of the last claim in an issued, unexpired patent within the licensed patents or a claim that has not been pending more than five years, subject to certain exceptions, which covers the sale of such licensed product or service, or (b) the end of any market exclusivity period granted by the relevant governmental authority in a country that prevents another party from marketing the same licensed product or service.

Novimmune IL-6r Agreement

In December 2016, we entered into a license and sublicense agreement with Novimmune (the Novimmune IL-6r Agreement), pursuant to which we obtained a worldwide, exclusive license to certain patents owned or controlled by Novimmune (the Novimmune IL-6r License), together with a sub-license to certain patent licenses from BMS (the BMS IL-6r Sub-License), and any associated know-how, biologic materials, clinical data or other technology relating to IL-6 receptor (IL-6r) mAbs and their use in order to research, develop, commercialize products and services. The Novimmune IL-6r License and BMS IL-6r Sub-License both confer the right to us to grant sub-licenses, and otherwise to employ third party manufacturers and distributors to produce and sell licensed products and services, respectively.

Pursuant to the Novimmune IL-6r Agreement, Novimmune granted the BMS IL-6r Sub-License. Novimmune effected such grant pursuant to the BMS R&C Agreement and the agreement for the IL-6r exclusive commercial license for the IL-6r antibody licensed product (NI-1201) between Novimmune and BMS dated September 2009 (the IL-6r Commercial License Agreement).

Under the Novimmune IL-6r Agreement, we have full control and authority over the research, development and commercialization of licensed products and services, and are required to exercise commercially reasonable efforts to commercialize such licensed products and services at all times.

Upon our entry into the Novimmune IL-6r Agreement we paid an upfront fee of $100,000 to Novimmune. For the term of the Novimmune IL-6r Agreement, we are obligated to pay to Novimmune a royalty of a low-single-digit percentage on net sales of licensed products and services, or low-double-digit percentage of any sub-license royalty revenue which we receive that arises from sales of licensed products and services, together with any amounts owed to BMS incurred pursuant to the BMS IL-6r Sub-License.

The BMS R&C Agreement and the IL-6r Commercial License Agreement were amended pursuant to an agreement between Novimmune and BMS dated December 2016 (the Novimmune Amendment Agreement). Pursuant to the Novimmune Amendment Agreement, in the event that Novimmune (or, as the case may be, a sublicensee) commercializes a combination product comprising NI-1201 and NI-0401, then such product shall be subject to a single royalty.

We may terminate the Novimmune IL-6r Agreement at any time on 90 days' written notice, and either party may terminate the Novimmune IL-6r Agreement by written notice for a payment breach or any other breach, subject to 45 day and 120 day cure periods, respectively. Absent early termination, the Novimmune IL-6r Agreement will continue until the later of, in all countries in which licensed

products are marketed pursuant to the Novimmune IL-6r Agreement, (a) the expiration of the last claim in an issued, unexpired patent within the licensed patents or a claim that has not been pending more than five years, subject to certain exceptions, which covers the sale of such licensed product or service, or (b) the end of any market exclusivity period granted by the relevant governmental authority in a country that prevents another party from marketing the same licensed product or service.

C. Organizational Structure

The following table sets out details of the Company's significant subsidiaries:

Name	Principal activity	Registered address	Percentage shareholding	Country of incorporation
Tiziana Pharma Limited	Clinical stage biotechnology company	3rd Floor, 11-12 St James's Square, London, SW1Y 4LB	100%	England & Wales
Tiziana Therapeutics Inc.	Clinical stage biotechnology company	420 Lexington Avenue Suite 2525 New York, NY 10170	100%	USA
Longevia Genomics S.r.l.	Biotechnology discovery company	Via Constantinopli 42 09100- Cagliria (CA)	100%	Italy

D. Government Regulation

Overview

Government authorities in most jurisdictions extensively regulate the research, development, clinical testing, manufacture, distribution and marketing of pharmaceutical products such as those that the Company is developing. Obtaining regulatory approvals and ensuring subsequent compliance with applicable laws and regulations requires the expenditure of substantial time and financial and managerial resources. Regulatory requirements in different jurisdictions vary, and the timing and success of efforts to obtain regulatory approvals can be highly uncertain. Development of a successful drug candidate, from identification of a candidate drug compound, through preclinical and clinical testing, to registration, typically takes more than ten years.

Drug development is a highly structured process divided into two major stages, preclinical and clinical. In the preclinical stage, the toxicology and mode of action of an active compound is evaluated. The clinical stage is designed to prove the safety of any new pharmaceutical, determine dosage requirements and, predominantly in the later phases, prove its therapeutic utility. This stage is carried out in three phases, which, as a developer moves through the phases, require increasingly large, complex, expensive and time-consuming clinical studies. During Phase 1, the product candidate is initially given to a small number of healthy human subjects or patients and tested for safety, tolerance, absorption, metabolism, distribution and excretion. During Phase 2, additional trials are conducted in a larger, but still relatively limited, patient population to verify that the product candidate has the desired effect and to identify optimal dosage levels. Furthermore, possible adverse effects and safety risks are identified. The therapeutic utility of the product candidate for specific targeted diseases is also studied in more depth. During Phase 3, trials are undertaken to further evaluate dosage, to provide statistically significant evidence of clinical effectiveness and to further study the safety in an expanded patient population at multiple clinical trial sites. Phase 3 trials may require several hundreds or thousands of patients and are therefore the most expensive and time-consuming to conduct. At any time during one of the phases, a trial may produce a negative result, in which case the developer may choose to end the development project.

Following completion of the Phase 3 trials, the developer submits all the preclinical and clinical trial documentation as well as extensive data characterising the manufacturing process to the regulator to seek regulatory approval to market the formulation as a pharmaceutical product. The regulator reviews all the information related to the safety of the active compound, and whether the pharmacological effect claimed by the developer on the proposed label can be substantiated by the results of the clinical trials. The regulator has the option to decide to approve the application as requested, ask for changes to the claims made by the developer, ask for more information, require that further clinical trials are undertaken, or refuse to approve the formulation for sale.

Even after initial regulatory approval has been obtained, further studies, including Phase 4 post-approval safety studies, may be required to provide additional data on safety and will be required to gain approval for the use of a product as a treatment for clinical indications other than those for which the product was initially tested. There are also continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data. In addition, regulatory authorities require post-marketing reporting to monitor the adverse effects of the product. Results of post-approval programmes may limit or expand the further marketing of the products. Further, if there are any modifications to the product, including changes in indication, manufacturing process or labeling, or a change in the manufacturing facility, an application seeking approval of such changes or, as the case may be, notification, must be submitted to the relevant regulatory authorities before the modified product can be commercialised. Moreover, an approved drug product may be subject to a Risk Evaluation and Mitigation Strategy ("**REMS**"), which could impose a number of post-approval obligations, including (among other things) a communication plan for physicians regarding safe use of the drug, distribution and use restrictions, and/or periodic assessments of the effectiveness of the REMS. Finally, studies may be required as a contingency of regulatory approval (post-approval commitments), and completion of these studies within a regulator mandated time frame may be required.

European Union

The development, marketing and sale of medicinal products in the EU is subject to extensive pre and post marketing regulation by regulatory authorities at both the EU and national levels. The requirements, regulatory approvals and processes governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country, although there is some degree of EU wide harmonization.

Clinical Trials

Clinical trials of medicinal products in the EU must be conducted in accordance with EU and national regulations, focusing in particular on traceability, apply to clinical trials of advanced therapy medicinal products. If the sponsor of the clinical trial is not established within the EU, it must appoint an entity within the EU to act as its legal representative. The sponsor must take out a clinical trial insurance policy and, in most EU countries, the sponsor is liable to provide 'no fault' compensation to any study subject injured in the clinical trial.

Prior to commencing a clinical trial, the sponsor must obtain a clinical trial authorization from the relevant regulatory authority, and a positive opinion from an independent ethics committee. The application for a clinical trial authorization must include, among other things, a copy of the trial protocol and an investigational medicinal product dossier containing information about the manufacture and quality of the medicinal product under investigation. Currently, clinical trial authorization applications must be submitted to the regulatory authority in each EU member state in which the trial will be conducted. Under the new Regulation on Clinical Trials, which is currently expected to take effect in October 2018, there will be a centralized application procedure where one national authority takes the lead in reviewing the application and the other national authorities have only a limited involvement. Any substantial changes to the trial protocol or other information submitted with the clinical trial applications must be notified to or approved by the relevant competent authorities and ethics committees. Medicines used in clinical trials must be manufactured in accordance with cGMP.

Marketing Approval

In the EU medicinal products can only be commercialised after obtaining an MA. There are three procedures for obtaining MAs: the centralised procedure, the decentralised procedure and the mutual recognition procedure/national procedure.

The Community marketing authorisation, which is issued by the European Commission through the centralised procedure, based on the opinion of the Committee for Medicinal Products for Human Use of the EMA, is valid throughout the entire territory of the EU. The centralized procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, and medicinal products containing a new active substance indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, autoimmune and viral diseases. The centralized procedure is optional for products containing a new active substance not yet authorised in the EU, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.

MAs obtained using the decentralized procedure ("**DCP**") are available for products not falling within the mandatory scope of the Centralized Procedure. An identical dossier is submitted to the regulatory authorities of each of the member states in which the MA is sought, one of which is selected by the applicant as the Reference Member State ("**RMS**"). The competent authority of the RMS prepares a draft assessment report, a draft summary of the product characteristics and a draft of the labeling and package leaflet, which are sent to the other the concerned member states ("**CMS**")) for their approval. A CMS can raise an objection, based on the assessment report, the summary of product characteristics, the labelling and the package leaflet on the grounds of potential serious risk to public health. If no such objections are raised the product will be granted a national marketing authorisation in the RMS and all of the selected CMSs. Where a product has already been authorised for marketing in a member state of the EEA, this DCP approval can be recognised in other member states through the mutual recognition procedure.

MAs obtained using the national procedure are issued by a single regulatory authority of one of the member states of the EU and only apply to the territory covered by the relevant regulatory authority. They are available for products not falling within the mandatory scope of the centralised procedure. Once a product has been authorised for marketing in a member state of the EU through the national procedure, any application in another member state must be by the mutual recognition procedure whereby the MA can also be recognised in other member states through the mutual recognition procedure.

Under the procedures described above, before granting the MA, the EMA or the relevant regulatory authority of the member states of the EU makes an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and therapeutic utility.

The holder of a marketing authorisation in any member state of the EU is subject to various obligations under applicable EU regulations, such as pharmacovigilance obligations, requiring it to, among other things, report and maintain detailed records of adverse reactions, and to submit periodic safety update reports to the regulatory authorities. The holder must also ensure that the manufacturing and batch release of its product is in compliance with the applicable requirements. The MA holder is further obligated to ensure that the advertising and promotion of its products complies with applicable laws, which can differ from member state to member state of the EU.

Data Exclusivity

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

There is a special regime for biosimilars, or biological medicinal products that are similar to a reference medicinal product but that do not meet the definition of a generic medicinal product, for example, because of differences in raw materials or manufacturing processes. For such products, the results of appropriate preclinical or clinical trials must be provided, and guidelines from the EMA detail the type of quantity of supplementary data to be provided for different types of biological product. There are no such guidelines for complex biological products, such as gene or cell therapy medicinal products, and so it is unlikely that biosimilars of those products will currently be approved in the EU. However, guidance from the EMA states that they will be considered in the future in light of the scientific knowledge and regulatory experience gained at the time.

Orphan Medicinal Products

The EMA's Committee for Orphan Medicinal Products, or COMP, may recommend orphan medicinal product designation to promote the development of products that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions affecting not more than five in 10,000 persons in the EU. Additionally, designation is granted for products intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the product in the EU would be sufficient to justify the necessary investment in developing the medicinal product. The COMP may only recommend orphan medicinal product designation when the product in question offers a significant clinical benefit over existing approved products for the relevant indication. Following a positive opinion by the COMP, the European Commission adopts a decision granting orphan status. The COMP will reassess orphan status in parallel with EMA review of a marketing authorization application and orphan status may be withdrawn at that stage if it no longer fulfills the orphan criteria (for instance because in the meantime a new product was approved for the indication and no convincing data are available to demonstrate a significant benefit over that product). Orphan medicinal product designation entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity is granted following marketing authorization. During this period, the competent authorities may not accept or approve any similar medicinal product, unless it offers a significant clinical benefit. This period may be redacted to six years if the orphan medicinal product designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity.

United States

Standard Procedure

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act and its implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending NDAs, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties.

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

- completion of preclinical laboratory studies, animal studies and formulation studies in compliance with the FDA's good laboratory practice regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- approval by the IRB at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with applicable IND and other clinical trial-related regulations, sometimes referred to as GCPs

to establish the safety and clinical utility of the proposed product candidate for its proposed indication;

- submission to the FDA of a BLA or NDA;
- satisfactory completion of an FDA pre-approval inspection of the production facility or facilities where the product is produced to assess compliance with the FDA's cGMP requirements to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality, purity and potency;
- potential FDA audit of the preclinical and/or clinical trial sites that generated the data in support of the NDA; and
- FDA review and approval of the BLA or NDA prior to any commercial marketing or sale of the product in the United States.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

Clinical Trials

Clinical trials involve the administration of the IND to human patients under the supervision of qualified investigators in accordance with GCP requirements, which include the requirement that all research patients provide their informed consent in writing for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, an IRB at each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health for public dissemination on their website. Regulatory authorities, IRBs or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research patients are being exposed to an unacceptable health risk.

Marketing Approval

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

In addition, under the Pediatric Research Equity Act of 2003, as amended and reauthorised**,** certain NDAs or supplements to an NDA must contain data that are adequate to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations, and

to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements.

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

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

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

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter, or, in some cases, a complete response letter. A complete response letter generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA and may require additional clinical or preclinical testing in order for the FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorises commercial marketing of the drug with specific prescribing information for specific indications.

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

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may designate a biologic product as an "orphan drug" if it is intended to treat a rare disease or condition (generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a biologic product available in the United States for treatment of the disease or condition will be recovered from sales of the product).

If a product with orphan status receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, meaning that the FDA may not approve any other applications to market the same drug or biologic product for the same

indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity or if the party holding the exclusivity fails to assure the availability of sufficient quantities of the drug to meet the needs of patients with the disease or condition for which the drug was designated. Competitors, however, may receive approval of different products for the same indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity.

Post-Approval Requirements for the EU and United States

The FDA and the relevant regulatory authorities in the EU strictly regulate marketing, labeling, advertising and promotion of products that are placed on the market in their respective territories. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The regulatory authorities actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the relevant regulatory authorities, and are subject to periodic unannounced inspections by them to confirm compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior approval of the relevant regulatory authorities before being implemented. Regulations laid down by the FDA and the regulatory authorities in the EU also require investigation and correction of any deviations from the requirements of cGMP and impose reporting and documentation requirements upon the MA holder and any third party manufacturers that the MA holder may decide to use.

Other Healthcare Laws in the EU and United States

The Company will also be subject to healthcare regulation and enforcement by the U.S. federal government and the states and governments in the EU and any other countries in which the Company conducts its business, including its research, and the marketing and distribution of its product candidates and products once they have obtained an MA. Failure to comply with these laws, where applicable, can result in the imposition of significant civil penalties, criminal penalties, exclusion from participating in health care programmes, additional reporting requirements and oversight if the Company becomes subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws and other sanctions. The healthcare laws and regulations that may affect the Company's ability to operate in the United States include: the federal fraud and abuse laws, including the federal anti-kickback and false claims laws; federal data privacy and security laws; and federal transparency laws related to payments and/or other transfers of value made to physicians and other healthcare professionals and teaching hospitals. Many US states have similar laws and regulations that may differ from each other and federal law in significant ways. Moreover, several US states have enacted legislation requiring pharmaceutical manufacturers to, among other things, establish marketing compliance programmes, file periodic reports with the state, and make periodic public disclosures on sales and marketing activities, and prohibiting certain other sales and marketing practices. Rules and legislation covering more or less the same subject matter as those in the United States apply to in countries in the EU and to other countries. These can differ between jurisdictions and can sometimes result in lower or higher exposure in those countries than in the United States. Where a product is sold in a number of countries compliance efforts can therefore be complicated.

Coverage and Reimbursement in the EU and United States

Sales of products developed from the Company's product candidates, if approved, will depend, in part, on the extent to which such products will be covered by third party payors, such as government health care authorities, government health care programmes, commercial insurance and managed healthcare organisations. These third party payors are increasingly limiting coverage or reducing reimbursements for medical products and services. In the United States, no uniform policy of coverage and reimbursement for products exists among third party payors. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. In addition, the U.S. government, state legislatures and foreign governments have continued implementing cost-containment programmes, including price controls, restrictions on reimbursement and requirements for substitution of generic products.

Governments influence the price of medicinal products in the EU through their pricing and reimbursement rules and control of national healthcare systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost-effectiveness of a particular product candidate to currently available therapies. Other EU member states allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on healthcare costs in general in the EU governments influence the price of medicinal products through their pricing and reimbursement.

The adoption of price controls and cost-containment measures, and the adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit the Company's net revenue and results. Decreases in third party reimbursement for the Company's product candidates or a decision by a third party payor to not cover the Company's product candidates could reduce physician usage of the Company's product candidates, once approved, and have a material adverse effect on the Company's sales, results of operations and financial condition.

E. Property, Plant and Equipment

The below table contains information regarding existing or planned material tangible fixed assets owned or leased by Tiziana and its subsidiaries. We believe that suitable additional or substitute space will be available as needed to accommodate any future expansion of our operations.

Location	Tenure	Principal use	Size
55 Park Lane, Suite 14a, London W1K 1NA, United Kingdom	Annual Lease	Principal Office	652 square feet
420 Lexington Avenue Suite 2525 New York, United States	Five-year Lease	Principal Office	3,011 square feet
3805 Old Easton Road, Doylestown, PA, United States	Annual Lease	Research & Development Centre	451 square feet

ITEM 4A: UNRESOLVED STAFF COMMENTS

Not applicable.

ITEM 5: OPERATING AND FINANCIAL REVIEW AND PROSPECTS

The following discussion of our financial condition and results of operations should be read in conjunction with the consolidated historical financial statements as at December 31, 2015 and 2016 and for the two years ended December 31, 2016 (the "Consolidated Annual Financial Statements") and the unaudited condensed consolidated interim historical financial statements as at June 30, 2017 and for the three months ended June 30, 2017 and 2016 (the "Q2 Interim Results") and related notes (together the "Historical Financial Information"). The Historical Financial Information has been included in "Item 18. Financial Statements." The following discussion should also be read in conjunction with the other information relating to our business contained in this registration statement, including "Item 3.A. Selected Financial Data" and "Item 3.D. Risk Factors."

The Historical Financial Information has been prepared in accordance with IFRS.

The following discussion includes forward-looking statements that reflect our plans, estimates and beliefs and involves risks and uncertainties. Our actual results could differ materially from those discussed in these statements. Factors that could cause or contribute to these differences include, but are not limited to, those discussed below and elsewhere in this registration statement, particularly in "Item 3.D. Risk Factors."

References below to "2016" and "2015" are to the financial years ended December 31, 2016 and December 31, 2015, respectively. References to "Q2 2016" and "Q2 2015" are to the six-month interim financial periods ended June 30, 2017 and June 30, 2016, respectively.

Overview

Introduction to Tiziana

We are a biotechnology company that is focused on the discovery and development of novel molecules and related diagnostics to treat high unmet medical needs in oncology and immunology. We have expanded our pipeline of assets to include lead clinical stage development therapeutic candidates in both oncology and immune-inflammation, including Milciclib, which is an orally bioavailable, small molecule pan-inhibitor of cyclin-dependent kinases (CDK: 1, 2, 4, 5, and 7) as well as Src family kinases designed for hepatocellular cancer (HCC), Foralumab, which is the only fully human monoclonal anti-CD3 mAb in clinical development designed for non-alcoholic steatohepatitis (NASH) and primary biliary cholangitis (PBC)/primary sclerosing cholangitis (PSC). We also have a drug discovery pipeline of small molecule new chemical entities (NCEs) and biologics. We employ a lean and virtual R&D model using highly experienced teams of experts for each business function to maximize value accretion by focusing resources on the drug discovery and development processes. Our mission is to design and deliver next generation therapeutics and diagnostics for oncology and immune diseases of high unmet medical need by combining deep understanding of disease biology with clinical development expertise.

Foralumab, in-licensed from Novimmune SA, is the only fully human monoclonal anti-CD3 mAb in clinical development in contrast to the previous non-human or humanized anti-CD3 mAbs. We believe that oral administration of Foralumab has the potential to provide therapeutic utility while minimizing the toxicity and related side effects of existing treatments for inflammatory diseases such as NASH, PBS, PSC and other autoimmune and inflammatory diseases. Novimmune completed a Phase 1 clinical study of Foralumab administered via intravenous injection in patients with Crohn's disease in 33 patients, a Phase IIa clinical trial in kidney transplant patients with renal allografts in 11 patients and another Phase IIa trial in 24 Crohn's disease patients. A separate clinical study of oral administration of murine anti-CD3 (OKT3; murine mAb) in 27 hepatitis C virus infected patients and in 27 NASH patients was conducted. OKT3 mAb was observed to be well-tolerated orally and produced immunologic effects consistent with potential clinical benefit. We expect to initiate Phase II trials for Foralumab in the first half of 2018, in patients with NASH and PBC/PSC.

Milciclib (TZLS-201), acquired from Nerviano Medical Sciences S.r.l., is an orally bioavailable, small molecule pan-inhibitor of cyclin-dependent kinases (CDK: 1, 2, 4, 5, and 7) as well as Src family kinases. A unique feature of Milciclib is its ability to reduce microRNAs miR-221 and miR-222. These microRNAs are consistently upregulated in HCC patients and may contribute towards resistance to treatment with sorafenib, a multikinase inhibitor often prescribed to HCC patients. Thus, we believe Milciclib has potential to be developed as a drug candidate for treatment of HCC. Seven Phase I and Phase II clinical trials in approximately 285 patients, both as a monotherapy or in combination with gemcitabine, were completed or are ongoing. Milciclib was observed to be well-tolerated and showed initial signals of anti-tumor activity.

Cumulative Patient Exposure in Completed and Ongoing Milciclib Clinical Studies

Clinical Study	Drug	Indication	Number of Patients Treated
CDKO-125a-001 Phase I	Milciclib	Solid tumors	37
CDKO-125a-002 Phase I/II	Milciclib	Malignant glioma (Phase 1 Glioblastoma (Phase II)	62
CDKO-125a-003 Phase I	Milciclib	Solid tumors	30
CDKO-125a-004 Phase I	Milciclib + gemcitabine	Solid tumors	16
CDKO-125a-005/-006[1]/-007[1]Phase II	Milciclib	Malignant Pleural Mesothelioma (-005) Thymic carcinoma and malignant thymoma (-006[1] and -007[1])	Approximately 140[1]
		Total Patients Exposed	Approximately 285 [1]

Source: Development Safety Update Report No. 6, March 2, 2017, Tiziana Life Sciences PLC; Investigator Brochure, Version 11, 2015.

[1]Patients still continuing on medication

We initiated a Phase IIa trial for Milciclib as a monotherapy in enrolling approximately 10 patients with HCC in the first half of 2017 in Italy and Greece and expect to initiate a Phase IIb trial for Milciclib in combination with sorafenib in patients with HCC in H1 2018.

Since our inception in March 2014, we have devoted substantially all our resources to conducting preclinical studies and clinical trials, organizing and staffing our company, business planning, raising capital and establishing our intellectual property portfolio. We do not have any products approved for sale and have not generated any revenue from product sales. We have funded our operations to date primarily with proceeds from the sale of ordinary shares. Through December 31, 2016, we had received net cash proceeds of $18.3 million from sales of our ordinary shares.

Since our inception, we have incurred operating losses. Our net loss was $13.2 million and $5.5 million for the years ended December 31, 2015 and 2016, respectively. As of December 31, 2016, we had an accumulated profit of $12.3 million (following a capital reduction in September 2016). As of December 31, 2016, we had cash and cash equivalents of $5.8 million, and in August 2017, we secured the conversion of $18.2 million of convertible loan notes and accrued interest with our ordinary shares.

We expect to continue to incur significant expenses for the foreseeable future as we advance our product candidates through preclinical and clinical development and seek regulatory approval and pursue commercialization of any approved product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution.

Trend information

Recent developments

- In July 2017, we announced publication of a research article in a prestigious journal, Clinical Immunology, entitled: “Oral treatment with Foralumab, a fully human anti-CD3 monoclonal antibody, prevents skin xenograft rejection in humanized mice”. This is the first-ever published report demonstrating the potential of oral therapy with Foralumab for inflammatory diseases such as NASH. Foralumab is the only fully human engineered anti-CD3 mAb in clinical development to date.
- In July 2017, we announced enrollment of the first patient in a phase IIa clinical trial (CDK-125a-010) with Milciclib in patients with refractory hepatocellular carcinoma (“HCC”). Top line data from this trial, being conducted in Italy, Greece and Turkey, was announced on December 8, 2017 as a result of the IDMC completing an interim analysis of the safety and pharmacokinetic data from the first six patients who had received and completed an initial cycle of treatment with Milciclib and found that Milciclib was safe and well tolerated with no drug-related serious adverse effects in patients with unresectable or metastatic HCC. The primary objective of this multi-center, multi-country phase IIa clinical study is to evaluate the safety of Milciclib in HCC patients who fail to respond to or are intolerant to the existing standard of care treatment.
- On August 16, 2017, we announced that further to the proposals announced on July 12, 2017, the holders of the Company’s Convertible Loan Note (“CLN Holders”) and the Company’s Warrant Holders (“Warrant Holders”) have passed the resolutions that were put to them to convert all of the loan notes and vary the terms of the warrants substantially prior to the intended deadline for consent. Accordingly the full £12,969,219 (at par value) of the CLNs have now been converted into ordinary shares (including accrued interest), resulting in the issue of 27,645,013 new ordinary shares in the Company. Therefore the fully diluted issued share capital of the Company is 138,216,920 ordinary shares (assuming all options and warrants, vested and unvested, exercised and exercisable, were converted).
- On November 23, 2017, we announced that Milciclib met its primary endpoints in two phase II clinical trials in patients with thymic carcinoma and thymoma. The treatment requires with Milciclib (150mg/day; 7 days on/7 days off) was safe and well tolerated in these patients with continuing expose of up to 5 years. In both clinical trials it was demonstrated that treatment with Milciclib was efficacious and met progression free survival as the primary endpoint and overall survival as a secondary endpoint.
- Between November 20, 2017 and December 15, 2017 we raised an additional $823,812 (£625,000) through the wire of 416,666 new ordinary shares at a price of $1.98 (£1.50) per share.

Significant factors affecting our results of operations

Our results of operations have been affected during the periods under review, and will continue to be affected in the future, by the following factors:

Research and development

In January 2017, Tiziana finalised the acquisition of an exclusive world-wide license for NI-1201 (TZLS-501), a fully human anti-interleukin-6 receptor (IL-6R) monoclonal antibody (mAb), from Novimmune SA. In exchange for the exclusive license from Novimmune the Company agreed to an upfront cash payment, milestone payments, and a royalty on future sales.

Monoclonal antibodies against IL-6R have been explored as potential drugs to treat inflammation in the past. NI-1201's unique mechanism, however, has the potential to considerably increase anti-inflammatory activity as well as complementing the Company's program on Foralumab (TZLS-401), a fully human oral anti-CD3 mAb.

The acquisition of NI-1201 strengthens the Company's business strategy of developing novel fully human mAbs to treat life-threatening inflammatory diseases and rheumatoid arthritis. In addition, it represents an opportunity to expand the current research with Foralumab, the oral anti-CD3 mAb, to treat autoimmune and inflammatory diseases.

In April, 2017, the Company announced the approval in Israel of a phase II clinical trial protocol for testing Milciclib, a novel inhibitor of cell cycle dependent kinases (CDKs), in patients with refractory hepatocellular carcinoma ("HCC"). A similar clinical trial protocol has been submitted for approval in Italy, Turkey and Greece. The primary objective of these multi-centered, multi-country phase IIa clinical studies is to evaluate the safety of Milciclib in HCC patients who fail to respond or are intolerant to the existing standard of care treatment. In July 2017, it followed announcement of the enrolment of the first patient. Top line data from this trial was announced on December 8, 2017 as a result of the IDMC completing an interim analysis of the safety and pharmacokinetic data from the first 6 patients who had received and completed an initial cycle of treatment with Milciclib and found that Milciclib was safe and well tolerated with no drug-related series adverse effects in patients with unresectable or metastatic HCC.

In June 2017, the Company resolved to discontinue funding of its pre-clinical programme Bcl-3 inhibitors as potential cancer therapeutics, which includes the potential candidate CB1 ("TZLS-101"), to refocus efforts on other promising candidates in the Company's pipeline, which Tiziana believes have greater near-term potential to deliver value for shareholders. The Company retains all of the intellectual property relating to the Bcl-3 programme and will work with scientists at Cardiff University in examining the potential to develop the programme further with grant funding.

In July 2017, the Company announced publication of a research article in a prestigious journal, Clinical Immunology, entitled: "Oral treatment with Foralumab, a fully human anti-CD3 monoclonal antibody, prevents skin xenograft rejection in humanized mice". This is the first-ever published report demonstrating the potential of oral therapy with Foralumab (TZLS-401) for inflammatory diseases such as non-alcoholic steatohepatitis (NASH). Tiziana's Foralumab is the only fully human engineered anti-CD3 monoclonal antibody (mAb) in clinical development to date.

- On November 23, 2017 we announced that Milciclib met its primary endpoints in two phase II clinical trials in patients with thymic carcinoma and thymoma. The treatment regimen with Milciclib (150 mg/day; 7 days On/7 days Off) was safe and well tolerated in these patients with continuing expose of up to 5 years. In both clinical trials it was demonstrated that treatment with Milciclib was efficacious and met progression free survival as the primary endpoint and overall survival as a secondary endpoint.

The Company is currently preparing clinical trials to demonstrate clinical utility of Foralumab in patients, and the first study will determine the safety and effectiveness of Foralumab in patients with NASH and type 2 diabetes. Foralumab could potentially be an ideal option for patients with NASH in all stages of disease progression, as it targets a pathogenic mechanism which is common to all disease stages.

Legal proceedings

From time to time, we may be a party to litigation or subject to claims incident to the ordinary course of business. Although the results of litigation and claims cannot be predicted with certainty, we currently believe that the final outcome of these ordinary course matters will not have a material adverse effect on our business. Regardless of the outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors. We are not currently a party to any material legal proceedings.

Foreign currency translations

Items included in the financial statements are measured using the currency of the primary economic environment in which the entity operates (the functional currency). The consolidated financial statements are presented in U.S. dollars, which is our presentation currency.

Foreign currency transactions are translated into the functional currency using exchange rates prevailing at the dates of the transactions. Foreign exchange gains and losses resulting from the settlement of foreign currency transactions and from the translation at year-end exchange rates of monetary assets and liabilities denominated in foreign currencies are recognized in the income statement.

The financial statements of overseas subsidiary undertakings are translated into US dollars on the following basis:

- Assets and liabilities at the rate of exchange ruling at the year-end date.
- Profit and loss account items at the average rate of exchange for the year.

Exchange differences arising from the translation of the net investment in foreign entities, borrowings and other currency instruments designated as hedges of such investments, are taken to equity (and recognized in the statement of comprehensive income) on consolidation.

Components of Our Results of Operations

Revenues

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from the sale of products in the near future. If our development efforts for our product candidates are successful and result in regulatory approval, we may generate revenue in the future from product sales.

Operating Expenses

Research and Development Expenses

Research and development expenses consist primarily of costs incurred in connection with the research and development of our product candidates, which are partially offset by research and development tax credits provided by HM Revenue & Customs, or HMRC. We expense research and development costs as incurred. These expenses consist of:

- expenses incurred under agreements with contract research organizations, or CROs, contract manufacturing organizations, or 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 materials for preclinical studies and clinical trial materials;
- 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 and utilities; and
- fees for maintaining our third-party licensing agreements.

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.

Our direct research and development expenses are tracked on a program-by-program basis for our product candidates and consist primarily of external costs, such as fees paid to outside consultants, CROs and CMOs in connection with our preclinical development, manufacturing and clinical development activities. Our direct research and development expenses by program also include fees incurred under our license agreements. We do not allocate employee costs or facility expenses, including depreciation or other indirect costs, to specific programs because these costs are deployed across multiple programs and, as such, are not separately classified. We use internal resources primarily to oversee the research and discovery as well as for managing our preclinical

development, process development, manufacturing and clinical development activities. These employees work across multiple programs and, therefore, we do not track their costs by program.

The table below summarizes our research and development expenses incurred by program:

	Six months ended June 30	Year ended December 31,	
	2017	2016	2015
Direct research and development expense by program:	(in thousands)		
Foralumab	$ 431	$ 714	$ 530
Milciblib	1,206	2,087	6,630
BCL-3	357	328	293
TZLS-0501	-	-	-
Stemprinter	751	371	951
Total direct research and development expense	2,745	3,500	8,404
Personnel related (including share-based compensation)			
Research and development tax credit			
Indirect research and development expense	139	507	665
Total research and development expense	2,884	4,007	9,609

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials and related product manufacturing expenses. As a result, we expect that our research and development expenses will increase substantially over the next several years as we increase personnel costs and prepare for regulatory filings related to our product candidates. We also expect to incur additional expenses related to milestone, royalty payments and maintenance fees payable to third parties with whom we have entered into license agreements to acquire the rights related to our product candidates.

The successful development and commercialization of our product candidates 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 preclinical and clinical development of any of our product candidates 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 development and commercialization, including the uncertainty of:

- the scope, progress, outcome and costs of our preclinical development activities, clinical trials and other research and development activities;
- establishing an appropriate safety profile with IND- and CTA-enabling studies;
- 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-grade drug formulations that can be used in our clinical trials and 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

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 and administrative functions. General and administrative expenses also include professional fees for legal, consulting, accounting and audit services.

We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support our continued research activities and development of our product candidates. We also anticipate that we will incur increased accounting, audit, legal, regulatory, compliance, director and officer insurance costs, as well as investor and public relations expenses associated with being a public company.

Other Income (Expense)

Other expense consists of interest on a convertible loan note.

A. Results of Operations

The results of operations that follow reflect the historic periods under review and should not be taken as indicative of future performance. The following table sets out information relating to the consolidated interim and annual income statements during the periods under review.

The following table summarizes our results of operations for the years ended December 31, 2015 and 2016 , and the six months ended June 30, 2017 and 2016:

$ 000's	Six months ended June 30,			Year ended December 31,		
	2017	2016	Change	2016	2015	Change
Operating Expenses:						
Research and development	(2,884)	(985)	(1,899)	(4,007)	(9,609)	5,602
General and administrative	(1,804)	(1,880)	76	(5,872)	(3,557)	(2,315)
Total Operating expenses	(4,689)	(2,866)	(1,823)	(9,879)	(13,166)	3,287
Other Income/ (Expense)	(5)	11	(16)	(12)	(28)	15
Income Tax Provision	-	-	-	121	-	121
Net Loss	(4,693)	(2,855)	(1,839)	(9,770)	(13,193)	3,423
Other comprehensive loss:						
Foreign currency translation adjustment	(116)	-	(116)	650	3,063	(2,413)
Total Comprehensive Loss	(4,809)	(2,855)	(1,954)	(9,120)	(10,130)	1,010

Research and Development Expenses

Research and development activities were $9.6 million for the year ended December 31, 2015 compared to $4 million for the year ended December 31, 2016. The decrease of $5.6 million was primarily due to the one off spend on license fees in 2015.

Research and development activities were $2.9 million for the six months ended June 30, 2017 compared to $1 million for the six months ended June 30, 2016. The increase of $1.9 million was primarily due to increased spend on the clinical trials for Milciclib.

General and Administrative Expenses

General and administrative expenses were $3.6 and $5.8 million for the years ended December 31, 2015 and 2016. Within general and administrative expenses, there were increases in consultancy fees of $0.4m, legal and professional fees of $0.4 million, travel of $0.4 million, employee related costs of $0.2 million and audit and accountancy of $0.1 million.

General and administrative expenses were $1.9m and $1.8m for the six months ended June 30, 2017 and 2016.

Taxation.

The tax expense for a period represents the total of current taxation and deferred taxation. The charges in respect of current taxation are based on the estimated taxable profit for the relevant year. Taxable profit for the year is based on the profit as shown in the income statement, as adjusted for items of income or expenditure which are not deductible or chargeable for tax purposes. The current tax liability for the year is calculated using tax rates which have either been enacted or substantively enacted at the relevant balance sheet date.

B. Liquidity and Capital Resources

Since our inception, we have not generated any revenue and have incurred operating losses and negative cash flows from our operations. We have funded our operations to date primarily with proceeds from the sale of ordinary shares and convertible loan notes. Through December 31, 2016, we had received net cash proceeds of $18.6 million from sales of our ordinary shares and convertible loan notes. As of December 31, 2016, we had cash and cash equivalents of $5.8 million. In August 2017, we converted all of the outstanding convertible loan notes into 28,455,214 of our ordinary shares. Between November 20, 2017 and December 15, 2017 we raised a further $823,812 (£625,000) a total sale of 416,666 new ordinary shares at a price of $1.98 (£1.50) per share. Between January 15, 2018 and January 19, 2018 we raised a further $335,500 (£250,000), a total sale of 166,667 new ordinary shares at a price of $1.98 (£1.50) per share and issued a further 810,201 new ordinary shares to our former noteholders (to capitalize balances included in the figure of $16,733,146 (£12,696,219) capitalized on August 16, 2017. Cash received from these financings are invested in a money market fund with a view of liquidity and capital preservation.

Cash Flows

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

$000	***Six months ended June 30,***		***Year ended December 31,***	
	2017	**2016**	**2016**	**2015**
Net cash used in operating activities	(3,960)	(2,129)	(6,926)	(8,421)
Net cash used in investing activities	—	—	(342)	—
Net cash provided by financing activities	694	1,334	1,575	18,565
Effect of exchange rate changes on cash and cash equivalents	73	(545)	(1,633)	(547)
Net increase / (decrease) in cash and cash equivalents	(3,193)	(1,340)	(7,326)	9,597

Net Cash Used in Operating Activities

Our use of cash in each of the years ended December 31, 2015 and 2016 resulted primarily from our net losses, adjusted for non-cash charges and changes in components of working capital. Net cash used in operating activities of $3.2 million during the year ended December 31, 2016 decreased by $4.5 million compared to the year ended December 31, 2015. The decrease in net cash used in operating activities was primarily due to an decrease of $6.9 million in operating expenses, offset by a decrease of $3.2million in the share based payments costs as compared to the year ended December 31, 2015.

Our use of cash in the six months ended June 30, 2017 and 2016 resulted primarily from our net losses, adjusted for non-cash charges and changes in components of working capital. Net cash used in operating activities of $4.0 million during the six months ended June 30, 2017 increased by $1.8 million compared to the six months ended June 30, 2016. The increase in net cash used in operating activities was primarily due to an increase of $1.8 million in operating expenses.

Net Cash Used in Investing Activities

During the year ended December 31, 2016, we used $0.1 million of cash in investing activities for the purchases of property and equipment and the acquisition of SharDNA Srl.

Net Cash Provided by Financing Activities

During the years ended December 31, 2015 and 2016, net cash provided by financing activities was $18.6 million and $7.2 million, respectively, consisting of net cash proceeds from our sale and issuance of ordinary shares and convertible loan notes.

During the six months ended June 30, 2017 and 2016, net cash provided by financing activities was $0.7 million and $1.3 million, respectively, consisting of net cash proceeds from our sale and issuance of ordinary shares and convertible loan notes.

Funding Requirements

We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we advance the preclinical activities, manufacturing and clinical trials of our product candidates. In addition, following this direct listing, we expect to incur additional costs associated with operating as a public company. Our expenses will also increase as we:

- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- establish a sales, marketing and distribution infrastructure in anticipation of commercializing any product candidates for which we may obtain marketing approval and intend to commercialize on our own or jointly;
- hire additional clinical, medical and development personnel;
- expand our infrastructure and facilities to accommodate our growing employee base; and
- maintain, expand and protect our intellectual property portfolio.

We believe that our existing cash, will enable us to fund our operating expenses and capital expenditure requirements for the foreseeable future. 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. If we receive regulatory approval for our other product candidates, 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. Our future funding requirements will depend on and could increase significantly as a result of many factors, including:

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

- the costs, timing, receipt and terms of any marketing approvals from applicable regulatory authorities;
- the costs of future activities, including product sales, marketing, manufacturing and distribution, for any of our product candidates for which we receive marketing approval;
- the revenue, if any, received from commercial sale of our products, should any of our product candidates receive marketing approval;
- the costs and timing of hiring new employees to support our continued growth;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims; and
- the extent to which we acquire technologies.

Until such time, if ever, that we can generate product revenue sufficient to achieve profitability, we expect to finance our cash needs through equity offerings. To the extent that we raise additional capital through the sale of equity, your ownership interest will be diluted. 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 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.

Borrowings

In August 2017, we completed a conversion of all of our outstanding convertible loan notes through the issuance of 28,455,214 ordinary shares. As a result of the conversion the company is free of debt.

See “Item 3.B. Capitalization and Indebtedness” for details relating to our capitalization and indebtedness as at the dates indicated therein.

C. Research and Development Expenses, Patents and Licenses, etc.

See “Item 4.B.—Intellectual Property,” “Item 4.B.—Research and Development,” and “Item 5. Operating and Financial Review and Prospects.”

D. Trend Information

See “Item 5. Operating and Financial Review and Prospects—Trend Information.”

E. 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.

F. Tabular Disclosure of Contractual Obligations

The following table summarizes our contractual commitments and obligations as of June 30, 2017.

	PAYMENTS DUE BY PERIOD				
($ in thousands)	**TOTAL**	**LESS THAN 1 YEAR**	**BETWEEN 1 AND 3 YEARS**	**BETWEEN 3 AND 5 YEARS**	**MORE THAN 5 YEARS**
Borrowings	-	-	-	-	-
Operating lease obligations	911	231	680	-	-
Total	911	231	680	-	-

Please refer to “Item 4.B. Business Overview” and “Item 10.C. Material Contracts” for further details.

G. Safe Harbor

See “Cautionary Note Regarding Forward-Looking Statements” on page 1.

H. Critical Accounting Policies and Significant Judgments and Estimates

Our consolidated financial statements are prepared in accordance with IFRS. The preparation of our consolidated financial statements and related disclosures requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, costs and expenses, and the disclosure of contingent assets and liabilities in our consolidated financial statements. We base our estimates on historical experience, known trends and events and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in our consolidated financial statements, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

Accrued Research and Development Expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual costs. We make estimates of our accrued expenses as of each balance sheet date in the consolidated financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of these estimates with the service providers and make adjustments if necessary. Examples of estimated accrued research and development expenses include fees paid to:

- vendors in connection with preclinical development activities;
- CROs and investigative sites in connection with preclinical studies and clinical trials; and
- CMOs in connection with drug substance and drug product formulation of preclinical study and clinical trial materials.

We base our expenses related to preclinical studies and clinical trials on our estimates of the services received and efforts expended pursuant to quotes and contracts with multiple research institutions and CROs that conduct and manage preclinical studies and clinical trials on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the estimate, we adjust the accrual or the amount of prepaid expenses accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting amounts that are too high or too low in any particular period. To date, there have not been any material adjustments to our prior estimates of accrued research and development expenses.

Valuation of Share-Based Compensation and Tranche Obligations

Share-Based Compensation

We recognize compensation expense for equity awards based on the grant date fair value of the award. For equity awards that vest based on a service condition, the share-based compensation expense is recognized on a straight-line basis over the requisite service period. For equity awards that contain both performance and service conditions, we recognize share-based compensation expense ratably over the requisite service period when the achievement of a performance-based milestone is probable based on the relative satisfaction of the performance condition as of the reporting date. We use the fair value of our ordinary shares to determine the fair value of restricted share awards.

To date, the share-based awards granted to our employees and directors have been in the form of time and/or performance vesting share options and have been reported in our consolidated statements of operations as follows:

$000	**Six months ended June 30,**	**Ended December 31,**	
	2017	**2016**	**2015**
Employee costs	10	927	1,075

The calculation of the fair value of equity-settled share based awards and the resulting charge to the statement of comprehensive income requires assumptions to be made regarding future events and market conditions. These assumptions include the future volatility of the Company's share price. These assumptions are then applied to a recognised valuation model in order to calculate the fair value of the awards.

Where employees, directors or advisers are rewarded using share based payments, the fair value of the employees', directors' or advisers' services are determined by reference to the fair value of the share options / warrants awarded. Their value is appraised at the date of grant and excludes the impact of any nonmarket vesting conditions (for example, profitability and sales growth targets). Warrants issued in association with the issue of Convertible Loan Notes are also considered as share based payments and a share based payment charge is calculated for these too.

In accordance with IFRS 2, a charge is made to the Statement of Comprehensive Income for all share-based payments including share options based upon the fair value of the instrument used. A corresponding credit is made to a Share Based Payment Reserve, in the case of options / warrants awarded to employees, directors or advisers, and Shares To Be Issued

Reserve in the case of warrants issued in association with the issue of Convertible Loan Notes, net of deferred tax where applicable.

If vesting periods or other vesting conditions apply, the expense is allocated over the vesting period, based on the best available estimate of the number of share options / warrants expected to vest. Non-market vesting conditions are included in assumptions about the number of options / warrants that are expected to become exercisable.

Estimates are subsequently revised, if there is any indication that the number of share options / warrants expected to vest differs from previous estimates. No adjustment is made to the expense or share issue cost recognised in prior periods if fewer share options ultimately are exercised than originally estimated.

Upon exercise of share options / warrants, the proceeds received are allocated to share capital with any excess being recorded as share premium.

Where share options are cancelled, this is treated as an acceleration of the vesting period of the options. The amount that otherwise would have been recognised for services received over the vesting period is recognised immediately within the Statement of Comprehensive Income.

Share-based compensation expense totaled $1.1 million and $0.9 million for the years ended December 31, 2015 and 2016, respectively. As of December 31, 2016. We expect the impact of our share-based compensation expense for share option awards granted to employees, directors and other service providers to grow in future periods due to the potential increases in the value of our ordinary shares and headcount.

In conducting the valuations, we considered all objective and subjective factors that we believed to be relevant for each valuation conducted, including our best estimate of our business condition, prospects and operating performance at each valuation date. Within the valuations performed, a range of factors, assumptions and methodologies were used. The significant factors included:

- the lack of an active public market for our ordinary shares;
- our results of operations, financial position and the status of our research and preclinical development efforts;
- the material risks related to our business;
- our business strategy;
- the market performance of publicly traded companies in the life sciences and biotechnology sectors;
- the prices paid in recent transactions involving our ordinary shares;
- the likelihood of achieving a liquidity event for the holders of our ordinary shares, such as an initial public offering, or IPO, given prevailing market conditions; and
- any recent contemporaneous valuations of our ordinary shares prepared in accordance with methodologies outlined in the Practice Aid.

The dates of our valuations have not always coincided with the dates of our share grants. In determining the value of our ordinary shares set forth in the table above, our board of directors considered, among other things, the most recent sale and issuance of our ordinary shares, our stage of research and development, our operating and financial performance and current business conditions.

The estimates of fair value of our ordinary shares are highly complex and subjective. There are significant judgments and estimates inherent in the determination of the fair value of our ordinary shares. These judgments and estimates include assumptions regarding our future operating performance, and the determinations of the appropriate valuation methods. The assumptions underlying these valuations represent management's best estimates, which involve inherent uncertainties and the application of management judgment. If we had made different assumptions, our stock-based compensation expense, net loss and net loss per share could have been materially different. If we had made different assumptions, our net loss and net loss per ordinary share could have been materially different.

Taxation

The tax expense for a period represents the total of current taxation and deferred taxation. The charges in respect of current taxation are based on the estimated taxable profit for the relevant year. Taxable profit for the year is based on the profit as shown in the income statement, as adjusted for items of income or expenditure which are not deductible or chargeable for tax purposes. The current tax liability for the year is calculated using tax rates which have either been enacted or substantively enacted at the relevant balance sheet date.

Deferred tax is provided in full, using the liability method on temporary differences arising between the tax base of assets and liabilities and their carrying values in the financial statements. The deferred tax is not accounted for if it arises from initial recognition of an asset or liability in a transaction other than a business combination that at the time of the transaction affects neither accounting nor taxable profit or loss. Deferred tax is determined using tax rates which have been enacted or substantively enacted at the balance sheet date and are expected to apply when the related deferred tax asset is realised or the deferred income tax liability is settled.

Deferred tax assets are recognised to the extent that it is probable that future taxable profits will be available against which the temporary differences can be utilised.

Deferred tax is provided on temporary differences arising on investments in subsidiaries and associates, except where the timing of the reversal of the temporary difference is controlled by the group and it is probable that the temporary difference will not reverse in the foreseeable future.

ITEM 6: DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES

A. Directors and Senior Management

The following table sets forth information regarding our directors as of the date of this registration statement.

NAME	AGE	POSITION
Gabriele Marco Antonio Cerrone MBA[2]	45	Executive Chairman
Riccardo Dalla-Favera MD[1],[3]	65	Non-Executive Director
Willy Simon[3]	66	Non-Executive Director
Kunwar Shailubhai PhD MBA[1],[2]	60	Chief Executive Officer, Chief Scientific Officer and Executive Director

[1] Remuneration Committee member
[2] Nominating Committee member
[3] Audit Committee member

The following table sets forth information regarding our senior managers as of the date of this registration statement:

NAME	POSITION
Tiziano Lazzaretti	Chief Financial Officer
Betty Liong Chu	Global Clinical Trial Manager
Jules S. Jacob	Senior Director, CMC & Non-Clinical Development
Evangeline Priya Eddy PhD DABT	Senior Director, Safety and Toxicology
Vaseem A. Palejwala PhD	Director, Non-Clinical Studies

Biographies

Gabriele Marco Antonio Cerrone – *Executive Chairman*

Mr. Gabriele Marco Antonio Cerrone, is the Founder of the Company and has been its Executive Chairman since April 2017, Mr. Cerrone has a successful track record and extensive experience in the financing and restructuring of micro-cap biotechnology companies. Mr. Cerrone has founded nine biotechnology companies in oncology, infectious diseases and molecular diagnostics, and has taken six of these companies to NASDAQ and one to AIM. Mr. Cerrone co-founded Trovagene, Inc. (NASDAQ: TROV), a molecular diagnostic company and served as its co-chairman. Mr. Cerrone was a co-founder and served as chairman of both Synergy Pharmaceuticals, Inc. (NASDAQ: SGYP) and Callisto Pharmaceuticals, Inc. (OTCMKTS: CLSP), and was a director of and led the restructuring of Siga Technologies, Inc. (NASDAQ: SIGA). Mr. Cerrone co-founded FermaVir Pharmaceuticals, Inc. and served as chairman until its merger in September 2007 with Inhibitex, Inc. Mr. Cerrone served as a director of Inhibitex, Inc. until its US$2.5bn sale to BMS in 2012. Mr. Cerrone graduated of New York University's Stern School of Business with a masters in business administration (MBA).

Dr. Riccardo Dalla-Favera - *Non-Executive Director*

Dr. Riccardo Dalla-Favera currently serves as a Non-Executive Director of the Company and is a leader in the field of molecular oncology and has made fundamental contributions to the field of cancer, especially in the study of the molecular genetics of B cell malignancies. As a researcher, Dr. Dalla-Favera has contributed much of the current knowledge on the genetic lesions responsible for human B cell lymphoma, which have led to the development of diagnostic tests and are being tested as targets in clinical trials with lymphoma patients. A faculty member for more than 15 years, Dr. Dalla-Favera helped found and has led the Institute for Cancer Genetics at Columbia University since 1999. Dr. Dalla-Favera is the Percy and Joanne Uris Professor of Pathology and Professor of Genetics & Development at the Columbia University College of Physicians and Surgeons. Dr. Dalla-Favera is also a director of the Specialised Center for research on Lymphoma at Columbia University funded by the Leukemia Lymphoma Society. Dr. Dalla-Favera joined Columbia University's College of Physicians and Surgeons in the Department of Pathology in 1989. Dr. Dalla-Favera completed a fellowship at the National Cancer Institute and was previously a faculty member at New York University School of Medicine. Dr. Dalla-Favera co-founded Therasis, Inc. in 2007 and has since served as a director of that company. Dr. Dalla-Favera has been a member of the scientific advisory board of Trovagene, Inc. since April 2010. Dr. Dalla-Favera is currently serving as a member of the scientific advisory board of Xigen SA. Dr. Dalla-Favera was a director of the Herbert Irving Comprehensive Cancer Centre from 2005 2011. Dr. Dalla-Favera has served as the chair of the Scientific Advisory Board of the Yale Cancer Centre. Dr. Dalla-Favera served as the co-chair of the National Centre Institute Program Review Group for Leukemia, Lymphoma and Myeloma and as a member of the boards of the Scientific Counsellors of the National Institute of Environmental Health and the National Cancer Institute.

Willy Simon - *Non-Executive Director*

Willy Jules Simon has served as a Non-Executive Director of the Company since November 2015. Mr. Simon has served as non-executive chairman of Bever Holding b.v. a Dutch listed public company focused on real estate development since August 2007. Mr. Simon served as the Chief Executive officer of Fortis Investment Management from January 2000 to July 2002. Mr. Simon worked in banking at Kredietbank N.V. from August 1975 to December 1983 and at Citibank London from January 1984 to December 1996 before serving as an executive member of the board of Generale Bank NL from January 1997 to December 1999. From July 2004 until April 2012, he served as a non-executive director of Redi & Partners Ltd., a fund of funds. Mr. Simon was previously chairman of AIM-traded Velox3 plc (formerly 24/7 Gaming Group Holdings plc), a company focused on publishing and developing gaming software for the mobile gaming industry, from April 2012 until April 2014. Mr. Simon was a director of Playlogic Entertainment Inc., a NASDAQ OTC listed company focused on developing, publishing, and selling interactive software games, from December 2003 to September 2011. Mr. Simon acted as chairman of Bank Oyens & van Eeghen from September 2002 to December 2004. Mr. Simon holds a law degree from the University of Louvain and a post-graduate degree in European law and economics from Institut des Hautes Etudes Européennes, Strasbourg.

Dr. Kunwar Shailubhai - *Chief Executive Officer, Chief Scientific Officer and Executive Director*

Dr Kunwar Shalilubhai has served as Chief Executive Officer, Chief Scientific Officer and Executive Director of the Company since 2008. Dr. Shailubhai was a co-founder of Synergy Pharmaceuticals Inc. From March 2004 until July 2008, Dr. Shailubhai served as Senior Vice President, Drug Discovery of Synergy, which at that time was a subsidiary of Callisto Pharmaceuticals, Inc. From May 2003 until March 2004, Dr. Shailubhai served as executive vice president, Research and Development of Synergy DE. From 2001 to April 2003, Dr. Shailubhai held the position of vice president, Drug Discovery at Synergy DE where he was chiefly responsible for the preclinical development of our GC-C agonist program for drugs to treat colon cancer and gastro intestinal (GI) inflammation. Between 1993 and 2000, he was with Monsanto Company, serving as group leader of the cancer chemoprevention group. Dr. Shailubhai previously served as a senior staff fellow at the National Institutes of Health, and as an assistant professor at the University of Maryland. Dr. Shailubhai received his Ph.D. in microbiology in 1984 from the University of Baroda, India, and his MBA in 2001 from the University of Missouri, St. Louis.

Tiziano Lazzaretti - *Chief Financial Officer*

Mr. Lazzaretti has served as Chief Financial Officer of the Company since March 2016. Mr. Lazzaretti has extensive experience in the healthcare and pharmaceutical industries and joined the Company from Pharmentis Srl, a spin-off from Teva Ratiopharm, where he served as group finance director from 2011 to 2016. Mr. Lazzaretti was executive director at Alliance Boots Healthcare, an international pharmacy-led health and beauty group. Mr. Lazzaretti held senior positions at SNIA Spa, Accenture, and Fiat Group. Mr. Lazzaretti received his bachelor of science (BSc Hons) in accounting and finance from the University of Turin, Italy, was awarded a master in business administration from Bocconi University, Milan and studied corporate finance at the London Business School.

Jules S. Jacob - *Senior Director, CMC & Non-Clinical Development*

Mr. Jules Jacob has served as Senior Director of Chemistry, Manufacturing and Controls (CMC) and Non-Clinical Development of the Company since July 2017 and has over 25 years of drug development experience. Previously, Mr. Jacob was senior director of product development at Aprecia Pharmaceuticals Company, a drug delivery technology platform company, from March 2009 to July 2017, where he led the development of Spritam®, the first FDA-approved dosage form manufactured using 3-dimensional printing, and other 505(b)(2) pipeline products. Mr. Jacob was director of formulation development at Panacos Pharmaceuticals Inc., a drug company focused on HIV and other major human viral diseases, from March 2007 to December 2008, where he worked on the development of first-in-class maturation inhibitors for the treatment of HIV. Mr. Jacob was a founding scientist, director of research and development and director of technology development at

Spherics, Inc., a pharmaceutical company that engaged in developing and manufacturing oral pharmaceutical products for central nervous system conditions, GI disorders, and cancer, from February 2000 to February 2007. Mr. Jacob worked on the development of bioadhesive dosage forms for treatment of CNS disorders, through the 505(b)(2) regulatory pathway at Spherics Inc. Mr. Jacob holds over 30 issued patents (in the U.S. and internationally) and 38 U.S. patent applications in the fields of drug delivery (proteins, peptides, DNA), nanoencapsulation, microencapsulation, solid oral dosage formulation, polymer compositions, gene therapy, tumor immunotherapy, protein micronization and formulation, imaging and bioadhesion, and he has authored more than 30 scientific articles and book chapters. Mr. Jacob completed his undergraduate degree and graduate education in biological and medical sciences at Brown University and has an active visiting faculty appointment in the Department of Molecular Pharmacolgy, Physiology and Biotechnology at Brown University.

Dr. Evangeline Priya Eddy - *Senior Director, Safety & Toxicology*

Dr. Eddy has served as Senior Director, Safety & Toxicology the Company since January 2017 and has over 20 years of experience in drug discovery and development. Dr. Eddy served as senior director, toxicology and safety pharmacology at Synergy Pharmaceuticals Inc., where she was responsible for toxicology, ADME/PK and safety pharmacology studies to support NOA submission of dolcanatide. Dr. Eddy contributed to the NOA for Trulance™, and her work at Synergy also included the development of a delayed release formulation for dolcanatide, as well as involvement in the supply of API for GLP and feasibility studies. Dr. Eddy worked at Endo Pharmaceuticals as an associate director, toxicology and safety pharmacology from February 2011 to October 2012 and as senior director, preclinical development at Zelos Therapeutics from April 2008 to February 2011. Dr. Eddy worked at Millennium Pharmaceuticals (now a wholly-owned subsidiary of Takeda Pharmaceutical Company Limited) 2000 to 2003 and at SmithKline Beecham Pharmaceuticals (now GlaxoSmithKline) from August 1992 to February 1999 in the areas of drug discovery and development including early clinical development. Dr. Eddy received her Ph.D. degree in biochemistry from Osmania University, Hyderabad and is a board-certified toxicologist of the American Board of Toxicology. Before joining the pharmaceutical industry, Dr. Eddy worked at Case Western Reserve University in Cleveland, OH in the area of chemical carcinogenesis and environmental health sciences.

Dr. Vaseem A. Palejwala - *Director, Non-Clinical Studies*

Dr. Palejwala has served as Director, Non-Clinical Studies of the Company since January 2017 and has 18 years of experience in drug discovery and development. Dr. Palejwala also currently serves as director of discovery and preclinical research at Rasna Therapeutics, Inc. From January 2015 to January 2017, Dr. Palejwala served as director of discovery and preclinical research, and from December 2012 to December 2014 served as associate director of discovery and preclinical research, at Synergy Pharmaceuticals Inc. There Dr Palejwala actively contributed to establishing GI tract-related preclinical animal models for testing the efficacy and validating the mechanism of action for both plecanatide and dolcanatide. Dr. Palejwala also actively participated in preparation of the nonclinical pharmacology section of the NDA for Trulance®. From 2001 to 2012, Dr. Palejwala served as discovery scientist/manager at Sanofi S.A., *a* multinational pharmaceutical company, where he advanced both small molecule and biologic programs in immunology, inflammation, oncology, CNS and metabolic disorders and also contributed to establishing and managing high-throughput gene expression profiling platform capabilities. Dr. Palejwala holds a degree in microbiology and chemistry from Bombay University, as well as a master of science degree in microbiology and a Ph.D. in microbiology from the Maharaja Sayajirao University of Baroda.

Betty Liong Chu – *Global Clinical Trial Manager*

Betty Liong Chu has served as our Global Clinical Trial Manager since July 2017 and has over 10 years of experience in clinical trial management and operations. Ms. Chu worked as global clinical trial manager at ICON plc, a global CRO, from January 2008 to June 2017. Ms Chu worked at Metropolitan Research Associates, a small, privately-owned CRO from March 2006 to January 2008. Ms. Chu holds a degree in psychology from Barnard College and a masters degree in forensic psychology from John Jay College (CUNY).

Family Relationships

There are no family relationships among any of our executive officers or directors.

B. Compensation

Total Compensation for the Chairman and Non-Executive Directors

The table below sets out the total remuneration received by the Chairman and the Non-Executive Directors for the year ended December 31, 2016.

Name	Position	Fees earned or paid in cash ($)	Options awarded ($)	Total ($)
Gabriele Marco Antonio Cerrone	Chairman	98,696	150,151	248,847
Riccardo Dalla-Favera	Non – Executive Director	24,674	-	24,674
Willy Simon	Non – Executive Director	44,413	-	44,413

(1) The amounts have been translated into U.S. dollars from pounds Sterling based upon the exchange rate as certified by the Federal Reserve Bank of New York for customs purposes as of December 31, 2016. These translations are merely for the convenience of the reader and should not be construed as representations that the pounds Sterling amounts actually represent such U.S. dollar amounts or could be converted into U.S. dollars at the rate indicated.

(2) Represents the fair value of incentive stock options granted during the year to December 31, 2016 using the Black-Scholes model for computing stock-based compensation expense as of the date of grant.

Compensation of Executive Directors and Senior Managers

The table below sets the remuneration of each of the Executive Directors and Senior Managers for the financial year ended December 31, 2016.

Name	Position	Fees earned or paid in cash ($)	Options awarded ($)	Total ($)
Kunwar Shailubhai	Executive Director	24,674	-	24,674
Tiziano Lazzaretti	Chief Financial Officer	92,528	223,590	316,118

Tiziana Equity Incentive Plan

2016 Equity Incentive Plan

The 2016 Equity Incentive Plan, or the 2016 Plan was adopted by the Board on 23 May 2016 and approved by shareholders on 30 June 2016 and allows for the grant of equity and cash based incentive awards to eligible service providers. The material terms of the 2016 Plan are summarized below. Except where the context indicates otherwise, references hereunder to our ordinary shares shall be deemed to include a number of ADSs equal to an ordinary share.

Eligibility and Administration

Our employees, consultants and directors, and employees and consultants of our subsidiaries are eligible to receive awards under the 2016 Plan. The 2016 Plan is administered by our board of directors, which may delegate its duties and responsibilities to one or more committees of our directors and/or officers (referred to collectively as the plan administrator below), subject to the limitations

imposed under the 2016 Plan, stock exchange rules and other applicable laws. The plan administrator has the authority to take all actions and make all determinations under the 2016 Plan, to interpret the 2016 Plan and award agreements and to adopt, amend and repeal rules for the administration of the 2016 Plan as it deems advisable. The plan administrator also has the authority to determine which eligible service providers receive awards, grant awards, set the terms and conditions of all awards under the 2016 Plan, including any vesting and vesting acceleration provisions, and designate whether such awards will cover our ordinary shares or ADSs, subject to the conditions and limitations in the 2016 Plan.

Shares Available for Awards

An aggregate of options equal to 10% of the Company's ordinary share capital from time to time may be issued under the 2016 Plan. Pursuant to the terms of the 2016 Plan, awards may be issued under the 2016 Plan covering ADSs in lieu of the number of our ordinary shares that such ADSs represent. Shares issued under the 2016 Plan may be authorized but unissued shares, shares purchased on the open market, treasury shares or ADSs.

If an award under the 2016 Plan, or any prior equity incentive plan, expires, lapses or is terminated, exchanged for cash, surrendered, repurchased, canceled without having been fully exercised or forfeited, any unused shares subject to the award will, as applicable, become or again be available for new grants under the 2016 Plan. Awards granted under the 2016 Plan in substitution for any options or other equity or equity-based awards granted by an entity before the entity's merger or consolidation with us or our acquisition of the entity's property or stock will not reduce the shares available for grant under the 2016 Plan, but will count against the maximum number of shares that may be issued upon the exercise of incentive options.

Awards

The 2016 Plan provides for the grant of options, share appreciation rights, or SARs, restricted shares, dividend equivalents, restricted share units, or RSUs, and other share or cash-based awards. All awards under the 2016 Plan will be set forth in award agreements, which will detail the terms and conditions of awards, including any applicable vesting and payment terms and post-termination exercise limitations. A brief description of each award type follows.

Options and SARs

Options provide for the purchase of our ordinary shares in the future at an exercise price set on the grant date. SARs entitle their holder, upon exercise, to receive from us an amount equal to the appreciation of the shares subject to the award between the grant date and the exercise date. The plan administrator will determine the number of shares covered by each option and SAR, the exercise price of each option and SAR and the conditions and limitations applicable to the exercise of each option and SAR.

Restricted Shares and Restricted Share Units

Restricted shares are an award of nontransferable ordinary shares that remain forfeitable unless and until specified conditions are met and which may be subject to a purchase price. RSUs are contractual promises to deliver our ordinary shares in the future, which may also remain forfeitable unless and until specified conditions are met and may be accompanied by the right to receive the equivalent value of dividends paid on our ordinary shares prior to the delivery of the underlying shares. The plan administrator may provide that the delivery of the shares underlying RSUs will be deferred on a mandatory basis or at the election of the participant. The terms and conditions applicable to restricted shares and RSUs will be determined by the plan administrator, subject to the conditions and limitations contained in the 2016 Plan.

Other Share or Cash Based Awards.

Other share or cash based awards are awards of cash, fully-vested our ordinary shares and other awards valued wholly or partially by referring to, or otherwise based on, our ordinary shares or other property. Other share or cash based awards may be granted to participants and may also be available as a payment form in the settlement of other awards, as standalone payments and as payment in lieu of compensation to which a participant is otherwise entitled. The plan administrator will determine the terms and conditions of other share or cash based awards, which may include any purchase price, performance goal, transfer restrictions and vesting conditions.

Performance Criteria

The plan administrator may select performance criteria for an award to establish performance goals for a performance period.

Certain Transactions

In connection with certain corporate transactions and events affecting our ordinary shares, including a change in control, another similar corporate transaction or event, another unusual or nonrecurring transaction or event affecting us or our financial statements or a change in any applicable laws or accounting principles, the plan administrator has broad discretion to take action under the 2016 Plan to prevent the dilution or enlargement of intended benefits, facilitate the transaction or event or give effect to the change in applicable laws or accounting principles. This includes canceling awards for cash or property, accelerating the vesting of awards, providing for the assumption or substitution of awards by a successor entity, adjusting the number and type of shares subject to outstanding awards and/or with respect to which awards may be granted under the 2016 Plan and replacing or terminating awards under the 2016 Plan. In addition, in the event of certain non-reciprocal transactions with our shareholders, the plan administrator will make equitable adjustments to the 2016 Plan and outstanding awards as it deems appropriate to reflect the transaction. Pursuant to the terms of their individual employment agreements, awards granted under the 2016 Plan to certain of our executives may become fully vested and exercisable upon a change in control.

Plan Amendment and Termination

Our board of directors may amend or terminate the 2016 Plan at any time; however, no amendment, other than an amendment that increases the number of shares available under the 2016 Plan, may materially and adversely affect an award outstanding under the 2016 Plan without the consent of the affected participant and shareholder approval will be obtained for any amendment to the extent necessary to comply with applicable laws. Further, the plan administrator cannot, without the approval of our shareholders, amend any outstanding option or SAR to reduce its price per share or cancel any outstanding option or SAR in exchange for cash or another award under the 2016 Plan with an exercise price per share that is less than the exercise price per share of the original option or SAR. The 2016 Plan will remain in effect until the tenth anniversary of its effective date unless earlier terminated by our board of directors. No awards may be granted under the 2016 Plan after its termination.

Transferability and Participant Payments

Except as the plan administrator may determine or provide in an award agreement, awards under the 2016 Plan are generally non-transferrable, except by will or the laws of descent and distribution, or, subject to the plan administrator's consent, pursuant to a domestic relations order, and are generally exercisable only by the participant. With regard to tax withholding obligations arising in connection with awards under the 2016 Plan, and exercise price obligations arising in connection with the exercise of options under the 2016 Plan, the plan administrator may, in its discretion, accept cash, wire transfer or cheque, our ordinary shares that meet specified conditions, a promissory note, a "market sell order," such other consideration as the plan administrator deems suitable or any combination of the foregoing.

Non-U.S. Participants

The plan administrator may modify awards granted to participants who are non-U.S. nationals or employed outside the United States or establish sub-plans or procedures to address differences in laws, rules, regulations or customs of such foreign jurisdictions.

C. Board Practices

Corporate Governance Practices

We are a "foreign private issuer," as defined by the SEC. As a result, in accordance with NASDAQ listing requirements, we may rely on home country governance requirements and certain exemptions thereunder rather than complying with NASDAQ corporate governance standards. While we voluntarily follow most NASDAQ corporate governance rules, we may choose to take advantage of the following limited exemptions:

- Exemption from filing quarterly reports on Form 10-Q containing unaudited financial and other specified information or current reports on Form 8-K upon the occurrence of specified significant events.
- Exemption from Section 16 rules requiring insiders to file public reports of their stock ownership and trading activities and liability for insiders who profit from trades in a short period of time, which will provide less data in this regard than shareholders of U.S. companies that are subject to the Exchange Act.
- Exemption from the NASDAQ requirement requiring disclosure of any waivers of the code of business conduct and ethics for directors and officers.
- Exemption from the requirement that our board have a compensation committee that is composed entirely of independent directors with a written charter addressing the committee's purpose and responsibilities.
- Exemption from the requirement to have independent director oversight of director nominations.

We intend to follow U.K. corporate governance practices in lieu of NASDAQ corporate governance requirements as follows:

- We do not intend to follow NASDAQ Rule 5620(c) regarding quorum requirements applicable to meetings of shareholders. Such quorum requirements are not required under English law. In accordance with generally accepted business practice, our Articles of Association will provide alternative quorum requirements that are generally applicable to meetings of shareholders.
- We do not intend to follow NASDAQ Rule 5605(b)(2), which requires that independent directors regularly meet in executive sessions where only independent directors are present. Our independent directors may choose to meet in executive sessions at their discretion.

Although we may rely on certain home country corporate governance practices, we must comply with NASDAQ's Notification of Noncompliance requirement (NASDAQ Rule 5625) and the Voting Rights requirement (NASDAQ Rule 5640). Further, we must have an audit committee that satisfies NASDAQ Rule 5605(c)(3), which addresses audit committee responsibilities and authority and requires that the audit committee consist of members who meet the independence requirements of NASDAQ Rule 5605(c)(2)(A)(ii).

We intend to take all actions necessary for us to maintain compliance as a foreign private issuer under the applicable corporate governance requirements of the Sarbanes-Oxley Act, the rules adopted by the SEC and NASDAQ listing rules. Accordingly, our shareholders will not have the same protections afforded to shareholders of companies that are subject to all of the corporate governance requirements of NASDAQ. For an overview of our corporate governance principles, see the section titled "Description of Share Capital and Articles of Association—Differences in Corporate Law."

Composition of Our Board of Directors

Our board of directors is currently composed of four members. Our board of directors has determined that, of our four directors, none have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of two of the directors, Mr. Dalla-Favera and Mr. Simon, and that each of these directors is "independent" as that term is defined under NASDAQ rules.

In accordance with our Articles of Association to be in effect upon the filing of this registration statement, one-third of our directors will retire from office at every annual general meeting of shareholders. Retiring directors will be eligible for re-election and if the retiring directors consent to act, they will be re-elected by default. See "Description of Share Capital and Articles of Association—Articles of Association—Board of Directors."

Committees of Our Board of Directors

Our board of directors has three standing committees: an audit committee, a remuneration committee and a nominating committee.

Audit Committee

The audit committee, which consists of Dr. Dalla-Favera and Mr. Simon, assists the board of directors in overseeing our accounting and financial reporting processes. Mr. Simon serves as chairman of the audit committee. The audit committee consists exclusively of members of our board who are financially literate, and Mr. Simon is considered an "audit committee financial expert" as defined by applicable SEC rules and has the requisite financial sophistication as defined under the applicable NASDAQ rules and regulations.

Our board has determined that all of the members of the audit committee satisfy the "independence" requirements set forth in Rule 10A-3 under the Exchange Act. The audit committee will be governed by a charter that complies with NASDAQ rules.

The audit committee's responsibilities include:

- recommending the appointment of the independent auditor to the general meeting of shareholders;
- the appointment, compensation, retention and oversight of any accounting firm engaged for the purpose of preparing or issuing an audit report or performing other audit services;
- pre-approving the audit services and non-audit services to be provided by our independent auditor before the auditor is engaged to render such services;
- evaluating the independent auditor's qualifications, performance and independence, and presenting its conclusions to the full board of directors on at least an annual basis;
- reviewing and discussing with management and our independent registered public accounting firm our financial statements and our financial reporting process; and
- reviewing, approving or ratifying any related party transactions.

Remuneration Committee

The remuneration committee consists of Dr. Dalla-Favera and Dr. Shailubhai. Dr. Dalla-Favera serves as chairman of the remuneration committee. Under SEC and NASDAQ rules, there are heightened independence standards for members of the remuneration committee, including a prohibition against the receipt of any compensation from us other than standard board member fees.

The remuneration committee's responsibilities include:

- identifying, reviewing and proposing policies relevant to the compensation and benefits of our directors and executive officers;

- evaluating each executive officer's performance in light of such policies and reporting to the board; and
- overseeing and administering our employee share option scheme or equity incentive plans in operation from time to time.

Nominating Committee

The nominating committee consists of Mr. Cerrone and Dr. Shailubai. Mr. Cerrone will serve as chairman of the nominating committee.

The nominating committee's responsibilities include:

- drawing up selection criteria and appointment procedures for directors;
- recommending nominees for election to our board of directors and its corresponding committees;
- assessing the functioning of individual members of our board of directors and executive officers and reporting the results of such assessment to the board of directors; and
- developing corporate governance guidelines.

Code of Business Conduct and Ethics

In connection with the filing of this registration statement, we will adopt a Code of Business Conduct and Ethics applicable to our employees, executive officers and directors.

Compensation of Executive Officers and Directors

For the year ended December 31, 2016, the aggregate compensation accrued or paid to the members of our board of directors and our executive officers for services in all capacities was $0.2 million.

Executive Director Service Agreement

Dr. Kunwar Shailubhai

We entered into an employment agreement with Dr. Kunwar Shailubhai in May 2017. This agreement entitles Dr. Shailubhai to receive an initial annual base salary of $300,000 per year. Dr. Shailubhai is eligible to receive an annual bonus of up to 35% of his base salary, such bonus amount to be determined in the company's sole discretion. Dr. Shailubhai is also entitled to the same fringe benefits as we provide to our other executives from time to time and is eligible to receive employee share incentives. The vesting of any unvested employee share incentives held by Dr. Shailubhai will accelerate in the event his employment is terminated without cause (as such term is defined in his employment agreement), or if he resigns for good reason (as such term is defined in his employment agreement) and, in each case, such termination is upon the consummation of or within 12 months following a change of control of the company. If Dr. Shailubhai's employment with the company is terminated without cause, or if he resigns for good reason, Dr. Shailubhai will also be entitled to receive severance equal to continuation of his base salary as then currently in effect for 12 months following his date of termination and will be eligible for reimbursement for medical coverage premiums for up to the same period. Dr. Shailubhai, his spouse and eligible dependents are entitled to stay on our health insurance plans for a period of 12 months following his termination for any reason. Dr. Shailubhai's severance benefits are conditioned on, among other things, his execution of our standard separation agreement and a general release of claims in our favor.

The agreement provides that Dr. Shailubhai's employment with us is at-will. If required by the company, the agreement further provides that Dr. Shailubhai will resign from his position on our board of directors effective as of the date of his termination for any reason. The agreement further contains a six-month non-competition covenant and a 12-month non-solicitation covenant by Dr. Shailubhai.

Non-Executive Director Service Contracts

The remuneration of our non-executive directors is determined by our board as a whole, based on a review of current practices in other companies. We intend to enter into service contracts with our directors for their services or amend and restate any prior service contracts in place prior to, or as soon as practicable, following the filing of this registration statement.

D. Employees

As of December 31, 2016, 2015 and 2014, we had 9, 2 and 3 employees, respectively. All of our employees were based in the United Kingdom, except that, as of December 31, 2016, we had 3 employees based outside of the United Kingdom. All of our employees were engaged in either administrative or research and development functions. None of our employees are covered by a collective bargaining agreement.

Insurance and Indemnification

To the extent permitted by the Companies Act, we are empowered to indemnify our directors against any liability they incur by reason of their directorship. We maintain directors' and officers' insurance to insure such persons against certain liabilities. We expect to enter into a deed of indemnity with each of our directors and executive officers prior to, or as soon as practicable, following the filing of this registration statement.

In addition to such indemnification, we provide our directors and executive officers with directors' and officers' liability insurance.

Insofar as indemnification of liabilities arising under the Securities Act may be permitted to our board of directors, executive officers, or persons controlling us pursuant to the foregoing provisions, we have been informed that, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

E. Share Ownership

See "Item 7. Major Shareholders and Related Party Transactions."

ITEM 7: MAJOR SHAREHOLDERS AND RELATED PARTY TRANSACTIONS

A. Major Shareholders

The Disclosure Guidance and Transparency Rules of the UK Financial Conduct Authority provide that a person or corporate entity that acquires an interest that reaches or exceeds 3% of the ordinary shares is required to notify the Company of that interest. If such interest subsequently reaches, exceeds or falls below a whole percentage point, this must also be notified. Similarly, a notification is required once the interest falls below 3% of the ordinary shares. The following table sets forth information with respect to the beneficial ownership of ordinary shares as of September 30, 2017, in respect of:

- each of our directors, executive officers and senior managers individually and as a group; and
- each person, or group of affiliated persons, who is known by us to own beneficially 3% or more of our ordinary shares.

As a number of our ordinary shares are held in book-entry form, we are not aware of the identity of all our shareholders. As of September 30, 2017, we had 0 ordinary shares held by 0 U.S. resident shareholders of record, representing approximately 0% of total voting power.

Beneficial ownership is determined in accordance with the rules and regulations of the SEC. In computing the number of ordinary shares beneficially owned by a person and the percentage ownership of that person, we have included ordinary shares that the person has the right to acquire within 60 days of September 30, 2017, including through the exercise of any option, warrant or other right or the conversion of any other security. These ordinary shares, however, are not included in the

computation of the percentage ownership of any other person. All ordinary shares have the same voting rights.

Significant Changes in Ownership:

2015/2016
No notifications were received during 2015 or 2016.

2017:
In June 2017, Planwise Group Limited** notified an increase in interest to 63,680,404 ordinary shares, which represents 66.20% of the issued share capital of the Company.

	Ordinary shares*	
	Number	**Percentage**
Planwise Group Limited**	63,680,404	66.20%
Nerviano Medical Sciences S.r.l.	4,233,616	4.49%
Maria McGuigan	3,114,618	3.30%
G Cerrone		
R Dalla Favera		
K Shailubhai		
W Simon		

* Based on 138,216,920 ordinary shares outstanding as of September 30, 2017, which comprise our entire issued and outstanding share capital as of that date.

** Mr. Gabriele Cerrone is the ultimate beneficial owner of the entire issued share capital of Planwise Group Limited, which is a private limited company incorporated under the laws of the British Virgin Islands with company number 1686824 and its registered office at Offshore Incorporations, Centre PO Box 957, Road Town, Tortola, British Virgin Islands.

B. Related Party Transactions

Financial year ended December 31, 2016

As at December 31, 2016, we had transferred $5,164,364 in total to Tiziana Pharma Limited during the year. Included within other debtors on our financial statements at the balance sheet date is $5,164,364 (2015: $3,603,797) owed by Tiziana Pharma Limited. During the year, we transferred $1,181,525 (2015: $247,612) to Tiziana Therapeutics Inc. This balance is included within other debtors.

Financial year ended December 31, 2015

As at December 31, 2015, we had loaned $2,906,202 in total and had recharged costs of $697,595 to Tiziana Pharma Limited during the year. Included within other debtors on our financial statements at the balance sheet date is $3,603,797 owed by Tiziana Pharma Limited. During the year, we loaned $247,611 to Tiziana Therapeutics Inc.

Financial year ended December 31, 2014

As at December 31, 2014, we had loaned $1,339,747 and recharged costs of $120,641 to Tiziana Pharma Limited. Included within other debtors on our financial statements at the balance sheet date is $570,895 owed by Tiziana Pharma Limited.

C. Interests of Experts and Counsel

Not applicable.

ITEM 8: FINANCIAL INFORMATION

A. Consolidated Statements and Other Financial Information

See “Item 18. Financial Statements” for a list of all financial statements filed as part of this registration statement.

Legal Proceedings

Save as disclosed in this paragraph, there are no governmental, legal or arbitration proceedings (including any such proceedings which are pending or threatened of which the Company is aware), which may have, or have had during the 12 months prior to the date of this registration statement, a significant effect on the Company’s and/or our financial position or profitability. In addition to the proceedings set out in this section, the Company is involved in other legal proceedings and claims in the ordinary course of business.

B. Significant Changes

For information on any significant changes that may have occurred since the date of our annual financial statements, see “Item 5. Operating and Financial Review and Prospects.”

ITEM 9: THE OFFER AND LISTING

A. Offering and Listing Details

The principal trading market for our ordinary shares is AIM, of the London Stock Exchange, where our ordinary shares have been listed since 2014. The following table sets forth, for the periods indicated, the reported high and low closing prices on the London Stock Exchange for our ordinary shares in pounds Sterling. See “Exchange Rate Information” on page 4 for the exchange rates applicable to the periods set forth below.

	High £	Low £
Annual:		
Fiscal year ended December 31, 2014	0.77	0.16
Fiscal year ended December 31, 2015	2.52	0.43
Fiscal year ended December 31, 2016	2.25	0.91
Fiscal year ended December 31, 2017	2.40	1.39
Quarterly:		
Fiscal year ended December 31, 2017	1.79	1.40
Third quarter		
Second quarter	2.40	1.02
First quarter	2.15	1.60
Fiscal year ended December 31, 2016		
Fourth quarter	2.25	1.75
Third quarter	2.03	1.27
Second quarter	1.69	0.91
First quarter	2.33	1.17
Most Recent Six Months:		
January 2018	1.44	1.35
December 2017	1.53	1.39
November 2017	1.75	1.41
October 2017	1.55	1.43
September 2017	1.60	1.40
August 2017	1.66	1.45
July 2017	1.80	1.55

For a description of the rights of our ADSs, see “Item 12.D. — American Depositary Shares.”

B. Plan of Distribution

Not applicable.

C. Markets

Our ordinary shares are trading on the London Stock Exchange. We are in the process of applying to have our ADSs listed on the NASDAQ Capital Market under the symbol "TILS." We make no representation that such application will be approved or that our ADSs will trade on such market either now or at any time in the future.

D. Selling Shareholders

Not applicable.

E. Dilution

Not applicable.

F. Expenses of the Issue

Not applicable.

ITEM 10: ADDITIONAL INFORMATION

A. Share Capital

Current authorized share capital

Not applicable.

Current issued share capital

Our share capital as of September 30, 2017 consists of 138,216,920 ordinary shares with a nominal value of £0.03 per share.

As at September 30, 2017, our issued and fully paid share capital was as follows:

Class of share	Issued and fully paid shares	Amount £
Ordinary shares	123,827,938	3,714,838

History of share capital

The following changes have occurred in our issued share capital in the last three years:

(A) On January 20, 2015, we issued 4,233,616 ordinary shares to Nerviano in connection with entry into the Nerviano Agreement, at a price of £0.505 per ordinary share, for an aggregate consideration of £2,137,976, following which we had 88,905,928 ordinary shares in issue.

(B) On March 20, 2015, we issued 28,000 ordinary shares to option holders following the exercise of options, at an exercise price of £0.03 per ordinary share, for an aggregate consideration of £840, following which we had 88,933,928 ordinary shares in issue.

(C) On March 31, 2015, we completed a placing and issued 3,400,000 ordinary shares to new investors, at a price of £0.75 per ordinary share, for a net consideration of £2,550,000, following which we had 92,333,928 ordinary shares in issue.

(D) On October 30, 2015, we issued 58,222 ordinary shares to warrant holders following the exercise by such warrant holders of existing warrants, at an exercise price of £1.50 per ordinary share, for an aggregate consideration of £87,333, following which we had 92,392,150 ordinary shares in issue.

(E) On April 28, 2016, we issued 1,095,000 ordinary shares to warrant holders following the exercise by such warrant holders of existing warrants, at an exercise price of £0.20 per ordinary share, for an aggregate consideration of £219,000, following which we had 93,487,150 ordinary shares in issue.

(F) On June, 29, 2016, we issued 206,250 ordinary shares to warrant holders following the exercise by such warrant holders of existing warrants, at an exercise price of £0.32 per ordinary share, for an aggregate consideration of £66,000 and a further 700,000 ordinary shares following the conversion of convertible loan note holders, at a conversion price of £0.24, for an aggregate consideration of £168,000, following which we had 94,393,400 ordinary shares in issue.

(G) On June 30, 2016, we issued one ordinary share pursuant to the terms of a deferred share buyback, at a price of £1.50 per ordinary share, for an aggregate consideration of £1.50, following which we had 94,393,401 ordinary shares in issue.

(H) On March 24, 2017, we issued 1,789,524 ordinary shares to warrant holders following the exercise by such warrant holders of existing warrants, at an exercise price of £0.32 per ordinary share, for an aggregate consideration of £572,648, following which we had 96,182,925 ordinary shares in issue.

(I) On August 16, 2017, we issued 27,645,013 ordinary shares to convertible loan note holders on conversion of all outstanding convertible loan notes, following which we had 123,827,938 ordinary shares in issue.

(J) On November 20, 2017 the Company issued 100,000 new ordinary shares at £1.50 per share to raise £150,000, each new ordinary share was issued with a warrant to subscribe for one additional share at a price of £1.60, for a 5 year period.

(K) On November 27, 2017 the Company issued 183,333 new ordinary shares at £1.50 per share to raise £275,000, each new ordinary share was issued with a warrant to subscribe for one additional share at a price of £1.60 for a five year period.

(L) On December 15, 2017 the Company issued 133,333 new ordinary shares at £1.50 per share to raise £200,000, each new ordinary share was issued with a warrant to subscribe for one additional share at a price of £1.60 for a five year period. In addition the Company granted a further 31,667 warrants on identical terms in lieu of fees and commissions on the funds raised.

(M) On January 15, 2018 the Company issued 100,000 new ordinary shares at £1.50 per share to raise £150,000, each new ordinary share was issued with a warrant to subscribe for one additional share at a price of £1.60 for a five year period. In addition the Company granted a further 63,334 warrants on identical terms in lieu of fees and commissions on the funds raised. The Company also issued a further 801,201 ordinary shares, credited as fully paid, to former holders of convertible loan notes (including in the face value capitalized at (I) above).

(N) On January 19, 2018 the Company issued 66,667 new ordinary shares at a price of £1.50 per share to raise £100,000, each new ordinary share was issued with a warrant attached to subscribe for one additional share at a price of £1.60 for a five year period. In addition the Company granted a further 66,667 warrants on identical terms in lieu of fees and commissions on the funds raised.

Information about the Ordinary Shares

In accordance with our Articles of Association to be in effect upon the filing of this registration statement, the following summarizes the rights of holders of our ordinary shares:

- each holder of our ordinary shares is entitled to one vote per ordinary share on all matters to be voted on by shareholders generally;
- the holders of the ordinary shares shall be entitled to receive notice of, attend, speak and vote at our general meetings; and
- holders of our ordinary shares are entitled to receive such dividends as are recommended by our directors and declared by our shareholders.

Registered Shares

We are required by the Companies Act to keep a register of our shareholders. Under English law, the ordinary shares are deemed to be issued when the name of the shareholder is entered in our share register. The share register therefore is prima facie evidence of the identity of our shareholders, and the shares that they hold. The share register generally provides limited, or no, information regarding the ultimate beneficial owners of our ordinary shares. Our share register is maintained by our registrar, Link Asset Services plc.

Potential future holders of our ADSs will not be treated as one of our shareholders and their names will therefore not be entered in our share register. The depositary, the custodian or their nominees will be the holder of the shares underlying our ADSs. Potential future holders of our ADSs have a right to receive the ordinary shares underlying their ADSs. For discussion on our ADSs and ADS holder rights, see “Description of American Depositary Shares” in this prospectus.

Under the Companies Act, we must enter an allotment of shares in our share register as soon as practicable and in any event within two months of the allotment. We will perform all procedures necessary to update the share register to reflect any ordinary shares being sold in any potential offering, including updating the share register with the number of ordinary shares to be issued to the depositary upon the closing of any such offering in the future. We also are required by the Companies Act to register a transfer of shares (or give the transferee notice of and reasons for refusal as the transferee may reasonably request) as soon as practicable and in any event within two months of receiving notice of the transfer.

We, any of our shareholders, or any other affected person may apply to the court for rectification of the share register if:

- the name of any person, without sufficient cause, is wrongly entered in or omitted from our register of members; or
- there is a default or unnecessary delay in entering on the register the fact of any person having ceased to be a member or on which we have a lien, provided that such delay does not prevent dealings in the shares taking place on an open and proper basis.

Preemptive Rights

English law generally provides shareholders with preemptive rights when new shares are issued for cash; however, it is possible for the articles of association, or shareholders in general meeting, to exclude preemptive rights. Such an exclusion of preemptive rights may be for a maximum period of up to five years from the date of adoption of the articles of association, if the exclusion is contained in the articles of association, or from the date of the shareholder resolution, if the exclusion is by shareholder resolution. In either case, this exclusion would need to be renewed by our shareholders upon its expiration (i.e., at least every five years). Typically UK public companies renew the disapplication of pre-emption rights on an annual basis or their annual general meeting. On 29 June 2017, our shareholders approved the exclusion of preemptive rights for a period of 15 months or the date of the next annual general meeting, which exclusion is for a number of shares equal to 20% of the issued share capital at the time of passing of the resolution and which will need to be renewed upon expiration (i.e., the earlier of 15 months from the date of passing the resolution on the date of the next annual general meeting) to remain effective.

Articles of Association

Our Articles of Association, or the Articles, were adopted by a special resolution of the founder shareholder passed at a general meeting on 30 June 2016. A summary of the terms of the Articles is set out below. The summary below is not a complete copy of the terms of the Articles.

The Articles contain no specific restrictions on our purpose and therefore, by virtue of section 31(1) of the Companies Act, our purpose is unrestricted.

The Articles contain, among other things, provisions to the following effect:

Share Capital

Our share capital currently consists of ordinary shares. We may issue shares with such rights or restrictions as may be determined by ordinary resolution, including shares which are to be redeemed, or are liable to be redeemed at our option or the holder of such shares.

Voting

The shareholders have the right to receive notice of, and to vote at, our general meetings. Each shareholder who is present in person (or, being a corporation, by representative) at a general meeting

on a show of hands has one vote and, on a poll, every such holder who is present in person (or, being a corporation, by representative) or by proxy has one vote in respect of every share held by him.

Variation of Rights

Whenever our share capital is divided into different classes of shares, the special rights attached to any class may be varied or abrogated either with the consent in writing of the holders of three-fourths in nominal value of the issued shares of that class or with the sanction of a special resolution passed at a general meeting of the holders of the shares of that class and may be so varied and abrogated whilst the company is a going concern.

Dividends

We may, subject to the provisions of the Companies Act and the Articles, by ordinary resolution from time to time declare dividends to be paid to shareholders not exceeding the amount recommended by our board of directors. Subject to the provisions of the Companies Act, in so far as, in the board of directors' opinions, our profits justify such payments, the board of directors may pay interim dividends on any class of our shares.

Any dividend unclaimed after a period of 12 years from the date such dividend was declared or became payable shall, if the board of directors resolve, be forfeited and shall revert to us. No dividend or other moneys payable on or in respect of a share shall bear interest as against us.

Transfer of Ordinary Shares

Each member may transfer all or any of his shares which are in certificated form by means of an instrument of transfer in any usual form or in any other form which the board of directors may approve. Each member may transfer all or any of his shares which are in uncertificated form by means of a "relevant system" (i.e., the CREST System) in such manner provided for, and subject as provided in, the CREST Regulations.

The Board may, in its absolute discretion, refuse to register a transfer of certificated shares unless:

(i) it is for a share which is fully paid up;

(ii) it is for a share upon which the company has no lien;

(iii) it is only for one class of share;

(iv) it is in favor of a single transferee or no more than four joint transferees;

(v) it is duly stamped or is duly certificated or otherwise shown to the satisfaction of the board of directors to be exempt from stamp duty; and

(vi) it is delivered for registration to the registered office of the company (or such other place as the board of directors may determine), accompanied (except in the case of a transfer by a person to whom the company is not required by law to issue a certificate and to whom a certificate has not been issued or in the case of a renunciation) by the certificate for the shares to which it relates and such other evidence as the board of directors may reasonably require to prove the title of the transferor (or person renouncing) and the due execution of the transfer or renunciation by him or, if the transfer or renunciation is executed by some other person on his behalf, the authority of that person to do so.

The board of directors may refuse to register a transfer of uncertificated shares in any circumstances that are allowed or required by the CREST Regulations and the CREST System.

Allotment of Shares and Preemption Rights

Subject to the Companies Act and to any rights attached to existing shares, any share may be issued with or have attached to it such rights and restrictions as the company may by ordinary resolution determine, or if no ordinary resolution has been passed or so far as the resolution does not make specific provision, as the board of directors may determine (including shares which are to be redeemed, or are liable to be redeemed at the option of the company or the holder of such shares).

In accordance with section 551 of the Companies Act, the board of directors may be generally and unconditionally authorized to exercise all the powers of the company to allot shares up to an aggregate nominal amount equal to the amount stated in the relevant ordinary resolution authorizing such allotment.

The provisions of section 561 of the Companies Act (which confer on shareholders rights of preemption in respect of the allotment of equity securities which are paid up in cash) apply to the company except to the extent disapplied by special resolution of the company. Such preemption rights have been disapplied, in part, pursuant to the special resolution passed on June 29, 2017.

Alteration of Share Capital

The company may by ordinary resolution consolidate or divide all of its share capital into shares of larger nominal value than its existing shares, or cancel any shares which, at the date of the ordinary resolution, have not been taken or agreed to be taken by any person and diminish the amount of its share capital by the nominal amount of shares so cancelled or sub-divide its shares, or any of them, into shares of smaller nominal value.

The company may, in accordance with the Companies Act, reduce or cancel its share capital or any capital redemption reserve or share premium account in any manner and with and subject to any conditions, authorities and consents required by law.

Board of Directors

Unless otherwise determined by the company by ordinary resolution, the number of directors (other than any alternate directors) shall not be less than two, but there shall be no maximum number of directors.

Subject to the Articles and the Companies Act, the company may by ordinary resolution appoint a person who is willing to act as a director and the board of directors shall have power at any time to appoint any person who is willing to act as a director, in both cases either to fill a vacancy or as an addition to the existing board of directors.

At the first annual general meeting following an acquisition (as defined in the Articles), all directors shall retire from office and may offer themselves for reappointment by the shareholders by ordinary resolution.

At every subsequent annual general meeting any director who either (i) has been appointed by the board of directors since the last annual general meeting or (ii) was not appointed or reappointed at one of the preceding two annual general meetings, must retire from office and may offer themselves for reappointment by the shareholders by ordinary resolution.

Subject to the provisions of the Articles, the board of directors may regulate their proceedings as they deem appropriate. A director may, and the secretary at the request of a director shall, call a meeting of the directors.

The quorum for a meeting of the board of directors shall be fixed from time to time by a decision of the board of directors, but it must never be less than two and unless otherwise fixed, it is two.

Questions and matters requiring resolution arising at a meeting shall be decided by a majority of votes of the participating directors, with each director having one vote. In the case of an equality of votes, the chairman will only have a casting vote or second vote when an acquisition has been

completed. The entering into any acquisition requires the consent of 75% of the directors present and entitled to vote.

Directors shall be entitled to receive such remuneration as the board shall determine for their services to the company as directors, and for any other service which they undertake for the company provided that the aggregate fees payable to the directors must not exceed £250,000 per annum. The directors shall also be entitled to be paid all reasonable expenses properly incurred by them in connection with their attendance at meetings of shareholders or class meetings, board of director or committee meetings or otherwise in connection with the exercise of their powers and the discharge of their responsibilities in relation to the company.

The board of directors may, in accordance with the requirements in the Articles, authorize any matter proposed to them by any director which would, if not authorized, involve a director breaching his duty under the Companies Act, to avoid conflicts of interests.

A director seeking authorization in respect of such conflict shall declare to the board of directors the nature and extent of his interest in a conflict as soon as is reasonably practicable. The director shall provide the board with such details of the matter as are necessary for the board to decide how to address the conflict together with such additional information as may be requested by the board.

Any authorization by the board of directors will be effective only if:

(i) to the extent permitted by the Companies Act, the matter in question shall have been proposed by any director for consideration in the same way that any other matter may be proposed to the directors under the provisions of the Articles;

(ii) any requirement as to the quorum for consideration of the relevant matter is met without counting the conflicted director and any other conflicted director; and

(iii) the matter is agreed to without the conflicted director voting or would be agreed to if the conflicted director's and any other interested director's vote is not counted.

Subject to the provisions of the Companies Act, every director, secretary or other officer of the company (other than an auditor) is entitled to be indemnified against all costs, charges, losses, damages and liabilities incurred by him in the actual purported exercise or discharge of his duties or exercise of his powers or otherwise in relation to them.

General Meetings

The company must convene and hold annual general meetings in accordance with the Companies Act. Under the Companies Act, an annual general meeting must be called by notice of at least 21 days.

No business shall be transacted at any general meeting unless a quorum is present when the meeting proceeds to business, but the absence of a quorum shall not preclude the choice or appointment of a chairman of the meeting which shall not be treated as part of the business of the meeting. Save as otherwise provided by the Articles, two shareholders present in person or by proxy and entitled to vote shall be a quorum for all purposes.

Borrowing Powers

Subject to the Articles and the Companies Act, the board of directors may exercise all of the powers of the company to:

(a) borrow money;

(b) indemnify and guarantee;

(c) mortgage or charge;

(d) create and issue debentures and other securities; and

(e) give security either outright or as collateral security for any debt, liability or obligation of the company or of any third party.

The borrowing powers are restricted to the sum of £25,000,000 but this limit may be increased by ordinary resolutions of shareholders.

(ii) Capitalization of profits
The directors may, if they are so authorized by an ordinary resolution of the shareholders, decide to capitalize any undivided profits of the company (whether or not they are available for distribution), or any sum standing to the credit of the company's share premium account or capital redemption reserve. The directors may also, subject to the aforementioned ordinary resolution, appropriate any sum which they so decide to capitalize to the persons who would have been entitled to it if it were distributed by way of dividend and in the same proportions.

(iii) Uncertificated Shares
Subject to the Companies Act, the board of directors may permit title to shares of any class to be issued or held otherwise than by a certificate and to be transferred by means of a "relevant system" (i.e., the CREST System) without a certificate.

The board of directors may take such steps as it sees fit in relation to the evidencing of and transfer of title to uncertificated shares, any records relating to the holding of uncertificated shares and the conversion of uncertificated shares to certificated shares, or vice-versa.

The company may by notice to the holder of an uncertificated share, require that share to be converted into certificated form.

The board of directors may take such other action that the board considers appropriate to achieve the sale, transfer, disposal, forfeiture, re-allotment or surrender of an uncertified share or otherwise to enforce a lien in respect of it.

Other Relevant Laws and Regulations

Mandatory Bid

(i) The Takeover Code applies to the company. Under the Takeover Code, where:

(a) any person, together with persons acting in concert with him, acquires, whether by a series of transactions over a period of time or not, an interest in shares which (taken together with shares in which he is already interested, and in which persons acting in concert with him are interested) carry 30% or more of the voting rights of a company; or

(b) any person who, together with persons acting in concert with him, is interested in shares which in the aggregate carry not less than 30% of the voting rights of a company but does not hold shares carrying more than 50% of such voting rights and such person, or any person acting in concert with him, acquires an interest in any other shares which increases the percentage of shares carrying voting rights in which he is interested,

such person shall, except in limited circumstances, be obliged to extend offers, on the basis set out in Rules 9.3, 9.4 and 9.5 of the Takeover Code, to the holders of any class of equity share capital, whether voting or non- voting, and also to the holders of any other class of transferable securities carrying voting rights. Offers for different classes of equity share capital must be comparable; the Takeover Panel should be consulted in advance in such cases.

(ii) An offer under Rule 9 of the Takeover Code must be in cash and at the highest price paid for any interest in the shares by the person required to make an offer or any person acting in concert with him during the 12 months prior to the announcement of the offer.

(iii) Under the Takeover Code, a "concert party" arises where persons acting together pursuant to an agreement or understanding (whether formal or informal and whether or not in writing) actively cooperate, through the acquisition by them of an interest in shares in a company, to obtain or consolidate control of the company. "Control" means holding, or aggregate holdings, of an interest in shares carrying 30% or more of the voting rights of the company, irrespective of whether the holding or holdings give *de facto* control.

Squeeze-out

(i) Under sections 979 to 982 of the Companies Act, if an offeror were to acquire, or unconditionally contract to acquire, not less than 90% of the ordinary shares of the company, it could then compulsorily acquire the remaining 10%. It would do so by sending a notice to outstanding shareholders telling them that it will compulsorily acquire their shares, provided that no such notice may be served after the end of: (a) the period of three months beginning with the day after the last day on which the offer can be accepted; or (b) if earlier, and the offer is not one to which section 943(1) of the Companies Act applies, the period of six months beginning with the date of the offer.

(ii) Six weeks following service of the notice, the offeror must send a copy of it to the company together with the consideration for the ordinary shares to which the notice relates, and an instrument of transfer executed on behalf of the outstanding shareholder(s) by a person appointed by the offeror.

(iii) The company will hold the consideration on trust for the outstanding shareholders.

Sell-out

(i) Sections 983 to 985 of the Companies Act also give minority shareholders in the company a right to be bought out in certain circumstances by an offeror who has made a takeover offer. If a takeover offer relating to all the ordinary shares of the company is made at any time before the end of the period within which the offer could be accepted and the offeror held or had agreed to acquire not less than 90% of the ordinary shares, any holder of shares to which the offer related who had not accepted the offer could by a written communication to the offeror require it to acquire those shares. The offeror is required to give any shareholder notice of his right to be bought out within one month of that right arising. The offeror may impose a time limit on the rights of minority shareholders to be bought out, but that period cannot end less than three months after the end of the acceptance period, or, if longer a period of three months from the date of the notice.

(ii) If a shareholder exercises his rights, the offeror is bound to acquire those shares on the terms of the offer or on such other terms as may be agreed.

Shareholder Notification and Disclosure Requirements

(i) Shareholders are obliged to comply with the shareholding notification and disclosure requirements set out in Chapter 5 of the Disclosure Guidance and Transparency Rules, or DTRs. A shareholder is required pursuant to Rule 5 of the DTRs to notify the company if, as a result of an acquisition or disposal of shares or financial instruments, the shareholder's percentage of voting rights of the company reaches, exceeds or falls below 3% of the nominal value of the company's share capital or any 1% threshold above that.

(ii) The DTRs can be accessed and downloaded from the FCA's website at http://fshandbook.info/FS/html/FCA/DTR. Shareholders are urged to consider their notification and disclosure obligations carefully as a failure to make a required disclosure to the company may result in disenfranchisement.

Differences in Corporate Law

The applicable provisions of the Companies Act differ from laws applicable to U.S. corporations and their shareholders. Set forth below is a summary of certain differences between the provisions of the Companies Act applicable to us and the General Corporation Law of the State of Delaware relating to shareholders' rights and protections. This summary is not intended to be a complete discussion of the respective rights and it is qualified in its entirety by reference to Delaware law and English law.

	ENGLAND AND WALES	**DELAWARE**
Number of Directors	Under the Companies Act, a public limited company must have at least two directors and the number of directors may be fixed by or in the manner provided in a company's articles of association.	Under Delaware law, a corporation must have at least one director and the number of directors shall be fixed by or in the manner provided in the bylaws.
Removal of Directors	Under the Companies Act, shareholders may remove a director without cause by an ordinary resolution (which is passed by a simple majority of those voting in person or by proxy at a general meeting) irrespective of any provisions of any service contract the director has with the company, provided 28 clear days' notice of the resolution has been given to the company and its shareholders. On receipt of notice of an intended resolution to remove a director, the company must forthwith send a copy of the notice to the director concerned. Certain other procedural requirements under the Companies Act must also be followed, such as allowing the director to make representations against his or her removal either at the meeting or in writing.	Under Delaware law, any director or the entire board of directors may be removed, with or without cause, by the holders of a majority of the shares then entitled to vote at an election of directors, except (i) unless the certificate of incorporation provides otherwise, in the case of a corporation whose board of directors is classified, stockholders may effect such removal only for cause, or (ii) in the case of a corporation having cumulative voting, if less than the entire board of directors is to be removed, no director may be removed without cause if the votes cast against his removal would be sufficient to elect him if then cumulatively voted at an election of the entire board of directors, or, if there are classes of directors, at an election of the class of directors of which he is a part.

Vacancies on the Board of Directors	Under English law, the procedure by which directors, other than a company's initial directors, are appointed is generally set out in a company's articles of association, provided that where two or more persons are appointed as directors of a public limited company by resolution of the shareholders, resolutions appointing each director must be voted on individually.	Under Delaware law, vacancies and newly created directorships may be filled by a majority of the directors then in office (even though less than a quorum) or by a sole remaining director unless (i) otherwise provided in the certificate of incorporation or bylaws of the corporation or (ii) the certificate of incorporation directs that a particular class of stock is to elect such director, in which case a majority of the other directors elected by such class, or a sole remaining director elected by such class, will fill such vacancy.
Annual General Meeting	Under the Companies Act, a public limited company must hold an annual general meeting in each six-month period following the company's annual accounting reference date.	Under Delaware law, the annual meeting of stockholders shall be held at such place, on such date and at such time as may be designated from time to time by the board of directors or as provided in the certificate of incorporation or by the bylaws.

General Meeting	Under the Companies Act, a general meeting of the shareholders of a public limited company may be called by the directors. Shareholders holding at least 5% of the paid-up capital of the company carrying voting rights at general meetings (excluding any paid up capital held as treasury shares) can require the directors to call a general meeting and, if the directors fail to do so within a certain period, may themselves convene a general meeting.	Under Delaware law, special meetings of the stockholders may be called by the board of directors or by such person or persons as may be authorized by the certificate of incorporation or by the bylaws.
Notice of General Meetings	Under the Companies Act, at least 21 days' notice must be given for an annual general meeting and any resolutions to be proposed at the meeting. Subject to a company's articles of association providing for a longer period, at least 14 days' notice is required for any other general meeting of a public limited company. In addition, certain matters, such as the removal of directors or auditors, require special notice, which is 28 days' notice. The shareholders of a company may in all cases consent to a shorter notice period, the proportion of shareholders' consent required being 100% of those entitled to attend and vote in the case of an annual general meeting and, in the case of any other general meeting, a majority in number of the members having a right to attend and vote at the meeting, being a majority who together hold not less than 95% in nominal value of the shares giving a right to attend and vote at the meeting.	Under Delaware law, unless otherwise provided in the certificate of incorporation or bylaws, written notice of any meeting of the stockholders must be given to each stockholder entitled to vote at the meeting not less than ten nor more than 60 days before the date of the meeting and shall specify the place, date, hour and purpose or purposes of the meeting.
Proxy	Under the Companies Act, at any meeting of shareholders, a shareholder may designate another person to attend, speak and vote at the meeting on their behalf by proxy.	Under Delaware law, at any meeting of stockholders, a stockholder may designate another person to act for such stockholder by proxy, but no such proxy shall be voted or acted upon after three years from its date, unless the proxy provides for a longer period. A director of a Delaware corporation may not issue a proxy representing the director's voting rights as a director.

Preemptive Rights	Under the Companies Act, “equity securities,” being (i) shares in the company other than shares that, with respect to dividends and capital, carry a right to participate only up to a specified amount in a distribution, referred to as “ordinary shares,” or (ii) rights to subscribe for, or to convert securities into, ordinary shares, proposed to be allotted for cash must be offered first to the existing equity shareholders in the company in proportion to the respective nominal value of their holdings, unless an exception applies or a special resolution to the contrary has been passed by shareholders in a general meeting or the articles of association provide otherwise in each case in accordance with the provisions of the Companies Act.	Under Delaware law, shareholders have no preemptive rights to subscribe to additional issues of stock or to any security convertible into such stock unless, and except to the extent that, such rights are expressly provided for in the certificate of incorporation.
Authority to Allot	Under the Companies Act, the directors of a company must not allot shares or grant rights to subscribe for or convert any security into shares unless an exception applies or an ordinary resolution to the contrary has been passed by shareholders in a general meeting or the articles of association provide otherwise, in each case in accordance with the provisions of the Companies Act.	Under Delaware law, if the corporation’s charter or certificate of incorporation so provides, the board of directors has the power to authorize the issuance of stock. The board may authorize capital stock to be issued for consideration consisting of cash, any tangible or intangible property or any benefit to the corporation or any combination thereof. It may determine the amount of such consideration by approving a formula. In the absence of actual fraud in the transaction, the judgment of the directors as to the value of such consideration is conclusive.

Liability of Directors and Officers	Under the Companies Act, any provision, whether contained in a company's articles of association or any contract or otherwise, that purports to exempt a director of a company, to any extent, from any liability that would otherwise attach to him in connection with any negligence, default, breach of duty or breach of trust in relation to the company, is void. Any provision by which a company directly or indirectly provides an indemnity, to any extent, for a director of the company or of an associated company against any liability attaching to him in connection with any negligence, default, breach of duty or breach of trust in relation to the company of which he is a director is also void except as permitted by the Companies Act, which provides exceptions for the company to (i) purchase and maintain insurance against such liability; (ii) provide a "qualifying third party indemnity," or an indemnity against liability incurred by the director to a person other than the company or an associated company or criminal proceedings in which he is convicted; and (iii) provide a "qualifying pension scheme indemnity," or an indemnity against liability incurred in connection with the company's activities as trustee of an occupational pension plan.	Under Delaware law, a corporation's certificate of incorporation may include a provision eliminating or limiting the personal liability of a director to the corporation and its stockholders for damages arising from a breach of fiduciary duty as a director. However, no provision can limit the liability of a director for: ▪ any breach of the director's duty of loyalty to the corporation or its stockholders; ▪ acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law; ▪ intentional or negligent payment of unlawful dividends or stock purchases or redemptions; or ▪ any transaction from which the director derives an improper personal benefit.
Voting Rights	Under English law, unless a poll is demanded by the shareholders of a company or is required by the chairman of the meeting or the company's articles of association, shareholders shall vote on all resolutions on a show of hands. Under the Companies Act, a poll may be demanded by (i) not fewer than five shareholders having the right to vote on the resolution; (ii) any shareholder(s) representing not less than 10% of the total voting rights of all the shareholders having the right to vote on the resolution (excluding any voting rights attaching to treasury shares); or (iii) any shareholder(s) holding shares in the company conferring a right to vote on the resolution (excluding any voting rights attaching to treasury shares) being shares on which an aggregate sum has been paid up equal to not less than 10% of the total sum paid up on all the shares conferring that right. A company's articles of association may provide more extensive rights for shareholders to call a poll. Under English law, an ordinary resolution is passed on a show of hands if it is approved by a simple majority (more than 50%) of the votes cast by shareholders present (in person or by proxy) and entitled to vote. If a poll is demanded, an ordinary resolution is passed if it is approved by holders representing a simple majority of the total voting rights of shareholders present, in person or by proxy, who, being entitled to vote, vote on the resolution. Special resolutions require the affirmative vote of not less than 75% of the votes cast by shareholders present, in person or by proxy, at the meeting.	Delaware law provides that, unless otherwise provided in the certificate of incorporation, each stockholder is entitled to one vote for each share of capital stock held by such stockholder.

Shareholder Vote on Certain Transactions	The Companies Act provides for schemes of arrangement, which are arrangements or compromises between a company and any class of shareholders or creditors and used in certain types of reconstructions, amalgamations, capital reorganizations or takeovers. These arrangements require: ▪ the approval at a shareholders' or creditors' meeting convened by order of the court, of a majority in number of shareholders or creditors representing 75% in value of the capital held by, or debt owed to, the class of shareholders or creditors, or class thereof present and voting, either in person or by proxy; and ▪ the approval of the court.	Generally, under Delaware law, unless the certificate of incorporation provides for the vote of a larger portion of the stock, completion of a merger, consolidation, sale, lease or exchange of all or substantially all of a corporation's assets or dissolution requires: ▪ the approval of the board of directors; and ▪ the approval by the vote of the holders of a majority of the outstanding stock or, if the certificate of incorporation provides for more or less than one vote per share, a majority of the votes of the outstanding stock of the corporation entitled to vote on the matter.

Standard of Conduct for Directors	Under English law, a director owes various statutory and fiduciary duties to the company, including: ▪ to act in the way he considers, in good faith, would be most likely to promote the success of the company for the benefit of its members as a whole; ▪ to avoid a situation in which he has, or can have, a direct or indirect interest that conflicts, or possibly conflicts, with the interests of the company; ▪ to act in accordance with the company's constitution and only exercise his powers for the purposes for which they are conferred; ▪ to exercise independent judgment; ▪ to exercise reasonable care, skill and diligence; ▪ not to accept benefits from a third party conferred by reason of his being a director or doing, or not doing, anything as a director; and ▪ to declare any interest that he has, whether directly or indirectly, in a proposed or existing transaction or arrangement with the company.	Delaware law does not contain specific provisions setting forth the standard of conduct of a director. The scope of the fiduciary duties of directors is generally determined by the courts of the State of Delaware. In general, directors have a duty to act without self-interest, on a well- informed basis and in a manner they reasonably believe to be in the best interest of the stockholders. Directors of a Delaware corporation owe fiduciary duties of care and loyalty to the corporation and to its shareholders. The duty of care generally requires that a director act in good faith, with the care that an ordinarily prudent person would exercise under similar circumstances. Under this duty, a director must inform himself of all material information reasonably available regarding a significant transaction. The duty of loyalty requires that a director act in a manner he reasonably believes to be in the best interests of the corporation. He must not use his corporate position for personal gain or advantage. In general, but subject to certain exceptions, actions of a director are presumed to have been made on an informed basis, in good faith and in the honest belief that the action taken was in the best interests of the corporation. However, this presumption may be rebutted by evidence of a breach of one of the fiduciary duties. Delaware courts have also imposed a heightened standard of conduct upon directors of a Delaware corporation who take any action designed to defeat a threatened change in control of the corporation. In addition, under Delaware law, when the board of directors of a Delaware corporation approves the sale or break-up of a corporation, the board of directors may, in certain circumstances, have a duty to obtain the highest value reasonably available to the shareholders.
Stockholder Suits	Under English law, generally, the company, rather than its shareholders, is the proper claimant in an action in respect of a wrong done to the company or where there is an irregularity in the company's internal management. Notwithstanding this general position, the Companies Act provides that a court may allow a shareholder to bring a derivative claim (that is, an action in respect of and on behalf of the company) in respect of a cause of action arising from a director's negligence, default, breach of duty or breach of trust and (ii) a shareholder may bring a claim for a court order where the company's affairs have been or are being conducted in a manner that is unfairly prejudicial to some of its shareholders.	Under Delaware law, a stockholder may initiate a derivative action to enforce a right of a corporation if the corporation fails to enforce the right itself. The complaint must: ▪ state that the plaintiff was a stockholder at the time of the transaction of which the plaintiff complains or that the plaintiffs shares thereafter devolved on the plaintiff by operation of law; and ▪ allege with particularity the efforts made by the plaintiff to obtain the action the plaintiff desires from the directors and the reasons for the plaintiff's failure to obtain the action; or ▪ state the reasons for not making the effort. Additionally, the plaintiff must remain a stockholder through the duration of the derivative suit. The action will not be dismissed or compromised without the approval of the Delaware Court of Chancery

C. Material Contracts

Except as otherwise set forth below or as otherwise disclosed in this registration statement on Form 20-F (including the Exhibits), we are not currently, and have not been in the last two years, party to any material contract, other than contracts entered into in the ordinary course of business. See the section titled "Business-Collaboration and License Agreements" in Section 4B. herein.

D. Exchange Controls

Other than certain economic sanctions which may be in place from time to time, there are currently no UK laws, decrees or regulations restricting the import or export of capital or affecting the remittance of dividends or other payment to holders of ordinary shares who are non-residents of the United Kingdom. Similarly, other than certain economic sanctions which may be in force from time to time, there are no limitations relating only to nonresidents of the United Kingdom under English law or the Company's articles of association on the right to be a holder of, and to vote in respect of, the ordinary shares.

E. Taxation

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

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

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

If an entity that is classified as a partnership for U.S. federal income tax purposes holds ordinary shares or ADSs, the

U.S. federal income tax treatment of a partner will generally depend on the status of the partner and the activities of the partnership. Partnerships holding ordinary shares or ADSs and partners in such partnerships are encouraged to consult their tax advisers as to the particular U.S. federal income tax consequences of holding and disposing of ordinary shares or ADSs.

The discussion is based on the Internal Revenue Code of 1986, as amended, or the Code, administrative pronouncements, judicial decisions, final, temporary and proposed Treasury Regulations, and the income tax treaty between the United Kingdom and the United States, or the Treaty, all as of the date hereof, changes to any of which may affect the tax consequences described herein—possibly with retroactive effect.

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

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

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

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

(iv) a trust if (1) a U.S. court is able to exercise primary supervision over the administration of the trust and one or more U.S. persons have authority to control all substantial decisions of the trust or (2) the trust has a valid election to be treated as a U.S. person under applicable U.S. Treasury Regulations.

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

A partner in a partnership or other pass-through entity or arrangement classified as a partnership for U.S. federal income tax purposes that will hold our common stock should consult his, her or its own tax advisor regarding the tax consequences of acquiring, holding and disposing of our ADSs through a partnership or other pass-through entity, as applicable.

The discussion below assumes that the representations contained in the deposit agreement are true and that the obligations in the deposit agreement and any related agreement will be complied with in accordance with their terms. Generally, a holder of an ADS should be treated for U.S. federal income tax purposes as holding the ordinary shares represented by the ADS. Accordingly, no gain or loss will be recognized upon an exchange of ADSs for ordinary shares. The U.S. Treasury has expressed concerns that intermediaries in the chain of ownership between the holder of an ADS and the issuer of the security underlying the ADS may be taking actions that are inconsistent with the beneficial ownership of the underlying security. Accordingly the creditability of foreign taxes, if any, as described below, could be affected by actions taken by intermediaries in the chain of ownership between the holders of ADSs and our company if as a result of such actions the holders of ADSs are not properly treated as beneficial owners of the underlying ordinary shares.

Passive Foreign Investment Company Rules

If we are classified as a PFIC in any taxable year, a U.S. Holder will be subject to special rules generally intended to reduce or eliminate any benefits from the deferral of U.S. federal income tax that a U.S. Holder could derive from investing in a non-U.S. company that does not distribute all of its earnings on a current basis.

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

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

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

Based on our estimates of expected gross assets and income for the current taxable year, we anticipate being classified as a PFIC for the year ending December 31, 2017. However, there can be no assurance that we will be classified as a PFIC for the current taxable year or any prior or future taxable year.

A separate determination must be made after the close of each taxable year as to whether we are a PFIC for that year. As a result, our PFIC status may change from year to year. The total value of our assets for purposes of the asset test generally will be calculated using the market price of the ordinary shares or ADSs, which may fluctuate considerably. Fluctuations in the market price of the ordinary shares or ADSs may result in our being a PFIC for any taxable year. Because of the uncertainties

involved in establishing our PFIC status, our United States tax counsel expresses no opinion regarding our PFIC status.

If we are classified as a PFIC in any year with respect to which a U.S. Holder owns the ordinary shares or ADSs, we will continue to be treated as a PFIC with respect to such U.S. Holder in all succeeding years during which the U.S. Holder owns the ordinary shares or ADSs, regardless of whether we continue to meet the tests described above unless (i) we cease to be a PFIC and the U.S. Holder has made a "deemed sale" election under the PFIC rules, or (ii) the U.S. Holder makes a Qualified Electing Fund Election, or QEF Election, with respect to all taxable years during such U.S. Holders holding period in which we are a PFIC. We do not expect that a U.S. Holder will be eligible to make a QEF Election with respect to our ordinary shares or ADSs. If the "deemed sale" election is made, a U.S. Holder will be deemed to have sold the ordinary shares or ADSs the U.S. Holder holds at their fair market value and any gain from such deemed sale would be subject to the rules described below. After the deemed sale election, so long as we do not become a PFIC in a subsequent taxable year, the U.S. Holder's ordinary shares or ADSs with respect to which such election was made will not be treated as shares in a PFIC and the U.S. Holder will not be subject to the rules described below with respect to any "excess distribution" the U.S.Holder receives from us or any gain from an actual sale or other disposition of the ordinary shares or ADSs. U.S. Holders should consult their tax advisors as to the possibility and consequences of making a deemed sale election if we cease to be a PFIC and such election becomes available.

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

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

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

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

U.S. Holders can avoid the interest charge on excess distributions or gain relating to the ordinary shares or ADSs by making a mark-to-market election with respect to the ordinary shares or ADSs, provided that the ordinary shares or ADSs are "marketable." Ordinary shares or ADSs will be marketable if they are "regularly traded" on certain U.S. stock exchanges or on a foreign stock exchange that meets certain conditions. For these purposes, the ordinary shares or ADSs will be considered regularly traded during any calendar year during which they are traded, other than in de minimis quantities, on at least 15 days during each calendar quarter. Any trades that have as their principal purpose meeting this requirement will be disregarded. Our ADSs will be listed on NASDAQ, which is a qualified exchange for these purposes. Consequently, if our ADSs remain listed on

NASDAQ and are regularly traded, and you are a holder of ADSs, we expect the mark-to-market election would be available to U.S. Holders if we are a PFIC. Each U.S. Holder should consult its tax advisor as to the whether a mark-to-market election is available or advisable with respect to the ordinary shares or ADSs.

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

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

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

Taxation of Distributions

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

converted into U.S. dollars after the date of receipt. Such gain or loss would generally be treated as U.S.-source ordinary income or loss. The amount of any distribution of property other than cash (and other than certain pro rata distributions of ordinary shares or ADSs or rights to acquire ordinary shares or ADSs) will be the fair market value of such property on the date of distribution.

For foreign tax credit limitation purposes, our dividends will generally be treated as passive category income. Because no U.K. income taxes will be withheld from dividends on ordinary shares or ADSs, there will be no creditable foreign taxes associated with any dividends that a U.S. Holder will receive. The rules governing foreign tax credits are complex and U.S. Holders should therefore consult their tax advisers regarding the effect of the receipt of dividends for foreign tax credit limitation purposes.

Sale or Other Taxable Disposition of Ordinary Shares and ADSs

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

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

WE STRONGLY URGE YOU TO CONSULT YOUR TAX ADVISOR REGARDING THE POTENTIAL APPLICATION OF THE PFIC RULES TO ANY FUTURE INVESTMENT IN OUR ORDINARY SHARES OR ADSs.

Information Reporting and Backup Withholding

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

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

Information with Respect to Foreign Financial Assets

Certain U.S. Holders who are individuals (and, under regulations, certain entities) may be required to report information relating to the ordinary shares or ADSs, subject to certain exceptions (including an exception for ordinary shares or ADSs held in accounts maintained by certain U.S. financial institutions). Such U.S. Holders who fail to timely furnish the required information may be subject to a penalty. Additionally, if a U.S. Holder does not file the required information, the statute of limitations with respect to tax returns of the U.S. Holder to which the information relates may not close

until three years after such information is filed. U.S. Holders should consult their tax advisers regarding their reporting obligations with respect to their ownership and disposition of the ordinary shares or ADSs.

U.K. Taxation

The following is intended as a general guide to current U.K. tax law and HM Revenue & Customs, or HMRC, published practice applying as at the date of this registration statement (both of which are subject to change at any time, possibly with retrospective effect) relating to the holding of ADSs. It does not constitute legal or tax advice and does not purport to be a complete analysis of all U.K. tax considerations relating to the holding of ADSs, or all of the circumstances in which holders of ADSs may benefit from an exemption or relief from U.K. taxation. It is written on the basis that the company is and remains solely resident in the U.K. for tax purposes and will therefore be subject to the U.K. tax regime and not the U.S. tax regime save as set out above under “Material U.S. Federal Income Tax Considerations for U.S. Holders.”

Except to the extent that the position of non-U.K. resident persons is expressly referred to, this guide relates only to persons who are resident for tax purposes solely in the U.K. and do not have a permanent establishment or fixed base in any other jurisdiction with which the holding of the ADSs is connected, or U.K. Holders, who are absolute beneficial owners of the ADSs (and do not hold the ADSs through an Individual Savings Account or a Self-Invested Personal Pension) and any dividends paid in respect of the ADSs or underlying ordinary shares (where the dividends are regarded for U.K. tax purposes as that person’s own income). It is assumed that for the purposes of this guide that a holder of an ADS is the beneficial owner of the underlying ordinary share for U.K. direct tax purposes.

This guide may not relate to certain classes of U.K. Holders, such as (but not limited to):

- persons who are connected with the company;
- financial institutions;
- insurance companies;
- charities or tax-exempt organizations;
- collective investment schemes;
- pension schemes;
- brokers or dealers in securities or persons who hold ADSs otherwise than as an investment;
- persons who have (or are deemed to have) acquired their ADSs by virtue of an office or employment or who are or have been officers or employees of the company or any of its affiliates; and
- individuals who are subject to U.K. taxation on a remittance basis.

THESE PARAGRAPHS ARE A SUMMARY OF CERTAIN U.K. TAX CONSIDERATIONS AND ARE INTENDED AS A GENERAL GUIDE ONLY. IT IS RECOMMENDED THAT ALL HOLDERS OF ADSs OBTAIN ADVICE AS TO THE CONSEQUENCES OF THE ACQUISITION, OWNERSHIP AND DISPOSAL OF OUR ADSs IN ANY FUTURE OFFERING, IN THEIR OWN PARTICULAR CIRCUMSTANCES FROM THEIR OWN TAX ADVISORS. IN PARTICULAR, NON-U.K. RESIDENT OR DOMICILED PERSONS ARE ADVISED TO CONSIDER THE POTENTIAL IMPACT OF ANY RELEVANT DOUBLE TAXATION AGREEMENTS.

Dividends

Withholding Tax

Dividends paid by the company will not be subject to any withholding or deduction for or on account of U.K. tax.

Income Tax

An individual U.K. Holder may, depending on his or her particular circumstances, be subject to U.K. tax on dividends received from the company. An individual holder of ADSs who is not resident for tax purposes in the United Kingdom should not be chargeable to U.K. income tax on dividends received from the company unless he or she carries on (whether solely or in partnership) a trade, profession or vocation in the U.K. through a permanent establishment to which the ADSs are attributable.

Dividend income is treated as the top slice of the total income chargeable to U.K. income tax. An individual U.K. Holder who receives a dividend in the 2017/2018 tax year will be entitled to a tax-free allowance of £5,000. The allowance will reduce to £2,000 for dividends received on or after 6 April 2018.

Dividend income in excess of this tax-free allowance will be charged at 7.5% for basic rate taxpayers, 32.5% for higher rate taxpayers, and 38.1% for additional rate taxpayers.

Corporation Tax

A corporate holder of ADSs who is not resident for tax purposes in the United Kingdom should not be chargeable to U.K. corporation tax on dividends received from the company unless it carries on (whether solely or in partnership) a trade in the United Kingdom through a permanent establishment to which the ADSs are attributable.

Corporate U.K. Holders should not be subject to U.K. corporation tax on any dividend received from the company so long as the dividends qualify for exemption, which should be the case, although certain conditions must be met. If the conditions for the exemption are not satisfied, or such U.K. Holder elects for an otherwise exempt dividend to be taxable, U.K. corporation tax will be chargeable on the amount of any dividends (at the current main rate of 19%).

Chargeable Gains

A disposal or deemed disposal of ADSs by a U.K. Holder may, depending on the U.K. Holder's circumstances and subject to any available exemptions or reliefs (such as the annual exemption), give rise to a chargeable gain or an allowable loss for the purposes of U.K. capital gains tax and corporation tax on chargeable gains.

If an individual U.K. Holder who is subject to U.K. income tax at either the higher or the additional rate is liable to U.K. capital gains tax on the disposal of ADSs, the current applicable rate will be 20%. For an individual U.K. Holder who is subject to U.K. income tax at the basic rate and liable to U.K. capital gains tax on such disposal, the current applicable rate would be 10%, save to the extent that any capital gains exceed the unused basic rate tax band. In that case, the rate currently applicable to the excess would be 20%.

If a corporate U.K. Holder becomes liable to U.K. corporation tax on the disposal of ADSs, the main rate of U.K. corporation tax (currently 19%) would apply. An indexation allowance may be available to such a holder to give an additional deduction based on the indexation of its base cost in the shares by reference to U.K. retail price inflation over its holding period. An indexation allowance can only reduce a gain on a future disposal, and cannot create a loss. It should be noted that changes were announced in the Autumn Budget on 22 November 2017 and draft provisions are contained in Finance Bill 2017-18 (as published on 1 December 2017) which will (if enacted) restrict the application of indexation relief to assets acquired prior to 1 January 2018 and, in addition, will change the calculation of the relief for disposals (or deemed disposals) of such assets on or after 1 January 2018 so as to apply the Retail Price Index for December 2017 regardless of the actual date of disposal.

A holder of ADSs which is not resident for tax purposes in the U.K. should not normally be liable to U.K. capital gains tax or corporation tax on chargeable gains on a disposal of ADSs. However, an individual holder of ADSs who has ceased to be resident for tax purposes in the U.K. for a period of less than five years and who disposes of ADSs during that period may be liable on his or her return to the United Kingdom to U.K. tax on any capital gain realized (subject to any available exemption or relief).

Stamp Duty and Stamp Duty Reserve Tax

The discussion below relates to the holders of our ordinary shares or ADSs wherever resident.

Issue of Ordinary Shares

No U.K. stamp duty or stamp duty reserve tax, or SDRT, is payable on the issue of the underlying ordinary shares in the company.

Transfers of Ordinary Shares

Neither U.K. stamp duty nor SDRT should arise on transfers of the underlying ordinary shares (including instruments transferring ordinary shares and agreements to transfer ordinary shares) on the basis that the ordinary shares are admitted to trading on AIM, provided the following requirements are (and continue to be) met:

- the ordinary shares are admitted to trading on AIM, but are not listed on any market (with the term "listed" being construed in accordance with section 99A of the Finance Act 1986), and this has been certified to Euroclear; and
- AIM continues to be accepted as a "recognised growth market" as construed in accordance with section 99A of the Finance Act 1986).

In the event that either of the above requirements is not met, stamp duty or SDRT will apply to transfers of, or agreements to transfer, ordinary shares. Where applicable, the purchaser normally pays the stamp duty or SDRT.

Transfers of ADSs

No U.K. stamp duty will in practice be payable on a written instrument transferring an ADS provided that the instrument of transfer is executed and remains at all times outside the United Kingdom. Where these conditions are not met, the transfer of, or agreement to transfer, an ADS could, depending on the circumstances, attract a charge to U.K. stamp duty at the rate of 0.5% of the value of the consideration. No SDRT will be payable in respect of agreement to transfer an ADS.

F. Dividends and Paying Agents

We have never declared or paid a dividend, and we do not anticipate declaring or paying dividends in the foreseeable future. We intend to retain all available funds and any future earnings to fund the development and expansion of our business. See "Risk Factors—Risks Related to the Ownership of Our Securities—Because we do not anticipate paying any cash dividends on our ADSs in the foreseeable future, capital appreciation, if any, will be your sole source of gains and you may never receive a return on your investment."

Under English law, among other things, we may only pay dividends if we have sufficient distributable reserves (on a non-consolidated basis), which are our accumulated realized profits that have not been previously distributed or capitalized less our accumulated realized losses, so far as such losses have not been previously written off in a reduction or reorganization of capital.

G. Statements by Experts

The financial statements of Tiziana Life Sciences PLC as of December 31, 2016 and 2015 and for each of the three years in the period ended December 31, 2016 included in this Registration Statement have been so included in reliance on the audit report of Mazars LLP, independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting. Mazars LLP is a member of the Institute of Chartered Accountants of England and Wales.

H. Documents on Display

When this registration statement on Form 20-F becomes effective, we will be subject to the information reporting requirements of the Exchange Act applicable to foreign private issuers, and

under those requirements will file reports with the SEC. Those other reports or other information and this registration statement may be inspected without charge and copied at the public reference facilities of the SEC located at 100 F Street, N.E., Washington, D.C. 20549. You may also obtain copies of the documents at prescribed rates by writing to the Public Reference Section of the SEC at 100 F Street, N.E., Washington, DC 20549. Please call the SEC at 1-800-SEC-0330 for further information on the public reference room. The SEC also maintains a website at http://www.sec.gov from which certain filings may be accessed.

As a foreign private issuer, we will be exempt from the rules under the Exchange Act related to the furnishing and content of proxy statements, and our officers, directors and principal shareholders will be exempt from the reporting and short-swing profit recovery provisions contained in Section 16 of the Exchange Act. In addition, we will not be required under the Exchange Act to file annual, quarterly and current reports and financial statements with the SEC as frequently or as promptly as U.S. companies whose securities are registered under the Exchange Act. However, for so long as we are listed on NASDAQ, or any other U.S. exchange, and are registered with the SEC, we will file with the SEC, within 120 days after the end of each fiscal year, or such applicable time as required by the SEC, an annual report on Form 20-F containing financial statements audited by an independent registered public accounting firm, and will submit to the SEC, on a Form 6-K, unaudited quarterly financial information for the first three quarters of each year.

We will maintain a corporate website. Information contained on, or that can be accessed through, our website does not constitute a part of this registration statement on Form 20-F.

I. Subsidiary Information

For information on our subsidiaries, see "Item 4C. Organizational Structure."

ITEM 11: QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

We are exposed to market risks in the ordinary course of our business, which are principally limited to interest rate fluctuations and foreign currency exchange rate fluctuations. We maintain significant amounts of cash and cash equivalents that are in excess of federally insured limits in various currencies, placed with one or more financial institutions for varying periods according to expected liquidity requirements.

Interest Rate Risk

As of June 30, 2017 (unaudited), we had cash and cash equivalents of $2.6 million and as of December 31, 2016, we had cash and cash equivalents of $5.8 million. Our exposure to interest rate sensitivity is impacted by changes in the underlying U.S. and U.K. bank interest rates. Our surplus cash and cash equivalents have been invested in interest-bearing savings and money market accounts from time to time. We have not entered into investments for trading or speculative purposes. Due to the conservative nature of our investment portfolio, which is predicated on capital preservation of investments with short-term maturities, we do not believe an immediate one percentage point change in interest rates would have a material effect on the fair market value of our portfolio, and therefore we do not expect our operating results or cash flows to be significantly affected by changes in market interest rates.

Foreign Currency Exchange Risk

We maintain our consolidated financial statements in the functional currency pounds Sterling. Monetary assets and liabilities denominated in currencies other than the functional currency are translated into the functional currency at rates of exchange prevailing at the balance sheet dates. Non-monetary assets and liabilities denominated in foreign currencies are translated into the functional currency at the exchange rates prevailing at the date of the transaction. Exchange gains or losses arising from foreign currency transactions are included in the determination of net income (loss) for the respective periods.

For financial reporting purposes, our consolidated financial statements are prepared using the functional currency, and translated into the U.S. dollar. Assets and liabilities are translated at the exchange rates at the balance sheet dates and revenue and expenses are translated at the average exchange rates and shareholders' equity is translated based on historical exchange rates. Translation

adjustments are not included in determining net income (loss) but are included in foreign exchange adjustment to accumulate other comprehensive loss, a component of shareholders' equity.

We do not currently engage in currency hedging activities in order to reduce our currency exposure, but we may begin to do so in the future. Instruments that may be used to hedge future risks may include foreign currency forward and swap contracts. These instruments may be used to selectively manage risks, but there can be no assurance that we will be fully protected against material foreign currency fluctuations.

ITEM 12: DESCRIPTION OF SECURITIES OTHER THAN EQUITY SECURITIES

A. Debt Securities

Not applicable.

B. Warrants and Rights

We have 4,931,246 warrants outstanding to acquire new ordinary shares at various prices. A summary of the key terms of the warrants are set out below:

Class	No. outstanding	Exercise Price $	Exercise Price £	Final Exercise Date
"API"	329,926	$0.65	£0.50	12/31/2021
"Special"	600,000	$0.65	£0.50	12/31/2021
"C"	2,048,685	$0.87	£0.66	12/31/2021
"D"	50,000	$1.38	£1.05	12/31/2021
"E"	1,021,792	$3.29	£2.50	12/31/2021
"F"	189,176	$3.29	£2.50	12/31/2021
"G"	100,000	$2.21	£1.60	12/31/2023
"H"	183,333	$2.21	£1.60	12/31/2023
"I"	196,667	$2.21	£1.60	12/31/2023
"J"	131,667	$2.21	£1.60	1/15/2024
"K"	80,000	$2.21	£1.60	1/22/2024

C. Other Securities

Not applicable.

D. American Depositary Shares

The Bank of New York Mellon has agreed to act as the depositary for the ADSs. The Bank of New York Mellon's depositary offices are located at 101 Barclay Street, New York, New York 10286. The Bank of New York Mellon's principal executive office is located at 225 Liberty Street, New York, New York 10286. ADSs represent ownership interests in securities that are on deposit with the depositary. ADSs may be represented by certificates that are commonly known as American Depositary Receipts, or ADRs. The depositary typically appoints a custodian to safekeep the securities on deposit. In this case, the custodian is The Bank of New York Mellon (London Branch) located at One Canada Square, Canary Wharf, London E14 5AL.

We have appointed The Bank of New York Mellon as depositary pursuant to a deposit agreement. A copy of the deposit agreement is on file with the SEC under cover of a registration statement on Form F-6. You may obtain a copy of the deposit agreement from the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549 and from the SEC's website (www.sec.gov).

We are providing you with a summary description of the material terms of the ADSs and of your material rights as an owner of ADSs. Please remember that summaries by their nature lack the precision of the information summarized and that the rights and obligations of an owner of ADSs will be determined by reference to the terms of the deposit agreement and not by this summary. We urge you to review the deposit agreement in its entirety.

Each ADS represents the right to receive, and to exercise the beneficial ownership interests in, 5 ordinary shares that are on deposit with the depositary and/or custodian. An ADS also represents the right to receive, and to exercise the beneficial interests in, any other property received by the depositary or the custodian on behalf of the owner of the ADS but that has not been distributed to the owners of ADSs because of legal restrictions or practical considerations. We and the depositary may agree to change the ADS-to-ordinary share ratio by amending the deposit agreement. This amendment may give rise to, or change, the depositary fees payable by ADS owners. The custodian, the depositary and their respective nominees will hold all deposited property for the benefit of the holders and beneficial owners of ADSs. The deposited property does not constitute the proprietary assets of the depositary, the custodian or their nominees.

Beneficial ownership in the deposited property will under the terms of the deposit agreement be vested in the beneficial owners of the ADSs. The depositary, the custodian and their respective nominees will be the record holders of the deposited property represented by the ADSs for the benefit of the holders and beneficial owners of the corresponding ADSs. A beneficial owner of ADSs may or may not be the holder of ADSs. Beneficial owners of ADSs will be able to receive, and to exercise beneficial ownership interests

in, the deposited property only through the registered holders of the ADSs, the registered holders of the ADSs (on behalf of the applicable ADS owners) only through the depositary, and the depositary (on behalf of the owners of the corresponding ADSs) directly, or indirectly, through the custodian or their respective nominees, in each case upon the terms of the deposit agreement.

If you become an owner of ADSs, you will become a party to the deposit agreement and therefore will be bound to its terms and to the terms of any ADR that represents your ADSs. The deposit agreement and the ADR specify our rights and obligations as well as your rights and obligations as owner of ADSs and those of the depositary. As an ADS holder you appoint the depositary to act on your behalf in certain circumstances. The deposit agreement and the ADRs are governed by New York law. However, our obligations to the holders of ordinary shares will continue to be governed by the laws of England and Wales, which may be different from the laws of the United States.

In addition, applicable laws and regulations may require you to satisfy reporting requirements and obtain regulatory approvals in certain circumstances. You are solely responsible for complying with such reporting requirements and obtaining such approvals. Neither the depositary, the custodian, us or any of their or our respective agents or affiliates shall be required to take any actions whatsoever on your behalf to satisfy such reporting requirements or obtain such regulatory approvals under applicable laws and regulations.

As an owner of ADSs, we will not treat you as one of our shareholders and you will not have direct shareholder rights. The depositary will hold on your behalf the shareholder rights attached to the ordinary shares underlying your ADSs. As an owner of ADSs you will be able to exercise the shareholders rights for the ordinary shares represented by your ADSs through the depositary only to the extent contemplated in the deposit agreement. To exercise any shareholder rights not contemplated in the deposit agreement you will, as an ADS owner, need to arrange for the cancellation of your ADSs and become a direct shareholder.

As an owner of ADSs, you may hold your ADSs either by means of an ADR registered in your name, through a brokerage or safekeeping account, or through an account established by the depositary in your name reflecting the registration of uncertificated ADSs directly on the books of the depositary (commonly referred to as the direct registration system or DRS). The direct registration system reflects the uncertificated (book-entry) registration of ownership of ADSs by the depositary. Under the direct registration system, ownership of ADSs is evidenced by periodic statements issued by the depositary to the holders of the ADSs. The direct registration system includes automated transfers between the depositary and The Depository Trust Company, or DTC, the central book-entry clearing and settlement system for equity securities in the United States. If you decide to hold your ADSs through your brokerage or safekeeping account, you must rely on the procedures of your broker or bank to assert your rights as ADS owner. Banks and brokers typically hold securities such as the ADSs through clearing and settlement systems such as DTC. The procedures of such clearing and settlement systems may limit your ability to exercise your rights as an owner of ADSs. Please consult with your broker or bank if you have any questions concerning these limitations and procedures. All ADSs held through DTC will be registered in the name of a nominee of DTC. This summary description assumes you have opted to own the ADSs directly by means of an ADS registered in your name and, as such, we will refer to you as the “holder.” When we refer to “you,” we assume the reader owns ADSs and will own ADSs at the relevant time.

The registration of the ordinary shares in the name of the depositary or the custodian shall, to the maximum extent permitted by applicable law, vest in the depositary or the custodian the record ownership in the applicable ordinary shares with the beneficial ownership rights and interests in such ordinary shares being at all times vested with the beneficial owners of the ADSs representing the ordinary shares. The depositary or the custodian shall at all times be entitled to exercise the beneficial ownership rights in all deposited property, in each case only on behalf of the holders and beneficial owners of the ADSs representing the deposited property.

Dividends and Other Distributions

As a holder of ADSs, you generally have the right to receive the distributions we make on the securities deposited with the custodian. Your receipt of these distributions may be limited, however, by practical considerations and legal limitations. Holders of ADSs will receive such distributions under the terms of the deposit agreement in proportion to the number of ADSs held as of the specified record date, after deduction the applicable fees, taxes and expenses.

Distributions of Cash

Whenever we make a cash distribution for the securities on deposit with the custodian, we will deposit the funds with the custodian. Upon receipt of confirmation of the deposit of the requisite funds, the depositary will arrange for the funds to be converted into U.S. dollars and for the distribution of the U.S. dollars to the holders, subject to the laws and regulations of England and Wales.

The conversion into U.S. dollars will take place only if practicable and if the U.S. dollars are transferable to the United States. The depositary will apply the same method for distributing the proceeds of the sale of any property (such as undistributed rights) held by the custodian in respect of securities on deposit.

The distribution of cash will be made net of the fees, expenses, taxes and governmental charges payable by holders under the terms of the deposit agreement. The depositary will hold any cash amounts it is unable to distribute in a non-interest-bearing account for the benefit of the applicable holders and beneficial owners of ADSs until the distribution can be effected or the funds that the depositary holds must be escheated as unclaimed property in accordance with the laws of the relevant states of the United States.

Distributions of Shares

Whenever we make a free distribution of ordinary shares for the securities on deposit with the custodian, we will deposit the applicable number of ordinary shares with the custodian. Upon receipt of confirmation of such deposit, the depositary will either distribute to holders new ADSs representing the ordinary shares deposited or modify the ADS-to-ordinary shares ratio, in which case each ADS you hold will represent rights and interests in the additional ordinary shares so deposited. Only whole new ADSs will be distributed. Fractional entitlements will be sold and the proceeds of such sale will be distributed as in the case of a cash distribution.

The distribution of new ADSs or the modification of the ADS-to-ordinary share ratio upon a distribution of ordinary shares will be made net of the fees, expenses, taxes and governmental charges payable by holders under the terms of the deposit agreement. In order to pay such taxes or governmental charges, the depositary may sell all or a portion of the new ordinary shares so distributed.

No such distribution of new ADSs will be made if it would violate a law (e.g., the U.S. securities laws) or if it is not operationally practicable. If the depositary does not distribute new ADSs as described above, it may sell the ordinary shares received upon the terms described in the deposit agreement and will distribute the proceeds of the sale as in the case of a distribution of cash.

Distributions of Rights

Whenever we intend to distribute rights to purchase additional ordinary shares, we will give prior notice to the depositary and we will assist the depositary in determining whether it is lawful and reasonably practicable to distribute rights to purchase additional ADSs to holders.

The depositary will establish procedures to distribute rights to purchase additional ADSs to holders and to enable such holders to exercise such rights if it is lawful and reasonably practicable to make the rights available to holders of ADSs, and if we provide all of the documentation contemplated in the deposit agreement (such as opinions to address the lawfulness of the transaction). You may have to pay fees, expenses, taxes and other governmental charges to subscribe for the new ADSs

upon the exercise of your rights. The depositary is not obligated to establish procedures to facilitate the distribution and exercise by holders of rights to purchase new ordinary shares other than in the form of ADSs.

The depositary will *not* distribute the rights to you if:

- we do not timely request that the rights be distributed to you or we request that the rights not be distributed to you; or
- we fail to deliver satisfactory documents to the depositary; or
- it is not reasonably practicable to distribute the rights.

The depositary will sell the rights that are not exercised or not distributed if such sale is lawful and reasonably practicable. The proceeds of such sale will be distributed to holders as in the case of a cash distribution. If the depositary is unable to sell the rights, it will allow the rights to lapse.

Elective Distributions

Whenever we intend to distribute a dividend payable at the election of shareholders either in cash or in additional shares, we will give prior notice thereof to the depositary and will indicate whether we wish the elective distribution to be made available to you. In such case, we will assist the depositary in determining whether such distribution is lawful and reasonably practicable.

The depositary will make the election available to you only if it is reasonably practicable and if we have provided all of the documentation contemplated in the deposit agreement. In such case, the depositary will establish procedures to enable you to elect to receive either cash or additional ADSs, in each case as described in the deposit agreement.

If the election is not made available to you, you will receive either cash or additional ADSs, depending on what a shareholder in England and Wales would receive upon failing to make an election, as more fully described in the deposit agreement.

Other Distributions

Whenever we intend to distribute property other than cash, ordinary shares or rights to purchase additional ordinary shares, we will notify the depositary in advance and will indicate whether we wish such distribution to be made to you. If so, we will assist the depositary in determining whether such distribution to holders is lawful and reasonably practicable.

If it is reasonably practicable to distribute such property to you and if we provide all of the documentation contemplated in the deposit agreement, the depositary will distribute the property to the holders in a manner it deems practicable.

The distribution will be made net of fees, expenses, taxes and governmental charges payable by holders under the terms of the deposit agreement. In order to pay such taxes and governmental charges, the depositary may sell all or a portion of the property received.

The depositary will *not* distribute the property to you and will sell the property if:

- we do not request that the property be distributed to you or if we ask that the property not be distributed to you; or
- we do not deliver satisfactory documents to the depositary; or
- the depositary determines that all or a portion of the distribution to you is not reasonably practicable.

The proceeds of such a sale will be distributed to holders as in the case of a cash distribution.

Redemption

Whenever we decide to redeem any of the securities on deposit with the custodian, we will notify the depositary in advance. If it is practicable and if we provide all of the documentation contemplated in the deposit agreement, the depositary will provide notice of the redemption to the holders.

The custodian will be instructed to surrender the shares being redeemed against payment of the applicable redemption price. The depositary will convert the redemption funds received into U.S. dollars upon the terms of the deposit agreement and will establish procedures to enable holders to receive the net proceeds from the redemption upon surrender of their ADSs to the depositary. You may have to pay fees, expenses, taxes and other governmental charges upon the redemption of your ADSs. If less than all ADSs are being redeemed, the ADSs to be retired will be selected by lot or on a pro rata basis, as the depositary may determine.

Changes Affecting Ordinary Shares

The ordinary shares held on deposit for your ADSs may change from time to time. For example, there may be a change in nominal or par value, split-up, cancellation, consolidation or any other reclassification of such ordinary shares or a recapitalization, reorganization, merger, consolidation or sale of assets of the company.

If any such change were to occur, your ADSs would, to the extent permitted by law, represent the right to receive the property received or exchanged in respect of the ordinary shares held on deposit. The depositary may in such circumstances deliver new ADSs to you, amend the deposit agreement, the ADRs and the applicable Registration Statement(s) on Form F-6, call for the exchange of your existing ADSs for new ADSs and take any other actions that are appropriate to reflect as to the ADSs the change affecting the ordinary shares. If the depositary may not lawfully distribute such property to you, the depositary may sell such property and distribute the net proceeds to you as in the case of a cash distribution.

Issuance of ADSs upon Deposit of Ordinary Shares

Upon the effectiveness of this registration statement, the ordinary shares being offered pursuant to this registration statement will be deposited by us with the custodian. Upon receipt of confirmation of such deposit, the depositary will issue ADSs to the underwriters named in this registration statement. After the effectiveness of this registration statement, the ordinary shares that are being offered for sale pursuant to this registration statement will be deposited by us with the custodian. Upon receipt of confirmation of such deposit, the depositary will issue ADSs to the underwriters named in this registration statement.

After the closing of this offer, the depositary may create ADSs on your behalf if you or your broker deposit ordinary shares with the custodian. The depositary will deliver these ADSs to the person you indicate only after you pay any applicable issuance fees and any charges and taxes payable for the transfer of the ordinary shares to the custodian. Your ability to deposit ordinary shares and receive ADSs may be limited by United States and England and Wales legal considerations applicable at the time of deposit.

The issuance of ADSs may be delayed until the depositary or the custodian receives confirmation that all required approvals have been given and that the ordinary shares have been duly transferred to the custodian. The depositary will only issue ADSs in whole numbers.

When you make a deposit of ordinary shares, you will be responsible for transferring good and valid title to the depositary. As such, you will be deemed to represent and warrant that:

- the ordinary shares are duly authorized, validly issued, fully paid, non-assessable and legally obtained;

- all preemptive (and similar) rights, if any, with respect to such ordinary shares have been validly waived or exercised;
- you are duly authorized to deposit the ordinary shares;
- the ordinary shares presented for deposit are free and clear of any lien, encumbrance, security interest, charge, mortgage or adverse claim, and are not, and the ADSs issuable upon such deposit will not be, "restricted securities" (as defined in the deposit agreement); and
- the ordinary shares presented for deposit have not been stripped of any rights or entitlements.

If any of the representations or warranties are incorrect in any way, we and the depositary may, at your cost and expense, take any and all actions necessary to correct the consequences of the misrepresentations.

Transfer, Combination and Split Up of ADRs

As an ADR holder, you will be entitled to transfer, combine or split up your ADRs and the ADSs evidenced thereby. For transfers of ADRs, you will have to surrender the ADRs to be transferred to the depositary and also must:

- ensure that the surrendered ADR is properly endorsed or otherwise in proper form for transfer;
- provide such proof of identity and genuineness of signatures as the depositary deems appropriate;
- provide any transfer stamps required by the State of New York or the United States; and
- pay all applicable fees, charges, expenses, taxes and other government charges payable by ADR holders pursuant to the terms of the deposit agreement, upon the transfer of ADRs.

To have your ADRs either combined or split up, you must surrender the ADRs in question to the depositary with your request to have them combined or split up, and you must pay all applicable fees, charges and expenses payable by ADR holders, pursuant to the terms of the deposit agreement, upon a combination or split up of ADRs.

Withdrawal of Ordinary Shares Upon Cancellation of ADSs

As a holder, you will be entitled to present your ADSs to the depositary for cancellation and then receive the corresponding number of underlying ordinary shares at the custodian's offices. Your ability to withdraw the ordinary shares held in respect of the ADSs may be limited by United States and England and Wales considerations applicable at the time of withdrawal. In order to withdraw the ordinary shares represented by your ADSs, you will be required to pay to the depositary the fees for cancellation of ADSs and any charges and taxes payable upon the transfer of the ordinary shares. You assume the risk for delivery of all funds and securities upon withdrawal. Once canceled, the ADSs will not have any rights under the deposit agreement.

If you hold ADSs registered in your name, the depositary may ask you to provide proof of identity and genuineness of any signature and such other documents as the depositary may deem appropriate before it will cancel your ADSs.

The withdrawal of the ordinary shares represented by your ADSs may be delayed until the depositary receives satisfactory evidence of compliance with all applicable laws and regulations.

Please keep in mind that the depositary will only accept ADSs for cancellation that represent a whole number of securities on deposit.

You will have the right to withdraw the securities represented by your ADSs at any time except as a result of:

- temporary delays that may arise because (i) the transfer books for the ordinary shares or ADSs are closed, or (ii) ordinary shares are immobilized on account of a shareholders' meeting or a payment of dividends;
- obligations to pay fees, taxes and similar charges; and/or
- restrictions imposed because of laws or regulations applicable to ADSs or the withdrawal of securities on deposit.

The deposit agreement may not be modified to impair your right to withdraw the securities represented by your ADSs except to comply with mandatory provisions of law.

Voting Rights

As a holder, you generally have the right under the deposit agreement to instruct the depositary to exercise the voting rights for the ordinary shares represented by your ADSs. The voting rights of holders of ordinary shares are described in "Description of Share Capital and Articles of Association—Articles of Association" in this registration statement.

At our request, the depositary will distribute to you any notice of shareholders' meeting received from us together with information explaining how to instruct the depositary to exercise the voting rights of the securities represented by ADSs.

If the depositary timely receives voting instructions from a holder of ADSs, it will endeavor to vote the securities (in person or by proxy) represented by the holder's ADSs as follows:

- *In the event of voting by show of hands*, the depositary will vote (or cause the custodian to vote) all ordinary shares held on deposit at that time in accordance with the voting instructions received from a majority of holders of ADSs who provide timely voting instructions.
- In the event of voting by poll, the depositary will vote (or cause the custodian to vote) the ordinary shares held on deposit in accordance with the voting instructions received from the holders of ADSs.

Securities for which no voting instructions have been received will not be voted (except as otherwise contemplated herein). Please note that the ability of the depositary to carry out voting instructions may be limited by practical and legal limitations and the terms of the securities on deposit. We cannot assure you that you will receive voting materials in time to enable you to return voting instructions to the depositary in a timely manner.

Fees and Charges

As an ADS holder, you will be required to pay the following fees under the terms of the deposit agreement:

SERVICE	**FEES**
Issuance of ADSs (e.g., an issuance of ADS upon a deposit of ordinary shares or upon a change in the ADS(s)-to-ordinary shares ratio), excluding ADS issuances as a result of distributions of ordinary shares	Up to $0.05 per ADS issued
Cancellation of ADSs (e.g., a cancellation of ADSs for delivery of deposited property or upon a change in the ADS(s)-to-ordinary shares ratio)	Up to $0.05 per ADS cancelled
Distribution of cash dividends or other cash distributions (e.g., upon a sale of rights and other entitlements)	Up to $0.05 per ADS issued
Distribution of ADSs pursuant to (i) share dividends or other free share distributions, or (ii) exercise of rights to purchase additional ADSs	Up to $0.05 per ADS held Up to $0.05 per ADS held
Distribution of securities other than ADSs or rights to purchase additional ADSs (e.g., upon a spin-off)	Up to $0.05 per ADS held
****ADS Services	Up to $0.05 per ADS held on the applicable record date(s) established by the depositary

As an ADS holder you will also be responsible to pay certain charges such as:

- taxes (including applicable interest and penalties) and other governmental charges;
- the registration fees as may from time to time be in effect for the registration of ordinary shares on the share register and applicable to transfers of ordinary shares to or from the name of the custodian, the depositary or any nominees upon the making of deposits and withdrawals, respectively;

- certain cable, telex and facsimile transmission and delivery expenses;
- the expenses and charges incurred by the depositary in the conversion of foreign currency;
- the fees and expenses incurred by the depositary in connection with compliance with exchange control regulations and other regulatory requirements applicable to ordinary shares, ADSs and ADRs; and
- the fees and expenses incurred by the depositary, the custodian or any nominee in connection with the servicing or delivery of deposited property.

ADS fees and charges payable upon (i) the issuance of ADSs, and (ii) the cancellation of ADSs are charged to the person to whom the ADSs are issued (in the case of ADS issuances) and to the person whose ADSs are cancelled (in the case of ADS cancellations). In the case of ADSs issued by the depositary into DTC, the ADS issuance and cancellation fees and charges may be deducted from distributions made through DTC, and may be charged to the DTC participant(s) receiving the ADSs being issued or the DTC participant(s) holding the ADSs being cancelled, as the case may be, on behalf of the beneficial owner(s) and will be charged by the DTC participant(s) to the account of the applicable beneficial owner(s) in accordance with the procedures and practices of the DTC participants as in effect at the time. ADS fees and charges in respect of distributions and the ADS service fee are charged to the holders as of the applicable ADS record date. In the case of distributions of cash, the amount of the applicable ADS fees and charges is deducted from the funds being distributed. In the case of (i) distributions other than cash and (ii) the ADS service fee, holders as of the ADS record date will be invoiced for the amount of the ADS fees and charges and such ADS fees and charges may be deducted from distributions made to holders of ADSs. For ADSs held through DTC, the ADS fees and charges for distributions other than cash and the ADS service fee may be deducted from distributions made through DTC, and may be charged to the DTC participants in accordance with the procedures and practices prescribed by DTC and the DTC participants in turn charge the amount of such ADS fees and charges to the beneficial owners for whom they hold ADSs.

In the event of refusal to pay the depositary fees, the depositary may, under the terms of the deposit agreement, refuse the requested service until payment is received or may set off the amount of the depositary fees from any distribution to be made to the ADS holder. Certain of the depositary fees and charges (such as the ADS services fee) may become payable shortly after the closing of the ADS offering. Note that the fees and charges you may be required to pay may vary over time and may be changed by us and by the depositary. You will receive prior notice of such changes. The depositary may reimburse us for certain expenses incurred by us in respect of the ADR program, by making available a portion of the ADS fees charged in respect of the ADR program or otherwise, upon such terms and conditions as we and the depositary agree from time to time.

Amendments and Termination

We may agree with the depositary to modify the deposit agreement at any time without your consent. We undertake to give holders 30 days' prior notice of any modifications that would materially prejudice any of their substantial rights under the deposit agreement. We will not consider to be materially prejudicial to your substantial rights any modifications or supplements that are reasonably necessary for the ADSs to be registered under the Securities Act or to be eligible for book-entry settlement, in each case without imposing or increasing the fees and charges you are required to pay. In addition, we may not be able to provide you with prior notice of any modifications or supplements that are required to accommodate compliance with applicable provisions of law.

You will be bound by the modifications to the deposit agreement if you continue to hold your ADSs after the modifications to the deposit agreement become effective. The deposit agreement cannot be amended to prevent you from withdrawing the ordinary shares represented by your ADSs (except as permitted by law).

We have the right to direct the depositary to terminate the deposit agreement. Similarly, the depositary may in certain circumstances on its own initiative terminate the deposit agreement. In either case, the depositary must give notice to the holders at least 30 days before termination. Until termination, your rights under the deposit agreement will be unaffected.

Termination

After termination, the depositary will continue to collect distributions received (but will not distribute any such property until you request the cancellation of your ADSs) and may sell the securities held on deposit. After the sale, the depositary will hold the proceeds from such sale and any other funds then held for the holders of ADSs in a non-interest-bearing account. At that point, the depositary will have no further obligations to holders other than to account for the funds then held for the holders of ADSs still outstanding (after deduction of applicable fees, taxes and expenses).

In connection with the termination of the deposit agreement, the depositary may, independently and without the need for any action by us, make available to holders a means to withdraw the ordinary shares and other deposited securities represented by their ADSs and to direct the deposit of such ordinary shares and other deposited securities into an unsponsored American depositary shares program established by the depositary, upon such terms and conditions as the depositary may deem reasonably appropriate, subject however, in each case, to satisfaction of the applicable registration requirements by the unsponsored American depositary shares program under the Securities Act, and to receipt by the depositary of payment of the applicable fees and charges of, and reimbursement of the applicable expenses incurred by, the depositary.

Books of Depositary

The depositary will maintain ADS holder records at its depositary office. You may inspect such records at such office during regular business hours but solely for the purpose of communicating with other holders in the interest of business matters relating to the ADSs and the deposit agreement.

The depositary will maintain in New York facilities to record and process the issuance, cancellation, combination, split-up and transfer of ADSs. These facilities may be closed from time to time, to the extent not prohibited by law.

Transmission of Notices, Reports and Proxy Soliciting Material

The depositary will make available for your inspection at its office all communications that it receives from us as a holder of deposited securities that we make generally available to holders of deposited securities. Subject to the terms of the deposit agreement, the depositary will send you copies of those communications or otherwise make those communications available to you if we ask it to.

Limitations on Obligations and Liabilities

The deposit agreement limits our obligations and the depositary's obligations to you. Please note the following:

- We and the depositary are obligated only to take the actions specifically stated in the deposit agreement without negligence or bad faith.
- The depositary disclaims any liability for any failure to carry out voting instructions, for any manner in which a vote is cast or for the effect of any vote, provided it acts in good faith and in accordance with the terms of the deposit agreement.
- The depositary disclaims any liability for any failure to determine the lawfulness or practicality of any action, for the content of any document forwarded to you on our behalf or for the accuracy of any

translation of such a document, for the investment risks associated with investing in ordinary shares, for the validity or worth of the ordinary shares, for any tax consequences that result from the ownership of ADSs, for the credit-worthiness of any third party, for allowing any rights to lapse under the terms of the deposit agreement, for the timeliness of any of our notices or for our failure to give notice.

- We and the depositary will not be obligated to perform any act that is inconsistent with the terms of the deposit agreement.

- We and the depositary disclaim any liability if we or the depositary are prevented or forbidden from or subject to any civil or criminal penalty or restraint on account of, or delayed in, doing or performing any act or thing required by the terms of the deposit agreement, by reason of any provision, present or future of any law or regulation, or by reason of present or future provision of any provision of our Articles of Association, or any provision of or governing the securities on deposit, or by reason of any act of God or war or other circumstances beyond our control.

- We and the depositary disclaim any liability by reason of any exercise of, or failure to exercise, any discretion provided for in the deposit agreement or in our Articles of Association or in any provisions of or governing the securities on deposit.

- We and the depositary further disclaim any liability for any action or inaction in reliance on the advice or information received from legal counsel, accountants, any person presenting ordinary shares for deposit, any holder of ADSs or authorized representatives thereof, or any other person believed by either of us in good faith to be competent to give such advice or information.

- We and the depositary also disclaim liability for the inability by a holder to benefit from any distribution, offering, right or other benefit that is made available to holders of ordinary shares but is not, under the terms of the deposit agreement, made available to you.

- We and the depositary may rely without any liability upon any written notice, request or other document believed to be genuine and to have been signed or presented by the proper parties.

- We and the depositary also disclaim liability for any consequential or punitive damages for any breach of the terms of the deposit agreement.

- No disclaimer of any Securities Act liability is intended by any provision of the deposit agreement.

Pre-Release Transactions

Subject to the terms and conditions of the deposit agreement, the depositary may issue to broker/dealers ADSs before receiving a deposit of ordinary shares or release ordinary shares to broker/dealers before receiving ADSs for cancellation. These transactions are commonly referred to as “pre-release transactions,” and are entered into between the depositary and the applicable broker/dealer. The deposit agreement limits the aggregate size of pre-release transactions (not to exceed 30% of the ordinary shares on deposit in the aggregate) and imposes a number of conditions on such transactions (e.g., the need to receive collateral, the type of collateral required, the representations required from brokers, etc.). The depositary may retain the compensation received from the pre-release transactions.

Taxes

You will be responsible for the taxes and other governmental charges payable on the ADSs and the securities represented by the ADSs. We, the depositary and the custodian may deduct from any distribution the taxes and governmental charges payable by holders and may sell any and all property on deposit to pay the

taxes and governmental charges payable by holders. You will be liable for any deficiency if the sale proceeds do not cover the taxes that are due.

The depositary may refuse to issue ADSs, to deliver, transfer, split and combine ADRs or to release securities on deposit until all taxes and charges are paid by the applicable holder. The depositary and the custodian may take reasonable administrative actions to obtain tax refunds and reduced tax withholding for any distributions on your behalf. However, you may be required to provide to the depositary and to the custodian proof of taxpayer status and residence and such other information as the depositary and the custodian may require to fulfill legal obligations. You are required to indemnify us, the depositary and the custodian for any claims with respect to taxes based on any tax benefit obtained for you.

Foreign Currency Conversion

The depositary will arrange for the conversion of all foreign currency received into U.S. dollars if such conversion is practical, and it will distribute the U.S. dollars in accordance with the terms of the deposit agreement. You may have to pay fees and expenses incurred in converting foreign currency, such as fees and expenses incurred in complying with currency exchange controls and other governmental requirements.

If the conversion of foreign currency is not practical or lawful, or if any required approvals are denied or not obtainable at a reasonable cost or within a reasonable period, the depositary may take the following actions in its discretion:

- Convert the foreign currency to the extent practical and lawful and distribute the U.S. dollars to the holders for whom the conversion and distribution is lawful and practical.
- Distribute the foreign currency to holders for whom the distribution is lawful and practical.
- Hold the foreign currency (without liability for interest) for the applicable holders.

Governing Law/Waiver of Jury Trial

The deposit agreement and the ADRs will be interpreted in accordance with the laws of the State of New York. The rights of holders of ordinary shares (including ordinary shares represented by ADSs) is governed by the laws of England and Wales.

AS A PARTY TO THE DEPOSIT AGREEMENT, YOU WAIVE YOUR RIGHT TO TRIAL BY JURY IN ANY LEGAL PROCEEDING ARISING OUT OF THE DEPOSIT AGREEMENT OR THE ADRs AGAINST US AND/OR THE DEPOSITARY.

PART II

ITEM 13: DEFAULTS, DIVIDEND ARREARAGES AND DELINQUENCIES

None.

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

None.

ITEM 15: CONTROLS AND PROCEDURES

Not applicable.

ITEM 16A: AUDIT COMMITTEE FINANCIAL EXPERT

Not applicable.

ITEM 16B: CODE OF ETHICS

Not applicable.

ITEM 16C: PRINCIPAL ACCOUNTANT FEES AND SERVICES

Not applicable.

ITEM 16D: EXEMPTIONS FROM THE LISTING STANDARDS FOR AUDIT COMMITTEES

Not applicable.

ITEM 16E: PURCHASES OF EQUITY SECURITIES BY THE ISSUER AND AFFILIATED PURCHASERS

None.

ITEM 16F: CHANGE IN REGISTRANTS CERTIFYING ACCOUNTANT

None.

ITEM 16G: CORPORATE GOVERNANCE

Not applicable.

ITEM 16H: MINE SAFETY DISCLOSURE

Not applicable.

PART III

ITEM 17: FINANCIAL STATEMENTS

We have elected to furnish financial statements and related information specified in Item 18.

ITEM 18: FINANCIAL STATEMENTS

See the Financial Statements beginning on page F-1.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Shareholders of Tiziana Life Sciences plc

We have audited the accompanying consolidated balance sheets of Tiziana Life Sciences plc as of December 31, 2015 and 2016, and the related consolidated statements of operations and comprehensive loss, shareholders' equity and cash flows for each of the years then ended. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the consolidated financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Tiziana Life Sciences plc at December 31, 2015 and 2016, and the consolidated results of its operations and its cash flows for the years then ended in conformity with International Financial Reporting Standards as issued by the International Accounting Standards Board.

Mazars LLP

London, England

February 8, 2018

Consolidated Balance Sheets
(In thousands, except share and per share amounts)

	Six months to June 30, 2017 (unaudited)	Year ended December 31, 2016	2015
ASSETS			
Current assets:			
Cash and cash equivalents	$ 2,609	$ 5,802	$ 13,128
Prepayments and other receivables	428	395	512
Total current assets	3,037	6,197	13,640
Property and Equipment, net	27	35	—
Total non-current assets	27	35	—
Total assets	$ 3,064	$ 6,231	$ 13,640
LIABILITIES AND SHAREHOLDERS' EQUITY			
Liabilities:			
Current liabilities:			
Accounts payable and accrued expenses	$ 2,985	$ 2,143	$ 1,100
Total current liabilities	2,985	2,143	1,100
Total liabilities	2,985	2,143	1,100
Shareholders Equity:			
Called up share capital	6,970	6,903	15,563
Share premium	9,591	8,943	33,496
Share based payment reserve	2,657	2,647	1,503
Shares to be issued reserve (warrants)	307	271	162
Shares to be issued reserve	17,577	17,158	15,510
Merger relief reserve	—	—	9,448
Other reserve	(46,171)	(46,171)	(46,171)
Translation reserve	2,655	2,771	2,121
Retained earnings	6,492	11,566	(19,091)
Total shareholders' equity	79	4,088	12,540
Total liabilities and shareholders' equity	$ 3,064	$ 6,231	$ 13,640

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

Consolidated Statements of Operations and Comprehensive Loss
(In thousands, except share and per share amounts)

	Six months to June 30, 2017 (unaudited)	Year ended December 31,		
		2016	2015	2014
Revenue	$ —	$ —	$ —	$ —
Cost of revenue	—	—	—	—
Gross profit	—	—	—	—
Operating expenses:				
Research and Development	(2,885)	(4,007)	(9,609)	(1,309)
Operating Expenses	(1,804)	(5,872)	(3,557)	(2,944)
Cost of listing	—	-	—	(1,245)
Total operating expenses	(4,689)	(9,879)	(13,166)	(5,496)
Loss from operations	(4,689)	(9,879)	(13,166)	(5,496)
Other income/(expense):				
Finance Income/(expense)	(5)	(12)	(28)	(86)
Other income	(5)	(12)	(28)	(86)
Loss from operations before income taxes	(4,693)	(9,891)	(13,193)	(5,583)
Income tax provision	—	121	—	99
Loss for the year	(4,693)	(9,770)	(13,193)	(5,484)
Other Comprehensive Loss:				
Currency translation	(116)	650	3,063	(942)
Comprehensive loss	(4,809)	$(9,120)	$(10,130)	$(6,426)
Basic and diluted loss per share attributable to common shareholders	$ (0.05)	$ (0.10)	$ (0.11)	$ (0.28)

Consolidated Statements of Shareholders' Equity

(In thousands, except share amounts)

	Share Capital	Share Premium	Share Based Payment Reserve	Shares to Be Issued Reserve	Convertible Loan Note Reserve	Merger Reserve	Other Reserve	Retained[1] Earnings	Capital Redemption Reserve	Translation Reserve	Total Equity
Balance at 1 January 2015	**15,217**	**27,069**	**232**	**-**	**3,519**	**9,448**	**(46,171)**	**(5,604)**	**-**	**(942)**	**2,768**
Transactions with owners											
Issue of share capital	346	6,427	-	-	-	-	-	-	-	-	6,773
Share based payments (options)	-	-	1,433	-	-	-	-	-	-	-	1,433
Share based payments (warrants)	-	-	-	162	-	-	-	-	-	-	162
Convertible loan note – equity component	-	-	-	-	11,991	-	-	(456)	-	-	11,535
Options cancelled	-	-	(162)	-	-	-	-	162	-	-	-
Total transactions with owners	346	6,427	1,271	162	11,991	-	-	(294)	-	-	19,903
Comprehensive income											
Loss for the period	-	-	-	-	-	-	-	(13,193)	-		(13,193)
Translation income	-	-	-	-	-	-	-	-	-	3,063	3,063
Total comprehensive income	-	-	-	-	-	-	-	(13,193)	-	3,063	(10,130)
Balance at 31 December 2015	**15,563**	**33,496**	**1,503**	**162**	**15,510**	**9,448**	**(46,171)**	**(19,091)**	**-**	**2,121**	**12,540**
Transactions with owners											
Issue of share capital	84	546	-	-	-	-	-	-	-	-	630
Share based payment (options)	-	-	1,144	-	-	-	-	-	-	-	1,144
Share based payment (warrants)	-	-	-	109	-	-	-	-			109
Convertible loan note – equity component	-	-	-	-	1,649	-	-	(851)			798
Cancellation of deferred shares	(8,744)	-	-	-	-	-	-	-	8,744	-	-
Capital Reduction	-	(25,099)	-	-	-	(9,448)	-	41,292	(8,744)		(1,999)
Prior Year Adjustment	-	-	-	-	-	-	-	(14)			(14)
Total transactions with owners	(8,660)	(24,553)	1,144	109	1,649	(9,448)	-	40,427	-	-	(669)
Comprehensive income											
Loss for the period	-	-	-	-	-	-	-	(9,770)	-	-	(9,770)
Translation	-	-	-	-	-	-	--	-	-	650	650
Total comprehensive income	-	-	-	-	-	-	-	(9,770)	-	650	(9,120)
Balance at 31 December 2016	**6,903**	**8,943**	**2,647**	**271**	**17,158**	**-**	**(46,171)**	**11,566**	**-**	**2,771**	**4,088**
Issue of share capital	67	649	-	-	-	-	-	-	-	-	716
Share based payment (options)	-	-	10	-	-	-	-	-	-	-	10
Share based payment (warrants)	-	-	-	36	-	-	-	-			36
Convertible loan note – equity component	-	-	-	-	419	-	-	(381)			38
Total transactions with owners	67	649	10	36	419	-	-	(381)	-	-	801
Comprehensive income											
Loss for the period	-	-	-	-	-	-	-	(4,693)	-	-	(4,693)
Translation	-	-	-	-	-	-	--	-	-	(116)	(116)
Total comprehensive income	-	-	-	-	-	-	-	(4,693)	-	(116)	(4,809)
Balance at 30 June 2017 (unaudited)	**6,970**	**9,591**	**2,657**	**307**	**17,577**	**-**	**(46,171)**	**6,492**	**-**	**2,655**	**79**

1 As detailed in note 21, retained earnings which represents the cumulative profits (losses) of the entity that have not been distributed to shareholders, has been credited with $41m arising as part of a capital reduction exercise in 2016.

Consolidated Statements of Cash Flows
(In thousands, except share amounts)

	Six months to June 30 2017 (unaudited)	Year ended December 31, 2016	2015
CASH FLOWS FROM OPERATING ACTIVITIES:			
Net loss	$ (4,693)	$ (9,770)	$ (13,193)
Adjustments to reconcile net loss to net cash used in operating activities:			
Convertible loan interest accrued	5	12	—
Share based payment – options	10	1,257	1,486
Share based payment – warrants	36	121	156
Net (increase)/decrease in operating assets/other receivables	(12)	—	(234)
Net increase/(decrease) in operating liabilities /other liabilities	676	1,174	96
Depreciation	6	11	—
Other share based payments	—	—	3,268
Loss on foreign exchange	6	214	—
Lease adjustment	6	55	—
Net cash used in operating activities	(3,960)	(6,926)	(8,421)
CASH FLOWS FROM INVESTING ACTIVITIES:			
PPE	—	(48)	—
Acquisition of other investments	—	(294)	—
Net cash provided by investing activities	—	(342)	—
CASH FLOWS FROM FINANCING ACTIVITIES:			
Proceeds from issuance of ordinary shares	694	614	4,032
Proceeds from issuance of convertible loan notes	—	961	15,643
Fundraising cost	—	—	(1,110)
Net cash provided by financing activities	694	1,575	18,565
Net increase in cash and cash equivalents	(3,266)	(5,693)	10,144
Cash and cash equivalent, beginning of period	5,802	13,128	3,531
Exchange difference	73	(1,633)	(547)
Cash and cash equivalent, end of period	$ 2,609	$ 5,802	13,128

TIZIANA LIFE SCIENCES PLC

Notes to Consolidated Financial Statements

1. GENERAL INFORMATION

Tiziana Life Sciences PLC is a public limited company incorporated in the United Kingdom under the Companies Act and quoted on the AIM market of the London Stock Exchange (AIM: TILS). The address of its registered office is given on page 1. The principal activities of the Company and its subsidiaries (the Group) are that of a clinical stage biotechnology company focussed on targeted drugs to treat diseases in oncology and immunology.

These financial statements are presented in thousands of dollars ($'000) which is the presentational currency of the Company. The functional currency is Pounds sterling (£) indicative of the primary economic environment in which the Company operates.

The ultimate parent of the group is Planwise Group Limited, incorporated in the British Virgin Islands. Gabriele Cerrone is the ultimate beneficial owner of the entire issued share capital of Planwise Group Limited.

2. ACCOUNTING POLICIES

The principal accounting policies applied in the preparation of these consolidated financial statements are set out below. These policies have been applied consistently to all the years presented unless otherwise stated.

Basis of preparation

The consolidated financial statements of the Group and Company have been prepared in accordance with International Financial Reporting Standards (IFRS) as issued by the International Accounting Standards Board, IFRIC interpretations and the Companies Act 2006 as applicable to companies reporting under IFRS. These accounts have been prepared under the historical cost convention.

As permitted by section 408 of the Companies Act 2006, a separate profit and loss account for the Company has not been presented in these financial statements.

Going Concern

The financial statements have been prepared on the going concern basis, which contemplates continuity of normal business activities and the realisation of assets and discharge of liabilities in the normal course of business.

The directors believe that there are reasonable grounds to believe that the company and consolidated entity will be able to continue as going concerns, after consideration of the following factors;

- Cash and cash equivalents totaling $5.8m at 31 December 2016
- Conversion of warrants on 24th March 2017 raising approximately $700k before expenses

Accordingly, the directors believe that the company and consolidated entities will be able to continue as going concerns and that it is appropriate to adopt the going concern basis in the preparation of the financial statement. The financial statement does not include any adjustment relating to the amounts or classification of recorded assets or liabilities that might be necessary if the company and consolidated entities do not continue as going concerns.

Basis of consolidation

Subsidiary undertakings are all entities over which the Group has the power to govern the financial and operating policies of the subsidiary and therefore exercises control. The existence and effect of both current voting rights and potential voting rights that are currently exercisable or convertible are considered when assessing whether control of an entity is exercised. Subsidiaries are consolidated from the date at which the Group obtains control and are de-consolidated from the date at which control ceases.

Business combination

The consolidated position of the Group is as a result of the reverse acquisition of Alexander David Investments plc by Tiziana Pharma Ltd and the subsequent listing of the Company as Tiziana Life Sciences plc on 24 April 2014. Reverse acquisition for the business combination in the year as detailed below:

On 24th April 2014, the Company (Alexander David Investments plc, (ADI)) acquired via a share for share exchange the entire issued share capital of Tiziana Pharma Limited, whose principal activity is that of a clinical stage biotechnology company focussed on targeted drugs to treat diseases in oncology and immunology.

Due to the relative values of the companies, the former Tiziana Pharma Limited shareholders became majority shareholders with 96.1% of the enlarged share capital in ADI which was renamed Tiziana Life Sciences plc, and hence hold the majority of the voting rights. Furthermore, the executive management of Tiziana Pharma Limited became the executive management of Tiziana Life Sciences plc. A qualitative and quantitative analysis of these factors led the Directors to conclude that in this transaction Tiziana Pharma Limited has the controlling interest and should be treated as the accounting acquirer.

In determining the appropriate accounting treatment for the reverse acquisition, the Directors considered the Application Supplement to IFRS 3, Business combinations. However, they concluded that this transaction fell outside the scope of IFRS 3 since Tiziana Life Sciences plc, whose activity prior to the acquisition was purely the maintenance of the AIM listing, did not constitute a business. It was therefore determined that the transaction should be accounted for in a manner that was similar to the reverse acquisition accounting as described in IFRS 3, but without recognising goodwill.

The following accounting treatment has been applied in respect of the reverse acquisition;

- The assets and liabilities of the legal subsidiary, Tiziana Pharma Limited are recognised and measured in the consolidated financial statements at their pre-combination carrying amounts, without restatement to their fair value.
- The retained reserves recognised in the consolidated financial statements reflect the retained reserves of Tiziana Pharma Limited to the date of acquisition.
- In applying IFRS 3 by analogy, the equity structure appearing in the consolidated financial statements reflects the equity structure of the legal parent Tiziana Life Sciences plc, including the equity instruments issued under the share exchange to effect the business combination.
- A reverse acquisition reserve has been created to enable the presentation of a consolidated balance sheet which combines the equity structure of the legal parent with the non-statutory reserves of the legal subsidiary.
- Comparative numbers are based upon the consolidated financial statements of the legal subsidiary, Tiziana Pharma Limited for the year ended 31 December 2013 apart from the equity structure which reflects that of the parent.

Tiziana Pharma Limited was incorporated on 4th November 2013 and prepared its first set of financial statements to 31 December 2014. Therefore, the parent and subsidiary had the same reporting date but Tiziana Pharma Limited had a long period of account. No adjustment was made in the consolidated financial statements for the difference in length of reporting period because the only transaction in Tiziana Pharma Limited at 31 December 2013 was the issue of ordinary share capital of $1.65.

Inter-company transactions, balances and unrealised gains on transactions between group companies are eliminated upon consolidation. Unrealised losses are also eliminated. Accounting policies of subsidiaries have been changed where necessary to ensure consistency with the policies adopted by the group.

Segment reporting

Operating segments are reported in a manner consistent with the internal reporting provided to the Board. The Board allocates resources to and assess the performance of the segments. The Board considers there to be only one operating segment being the research and development of biotechnological and pharmaceutical products.

Taxation

The tax expense for a period represents the total of current taxation and deferred taxation. The charges in respect of current taxation are based on the estimated taxable profit for the relevant year. Taxable profit for the year is based on the profit as shown in the income statement, as adjusted for items of income or expenditure which are not deductible or chargeable for tax purposes. The current tax liability for the year is calculated using tax rates which have either been enacted or substantively enacted at the relevant balance sheet date.

Foreign currency translation

Items included in the financial statements of each of the Group's entities are measured using the currency of the primary economic environment in which the entity operates (the functional currency). The consolidated financial statements are presented in US dollars, which is the Group's presentation currency.

Foreign currency transactions are translated into the functional currency using exchange rates prevailing at the dates of the transactions. Foreign exchange gains and losses resulting from the settlement of foreign currency transactions and from the translation at year-end exchange rates of monetary assets and liabilities denominated in foreign currencies are recognized in the income statement.

The financial statements of overseas subsidiary undertakings are translated into US dollars on the following basis:

• Assets and liabilities at the rate of exchange ruling at the year-end date.

• Profit and loss account items at the average rate of exchange for the year.

Exchange differences arising from the translation of the net investment in foreign entities, borrowings and other currency instruments designated as hedges of such investments, are taken to equity (and recognized in the statement of comprehensive income) on consolidation.

License fees

Payments related to the acquisition of rights to a product or technology are capitalised as intangible assets if it is probable that future economic benefits from the asset will flow to the entity and the cost of the asset can be reliably measured.

Payments made which provide the right to perform research are carefully evaluated to determine whether such payments are to fund research or acquire an asset. Where fees related to research and development projects are recognised as an expense in the income statement, due to the uncertainty in the length of time that the Group will hold them the expense is recognised fully at the point of recognition.

Research and development

All on-going research and development expenditure is currently expensed in the period in which it is incurred. Due to the regulatory environment inherent in the development of the Group's products, the criteria for development costs to be recognised as an asset, as set out in IAS 38 'Intangible Assets', are not met until a product has been granted regulatory approval and it is probable that future economic benefit will flow to the Group. The Group currently has no qualifying expenditure.

Financial instruments

Financial assets

The Group classifies its financial assets into one of the categories discussed below, depending on the purpose for which the asset was acquired.

Loans and receivables

Loans and receivables are recognised initially at fair value and are subsequently measured at amortised cost, with no discounting where the effect is not material.

Cash and cash equivalents

Cash and cash equivalents comprise cash at bank and in hand and other short term highly liquid deposits with original maturities of three months or less. Bank overdrafts are shown within borrowings in current liabilities on the balance sheet.

Financial liabilities

The Group classifies its financial liabilities into one of the categories discussed below, depending on the purpose for which the liability was committed.

Trade and other payables

Trade and other payables are recognised initially at fair value and are subsequently measured at amortised cost using the effective interest method. As the payment period of trade payables is short future cash payments are not discounted as the effect is not material.

Share capital

Ordinary shares of the company are classified as equity.

Property, plant and equipment

(i) Recognition and measurement

Items of property, plant and equipment are measured at cost less accumulated depreciation and accumulated impairment losses. Costs include expenditures that are directly attributable to the acquisition of the asset. Purchased software that is integral to the functionality of the related equipment is capitalized as part of that equipment.

When parts of an item of property, plant and equipment have different useful lives, they are accounted for as separate items (major components) of property, plant and equipment.

Gains and losses on disposal of an item of property, plant and equipment are determined by comparing the proceeds from disposal with the carrying amount of property, plant and equipment, and are recognised in profit or loss. When revalued assets are sold, the amounts included in the revaluation reserve are transferred to retained earnings.

(ii) Depreciation
Depreciation is calculated on the depreciable amount, which is the cost of an asset, or other amount substituted for cost, less its residual value.

Depreciation is recognized in profit or loss on a straight-line basis over the estimated useful life of each part of an item of property, plant and equipment. Leased assets are depreciated over the shorter of the lease term and their useful lives unless it is reasonably certain that the Company will obtain ownership by the end of the lease term.

The estimated useful lives for the current period and the comparative period are as follows.

Plant and equipment	**3 years**
Fixtures and fittings	**5 years**

Depreciation methods, useful lives and residual values are reviewed at each reporting date. Depreciation is allocated to the operating expenses line of the income statement.

Impairment

A financial asset not carried at fair value is assessed at each reporting date to determine whether there is objective evidence that it should be impaired. A financial asset is impaired if objective evidence indicates that a loss event has occurred after the initial recognition of the asset, and that the loss event had a negative effect on the estimated future cash flows of that asset that can be estimated reliably.

Objective evidence that financial assets are impaired can include default or delinquency of a debtor, restructuring of an amount due to the Company on terms that the Company would not consider otherwise and indications that a debtor will enter bankruptcy.

Non-financial assets are tested for impairment whenever events or changes in circumstances indicate that the carrying amount may not be recoverable.

Non-financial assets are impaired when its carrying amount exceed its recoverable amount. The recoverable amount is measured as the higher of fair value less cost of disposal and value in use. The value in use is calculated as being net projected cash flows based on financial forecasts discounted back to present value.

Operating leases

Payments made under operating leases are recognised in profit and loss on a straight-line basis over the term of the lease. Lease incentives received are recognised as an integral part of the total lease expense, over the term of the lease.

Fair Value Measurement

Management have assessed the categorisation of the fair value measurements using the IFRS 13 fair value hierarchy. Categorisation within the hierarchy has been determined on the basis of the lowest level of input that is significant to the fair value measurement of the relevant asset as follows;

- Level 1 - valued using quoted prices in active markets for identical assets
- Level 2 - valued by reference to valuation techniques using observable inputs other than quoted prices included within Level 1;
- Level 3 - valued by reference to valuation techniques using inputs that are not based on observable market data.

Share based payments

The calculation of the fair value of equity-settled share based awards and the resulting charge to the statement of comprehensive income requires assumptions to be made regarding future events and market conditions. These assumptions include the future volatility of the Company's share price. These assumptions are then applied to a recognised valuation model in order to calculate the fair value of the awards.

Where employees, directors or advisers are rewarded using share based payments, the fair value of the employees', directors' or advisers' services are determined by reference to the fair value of the share options / warrants awarded. Their value is appraised at the date of grant and excludes the impact of any nonmarket vesting conditions (for example, profitability and sales growth targets). Warrants issued in association with the issue of Convertible Loan Notes are also considered as share based payments and a share based payment charge is calculated for these too.

In accordance with IFRS 2, a charge is made to the Statement of Comprehensive Income for all share-based payments including share options based upon the fair value of the instrument used. A corresponding credit is made to a Share Based Payment Reserve, in the case of options / warrants awarded to employees, directors or advisers, and Shares To Be Issued Reserve in the case of warrants issued in association with the issue of Convertible Loan Notes, net of deferred tax where applicable.

If vesting periods or other vesting conditions apply, the expense is allocated over the vesting period, based on the best available estimate of the number of share options / warrants expected to vest. Non market vesting conditions are included in assumptions about the number of options / warrants that are expected to become exercisable.

Estimates are subsequently revised, if there is any indication that the number of share options / warrants expected to vest differs from previous estimates. No adjustment is made to the expense or share issue cost recognised in prior periods if fewer share options ultimately are exercised than originally estimated.
exercise of share options / warrants, the proceeds received are allocated to share capital with any excess being recorded as share premium.

Where share options are cancelled, this is treated as an acceleration of the vesting period of the options. The amount that otherwise would have been recognised for services received over the remainder of the vesting period is recognised immediately within the Statement of Comprehensive Income.

All goods and services received in exchange for the grant of any share based payment are measured at their fair value.

Convertible loan notes

Under IAS 32 the liability and equity components of convertible loan notes must be presented separately on the Statement of Financial Position. The Group has examined the terms of each issue of convertible loan notes and determined their accounting treatment accordingly. Convertible loan notes are treated differently depending upon a number of factors.

Where there is no option to repay as cash and the interest rate is fixed

The Group considers these to be Convertible Equity Instruments and records the principal of the loan note as an equity liability in a Convertible loan note reserve. The accrued interest on the principal amount is also recorded in the Convertible loan note reserve. Upon redemption of the instrument and the issue of share capital, the amount is reclassified from the convertible loan note reserve to share capital and share premium.

Where there is no option to repay as cash and the interest rate is variable

The Group considers these to be Convertible Debt Instruments and records the principal of the loan note as a debt liability in the liabilities section of the balance sheet. The accrued interest on the principal amount is recorded in the income statement and as an increase in the debt liability. Upon redemption of the instrument and the issue of share capital, the amount is reclassified from the debt liability to share capital and share premium.

3. CRITICAL ACCOUNTING ESTIMATES AND JUDGEMENTS

The preparation of financial information in accordance with generally accepted accounting practice, in the case of the Group being International Financial Reporting Standards as adopted by the European Union, requires the directors to make estimates and judgements that affect the reported amount of assets, liabilities, income and expenditure and the disclosures made in the financial statements. Such estimates and judgements must be continually evaluated based on historical experience and other factors, including expectations of future events.

When entering into agreements with third parties which provide the rights to conduct research into specific biological processes the group account for these agreements as an expense if the agreements are 'milestone' in nature and relate to the Group's own research and development costs. Such agreements involve periodic payments and are evaluated as representing payments made to fund research.

The only other critical accounting estimates and judgements in the preparation of the financial statements were fair value estimates used in the calculation of share based payments and warrants which have been detailed above in note 2, accounting policies, and note 17, share based payments, to the accounts.

4. OPERATING LOSS

The Group and Company's operating loss are stated after charging the following:

	Six months to June 30 (Unaudited)	Year ended December 31		
	2017	**2016**	**2015**	**2014**
	$'000	$'000	$'000	$'000
Depreciation	6	11	-	-
Foreign exchange losses/(Gain)	6	215	(32)	3
	12	226	(32)	3

5. SEGMENTAL REPORTING

During the year under review Management identified the Group's only operating segment as the research and development of biotechnological and pharmaceutical products. This one segment is monitored and strategic decisions are made based upon it and other non-financial data collated from industry intelligence. The form of financial reporting reported to the Board is consistent with those presented in the annual financial statements.

6. AUDITOR'S REMUNERATION

	Six months to June 30 (Unaudited)	Year ended December 31		
	2017	2016	2015	2014
	$'000	$'000	$'000	$'000
Remuneration receivable by the Company's auditor for the audit of the consolidated and Company financial statements, including £9k for the audit of Company subsidiaries	-	49	-	-
Remuneration receivable by the Company's previous auditor for the audit of the consolidated and Company previous financial statements	-	-	30	63

7. EMPLOYEES

	Six months to June 30 (Unaudited)	Year ended December 31		
Group	2017	2016	2015	2014
Staff costs comprised:	$'000	$'000	$'000	$'000
Directors' salaries	146	214	304	259
Wages and salaries	523	786	29	20
Social security costs	11	38	30	41
Share based payment charge	10	1,015	461	541
	690	2,053	824	861
The average monthly number of employees, including directors, employed by the group during the year was:				
Corporate and administration	9	6	8	8
	9	6	8	8

8. REMUNERATION OF KEY MANAGEMENT PERSONNEL

	Six months to June 30 (Unaudited)	Year Ending December 31,		
Director	2017	2016	2015	2014
P. Boyd	-	-	86,986	84,480
W Simon	21,813	52,000	-	-
G. Cerrone	48,473	108,000	1,000	153,470
R. Dalla-Favera	12,118	27,000	53,000	-
K. Shailubhai	12,118	27,000	20,447	-
C. McGuigan	-	-	20,447	-
	94,522	214,000	302,880	237,950

The following share options were granted to directors in the year:

Director	Six months to June 30 (Unaudited) 2017 Number of options	Year Ending December 31, 2016 Number of options	2015 Number of options	2014 Number of options
R. Dalla-Favera	-	-	100,000	370,000
P. Boyd	-	-	300,000	937,500
A. Gutmann	-	-	-	80,000
G. Cerrone	-	3,259,403	2,000,000	1,200,000
K. Shailubhai	-	-	300,000	-
	-	3,259,403	2,700,000	2,587,500

The key management personnel of the Group are considered to be mostly represented by the directors.
No director has yet benefitted from any increase in the value of share capital since issuance of the options.

No director exercised share options in any of the periods. The company has not made any payments to defined benefit or defined contribution pension schemes on behalf of directors or employees.

9. FINANCE COSTS

Group	Six months to June 30 (Unaudited) 2017 $'000	Year Ending December 31, 2016 $'000	2015 $'000	2014 $'000
Loan interest paid on convertible loan notes (recognised as debt)	-	-	14	12
Finance charge accrued on convertible loan notes (recognised as debt)	5	12	14	12
Stamp duty paid on the reverse acquisition				63
	5	12	28	87

10. TAXATION

	2016 $'000	2015 $'000	2014 $'000
Group			
Current tax (credit)	(121)	-	(99)
Deferred tax			
Origination and reversal of timing differences	Nil	Nil	Nil
Total tax (credit) for period	(121)	-	(99)

The tax charge for the year is different from the standard rate of corporation tax in the United Kingdom of 21.49%. The difference can be reconciled as follows:

Loss before taxation	(9,770)	(13,193)	(5,484)
Loss charged at standard rate of corporation tax 20% (2015: 21.49%)	(1,953)	(2,669)	(1,264)
Tax calculated at the applicable rate based on loss for the year	1,656	2,334	740
Expenses not deductible for taxation	297	335	485
Adjustments due to prior periods	(121)	-	-
Additional deduction for R&D expenditure			(195)
Utilisation of tax losses			135
	(121)	-	(99)

No deferred tax asset has been recognised in respect of trading losses carried forward because of uncertainty as to when these losses will be recoverable.

11. LOSS PER SHARE

Basic loss per share is calculated by dividing the profit attributable to equity holders of the company by the weighted average number of ordinary shares in issue during the year.

	Six months to June 30 (Unaudited)	Year Ending December 31,		
	2017	**2016**	**2015**	**2014**
(Loss) attributable to equity holders of the company ($000)	(4,693)	(9,770)	(12,419)	(5,484)
Weighted average number of ordinary shares in issue	95,305,823	93,592,195	91,242,884	22,866,387
Basic loss per share (pence per share)	(4.9)	(10.4)	(13.6)	(24.0)

As the Group is reporting a loss from continuing operations for the year then, in accordance with IAS 33, the share options are not considered dilutive because the exercise of the share options would have an anti-dilutive effect. The basic and diluted earnings per share as presented on the face of the income statement are therefore identical. All earnings per share figures presented above arise from continuing and total operations and therefore no earnings per share for discontinued operations are presented.

12. PROPERTY, PLANT AND EQUIPMENT

Details of the Groups property, plant and equipment are as follows:

Group	Furniture and fixtures $'000	IT equipment $'000	Total $'000
Cost			
At 1 January 2016	-	-	-
Additions	15	30	45
Disposals	-	-	-
At 31 December 2016	15	30	45
Depreciation			
At 1 January 2016	-	-	-
Charge in year	1	9	10
At 31 December 2016	1	9	10
Net book value as at 31 December 2016	14	21	35
Net book value as at 31 December 2015	-	-	-

Group	Furniture and fixtures $'000	IT equipment $'000	Total $'000
Cost			
At 1 January 2017	-	-	-
Additions	15	30	45
Disposals	-	-	-
At 31 December 2016	15	30	45
Depreciation			
At 1 January 2017	1	9	10
Charge in period	2	6	8
At 30 June 2017	3	15	18
Net book value as at 30 June 2017 (unaudited)	12	15	27

13. OTHER RECEIVABLES

	Six months to June 30 (Unaudited)	Year Ending December 31,	
	2017 $'000	**2016** $'000	**2015** $'000
Group			
Other receivables	135	115	380
Taxation receivable	-	-	23
Prepayments	10	12	109
	145	127	512

There are no differences between the carrying amount and fair value of any of the trade and other receivables above.

14. OTHER ASSETS

In June 2016, the Board approved the purchase of the Data repository of DNA from SharDNA (an Italian entity in liquidation) for EUR 258,000, approximately $268,000.

Management recognizes that the transaction is not the purchase of a business but the purchase of key assets owned by SharDNA. These assets are to be owned by Tiziana Life Sciences PLC and will be loaned to its subsidiary Longevia SRL for no extra cost.

No research and development work has been carried out to this date, but Management anticipates that this will commence within the next 12 months.

As there is current legal action pending against the liquidators as to the validity to the sale of the assets, the Company is unable to utilise these assets until the legal action is resolved. For this reason, the investment has been recognised as a current asset until such a time that the Company is able to use this asset.

15. INVESTMENTS IN SUBSIDIARIES

The company's interest in subsidiary undertakings is as follows:

Name	Principal activity	Registered Address	Percentage shareholding	Country of incorporation
Tiziana Pharma Limited	Clinical stage biotechnology company	3rd Floor, 11-12 St James's Square, London, SW1Y 4LB	100%	England & Wales
Tiziana Therapeutics Inc	Clinical stage biotechnology company	420 Lexington Avenue Suite 2525 New York, NY 10170	100%	USA
Longevia Genomics SRL	Biotech Discovery Company	Via Constantinopli 42 09100- Cagliria (CA)	100%	Italy

Tiziana Therapeutics Inc was incorporated on 28 October 2015. This entity was set up to house the Company's US operations.

Longevia Genomics SRL was incorporated on 4 July 2016.This entity was established to enable the Company to carry out R&D activities in Sardinia.

16. SHARE CAPITAL

Company and Group	Number of shares	$000
In issue 1 January 2015:	205,862,224	15,217
Transactions in the year:		
Ordinary shares issued at 50.5 pence	4,233,616	191
Ordinary shares issued at 3.0 pence	28,000	1
Ordinary shares issued at 75 pence	3,400,000	151
Ordinary shares issued at 150 pence	58,222	3
In issue 31 December 2015	213,582,062	15,563
Transactions in the year:		
Ordinary shares issued at 3 pence	2,001,250	84
Sale of Deferred shares	1	-
Deferred shares transferred to Capital redemption reserve	(121,189,912)	(8,744)
In issue 31 December 2016	94,393,401	6,903
Transactions in the year:		
Warrants exercised during the period	1,789,524	67
In issue 30 June 2017	96,182,925	6,970

On 20 January 2015 the company issued a further 4,233,616 ordinary shares at 50.5 pence each credited as fully paid, as consideration to Nerviano on the execution of the licence agreement with Nerviano.

On 20 March 2015 the company issued a further 28,000 ordinary shares at 3 pence each in order to satisfy the exercise of options.

On 31 March 2015 the company issued a further 3,400,000 ordinary shares at 75 pence each by way of a further placing of ordinary shares to raise finance.

On 30 October 2015 the company issued a further 58,222 ordinary shares at 150 pence each in order to satisfy the exercise of warrants.

On 28 April 2016 the company issued a further 1,095,000 ordinary shares at 3 pence each in order to satisfy the exercise of warrants.

On 29 June 2016 the company issued a further 206,250 ordinary shares at 3 pence each in order to satisfy the exercise of warrants.

On 29 June 2016 the company issued a further 700,000 ordinary shares at 3 pence each in order to satisfy the exercise of a convertible loan note.

On 30 June 2016 the Company was authorized by ordinary resolution to repurchase the various classes of deferred shares in its capital then outstanding (such deferred shares being of no economic value to the holders); these deferred shares were repurchased for the aggregate sum of £1.00 financed out of the issue of one new ordinary share issued at a price of £1.50 for cash. The share capital attributable to the deferred shares was then transferred to a capital redemption reserve.

On 30 June 2016 the Company was authorized by special resolution of shareholders to effect a capital reduction. This process was approved by the High Court of England and Wales on 14 September 2016. The capital reduction involved the cancellation of the balance of the Company's share premium account and capital redemption reserve (and a balance standing to a merger relief reserve) and the application of these reserves to the then negative balance on the Company's retained earnings reserve, eliminating that negative balance and creating positive retained earnings.

On 30 June 2017, 1,789,524 shares were issued to warrant holders who exercised their warrants previously granted as an arrangement fee for subscribing to a convertible loan notes.

17. SHARE BASED PAYMENTS

Group and Company

Options

The company operates share-based payment arrangements to remunerate directors and key employees in the form of a share option scheme. The exercise price of the option is normally equal to the market price of an ordinary share in the company at the date of grant.

	2016		2015	
	Weighted Average exercise price (cents)	Options ('000)	Weighted Average exercise price (cents)	Options ('000)
Outstanding at 1 January	35	7,985	24	5,222
Granted	190	4,464	60	4,000
Cancelled	-	-	(22)	(1,237)
Outstanding at 31 December	90	12,449	41	7,985
Exercisable at 31 December	41	4,151,750	41	1,996,250

	2017		2016	
	Weighted Average exercise price (cents)	Options ('000)	Weighted Average exercise price (cents)	Options ('000)
Outstanding at 1 January	90	12,449	49	7,985
Granted	225	100	195	4,214
Outstanding at 30 June	97	12,549	94	12,199
Exercisable at 30 June	49	4,302	94	3,993

On 23 January 2015 2,050,000 options were granted at an exercise price of £0.35 per share and are exercisable for a period of 10 years from the date of vesting.

On 23 January 2015 600,000 options were granted at an exercise price of £0.50 per share and are exercisable for a period of 10 years from the date of vesting.

On 23 January 2015 300,000 options were granted at an exercise price of £0.57 per share and are exercisable for a period of 10 years from the date of vesting.

On 2 March 2015 600,000 options were granted at an exercise price of £0.55 per share and are exercisable for a period of 10 years from the date of vesting.

On 7 May 2015 1,237,500 options were cancelled at exercise prices of £0.15 and £0.35 per share and would have been exercisable for a period of 10 years from the date of vesting.

On 7 May 2015 150,000 options were granted at an exercise price of £0.15 per share and are exercisable before 31st January 2018

On 21 October 2015 600,000 options were granted at an exercise price of £2 per share and are exercisable before 21st October 2019

On 23 March 2016 400,000 options were granted at an exercise price of £1.26 per share and are exercisable before 23rd March 2026.

On 9 June 2016 105,000 options were granted at an exercise price of £1.50 per share and are exercisable for a period of 10 years from the date of vesting.

On 9 June 2016 3,259,403 options were granted at an exercise price of £1.50 per share and are exercisable with special conditions for a period of 15 years from the date of vesting.

On 5 November 2016, 100,000 options were granted at an exercise price of £1.86 per share and are exercisable for a period of 10 years from the date of vesting.

On 1 December 2016, 600,000 options were granted at an exercise price of £1.925 per share and are exercisable based upon performance conditions for a period of 5 years from the date of vesting. The performance conditions are based on the successful completion of human clinical trials for two of the R&D projects in the Groups pipeline.

On 10 March 2017, 100,000 options were granted at an exercise price of £1.725 per share and are exercisable for a period of 10 years from the date of vesting.

No options were exercised during the period to June 30 2017 and the period to 31st December 2016. 28,000 options were exercised during the year to 31st December 2015.

Share options outstanding at the end of the year have the following expiry date and exercise prices:

Date of issue	Number at 31 December 2016	Exercise price	Date from which exercisable	Expiry Date
24 April 2014	962,500	0.15	24 April 2015	24 April 2025
24 April 2014	962,500	0.15	24 April 2016	24 April 2026
24 April 2014	962,500	0.15	24 April 2017	24 April 2027
24 April 2014	962,500	0.15	24 April 2018	24 April 2028
25 June 2014	90,000	0.28	17 May 2015	17 May 2025
25 June 2014	90,000	0.28	17 May 2016	17 May 2026
25 June 2014	90,000	0.28	17 May 2017	17 May 2027
25 June 2014	90,000	0.28	17 May 2018	17 May 2028
25 June 2014	6,250	0.33	24 April 2015	24 April 2025
25 June 2014	6,250	0.33	24 April 2016	24 April 2026
25 June 2014	6,250	0.33	24 April 2017	24 April 2027
25 June 2014	6,250	0.33	24 April 2018	24 April 2028
07 July 2014	12,500	0.35	18 June 2015	18 June 2025
07 July 2014	12,500	0.35	18 June 2016	18 June 2026
07 July 2014	12,500	0.35	18 June 2017	18 June 2027
07 July 2014	12,500	0.35	18 June 2018	18 June 2028
23 January 2015	2,050,000	0.35	23 January 2015	23 January 2025
23 January 2015	150,000	0.5	1 October 2015	1 October 2025
23 January 2015	150,000	0.5	1 October 2016	1 October 2026
23 January 2015	150,000	0.5	1 October 2017	1 October 2027
23 January 2015	150,000	0.5	1 October 2018	1 October 2028
23 January 2015	75,000	0.57	12 September 2015	12 September 2025
23 January 2015	75,000	0.57	12 September 2016	12 September 2026
23 January 2015	75,000	0.57	12 September 2017	12 September 2027
23 January 2015	75,000	0.57	12 September 2018	12 September 2028
02 March 2015	150,000	0.55	2 March 2015	2 March 2025
02 March 2015	150,000	0.55	2 March 2016	2 March 2026
02 March 2015	150,000	0.55	2 March 2017	2 March 2027
02 March 2015	150,000	0.55	2 March 2018	2 March 2028
07 May 2015	150,000	0.15	24 April 2015	31 January 2018
21 October 2015	600,000	2.00	21 October 2016	21 October 2019

23 March 2016	100,000	1.26	23 March 2017	22 March 2026
23 March 2016	100,000	1.26	23 March 2018	22 March 2026
23 March 2016	100,000	1.26	23 March 2019	22 March 2026
23 March 2016	100,000	1.26	23 March 2020	22 March 2026
09 June 2016	26,250	1.50	09 June 2017	09 June 2027
09 June 2016	26,250	1.50	09 June 2018	09 June 2028
09 June 2016	26,250	1.50	09 June 2019	09 June 2029
09 June 2016	26,250	1.50	09 June 2020	09 June 2030
09 June 2016	3,259,403	1.50	If weighted average of an ordinary share is greater than £3 for 120 consecutive dealing days	15 years from vesting date
05 November 2016	100,000	1.86	05 November 2017	05 November 2027
01 December 2016	600,000	1.925	Successful completion of clinical trials within 24 months of 1st September 2016	5 years from vesting conditions being met
10 March 2017	25,000	1.725	10 March 2018	10 March 2028
10 March 2017	25,000	1.725	10 March 2019	10 March 2029
10 March 2017	25,000	1.725	10 March 2020	10 March 2030
10 March 2017	25,000	1.725	10 March 2021	10 March 2031

The total outstanding fair value of the share option instruments is deemed to be approximately $2,304,552 as at December 31, 2016 (2015: $1,433,311), and $2,618,136 at June 30, 2017 (2016: $1,302,394).

The Directors have used the Black-Scholes option pricing model to estimate the fair value of most of the options applying the assumptions below.

Historical volatility relies in part on the historical volatility of a group of peer companies that management believes is generally comparable to the Company.

The Company has not paid any dividends on common stock since its inception and does not anticipate paying dividends on its common stock in the foreseeable future.

The Company has estimated a forfeiture rate of zero.

	24 April 2014	**25 June 2014**	**7 July 2014**
Grant date share price	£0.12	£0.39	£0.44
Exercise share price	£0.15	£0.28 to £0.33	£0.35
Vesting periods	25% each	25% each	25% each
	Yr 1, Yr 2, Yr 3, Yr 4	Yr 1, Yr 2, Yr 3, Yr 4	Yr 1, Yr 2, Yr 3, Yr 4
Risk free rate	0.55% to 1.54%	0.55% to 1.54%	0.55% to 1.54%
Expected volatility	99% to 197%	99% to 197%	99% to 197%
Option life	10 years	10 years	10 years

	23 January 2015	**2 March 2015**	**7 May 2015**
Grant date share price	£0.575	£0.615	£0.465
Exercise share price	£0.35 to £0.57	£0.28 to £0.33	£0.15
Vesting periods	900,000 25% each	25% each	Immediate
	Yr 1, Yr 2, Yr 3, Yr 4	Yr 1, Yr 2, Yr 3, Yr 4	
	2.05m immediate		
Risk free rate	0.55% to 1.54%	0.55% to 1.54%	0.55% to 1.54%
Expected volatility	99% to 197%	99% to 197%	99% to 197%
Option life	10 years	10 years	2 years 9 months

	23 March 2016	9 June 2016	5 November 2016
Grant date share price	£1.26	£1.38	£1.86
Exercise share price	£1.26	£1.5	£1.86
Vesting periods	25% each	Immediate,25% each	33.3% each
	Yr 1, Yr 2, Yr 3, Yr 4	Yr 1, Yr 2, Yr 3, Yr 4	Yr 1, Yr 2, Yr 3
Risk free rate	0.55% to 1.54%	0.55% to 1.54%	0.55% to 1.54%
Expected volatility	99% to 197%	99% to 197%	99% to 197%
Option life	10 years	10-15 years	10 years

	1 December 2016	10 March 2017
Grant date share price	£1.86	£1.725
Exercise share price	£1.925	£1.725
Vesting periods	within 24 months of 1 September 2016	25% each
		Yr 1, Yr 2, Yr 3, Yr 4
Risk free rate	0.55% to 1.54%	0.55% to 1.54%
Expected volatility	99% to 197%	85% to 167%
Option life	2 years	10 years

For the options issued with a market condition attached, the Directors have used the Monte Carlo simulation to estimate the fair value of these options, the Company uses the following methods to determine its underlying assumptions:

- expected volatilities are based on the historical volatilities of the market
- the expected term of the awards is based on managements' assessment of when the market condition is likely to be achieved of 15 years
- a range of fair value's per share were produced and management have determined the most appropriate value based on their knowledge of the market and vesting conditions being fulfilled.

Warrants

The Directors have estimated the fair value of the warrants in services provided using an appropriate valuation model. The total fair value of the warrant instruments is deemed to be approximately $340,501. For each set of warrants, the charge has been expensed over the vesting period. A share based payment charge for the year of $120,441 (year to December 2015: $156,424) has been expensed in the statement of comprehensive income.

18. CONVERTIBLE LOAN NOTES

Group and Company

Planwise Convertible Loan Notes 2016

From the date of the reverse acquisition a convertible loan note of $247,000 was in existence as detailed in the Admission Document dated 31 March 2014. Proceeds of the subscriptions for the notes are to be used exclusively to finance the Company's on-going working capital requirements. The terms of the loan note are that the loan notes, plus accrued interest at a rate of 4 per cent above Bank of England base rate per annum, will convert into ordinary shares in the Company at a price of £0.10 per share at the election of Planwise any time after the second anniversary of the readmission to AIM on 24 April 2014. The Company considers this to be a Convertible Debt Instrument as detailed in the policy described at note 2.

Accounting for the convertible debt instrument

The net proceeds received from the issue of the Planwise Convertible Loan Note 2016 has been recorded as a debt liability in the balance sheet and the accrued interest charged to the income statement and the debt liability. The liability for the convertible debt instrument is;

Planwise Convertible Loan Note

	June 30, 2017 $000 (unaudited)	December 31, 2016 $000
Convertible loan notes issued	247	247
Accrued interest	36	31
	283	278

19. CONVERTIBLE EQUITY INSTRUMENTS

The principal amount of the Convertible Equity Instrument for Tranches A to F are recorded as shares to be issued reserve and the accrued interest also charged to the same reserve.

$000	A	B	C	D	E	F	Total
Balance as at January 1 2016	1,084	1,932	7,321	323	4,848	-	15,509
Convertible equity instruments issued	-	-	-	-	-	936	936
Addition to Equity (Interest)	58	158	325	13	305	51	911
Convertible equity instruments exercised		(198)					(198)
Balance as at December 31 2016	1,142	1.893	7,646	336	5,153	988	17,158
Addition to Equity (Interest)	29	49	159	7	148	27	419
Convertible equity instruments exercised	-	-	-	-	-	-	-
Balance as at June 30, 2017	1,171	1,942	7,805	343	5,301	1,015	17,577

20. SHARE PREMIUM

	Six months to June 30 (Unaudited)	Year Ending December 31,	
Group and Company	**2017**	**2016**	**2015**
	$000	$000	$000
Balance at 1 January	8,943	33,496	27,069
Premium on issue of shares	648	546	6,427
Capital reduction		(25,099)	-
Closing Balance	9,591	8,943	33,496

21. RESERVES

The shares to be issued reserve represent the value of equity shares which could be issued in future accounting periods if the warrants in issue are exercised.

The share based payment reserve represents the value of equity shares which could be issued in future accounting periods if the share based payment options in issue are exercised.

The merger relief reserve was created as a result of the reverse merger reverse acquisition of Alexander David Investments plc. The reserve represents the difference between the fair value of the consideration transferred and the nominal value of the shares. This reserve has been written off as part of the balance sheet capital reduction exercise described below.

The other reserve was created as a result of the reverse acquisition of Alexander David Investments plc in the year and the accounting treatment required, which is described in Note 2. The reserve is required due to the fact that the reverse acquisition accounting requires the legal parent's equity structure to be shown.

Retained earnings represent the cumulative profits / (losses) of the entity which have not been distributed to shareholders. This reserve has been credited as part of the capital reduction exercise described below.

On the 14th of September the High court granted the Company permission to cancel its share premium account and its capital redemption reserve. The order had previously been ratified at the AGM held on 30th June 2016.

The Company also decided to cancel its merger relief reserve as part of the capital reduction exercise.

22. FINANCIAL INSTRUMENTS

The main risks arising from the Group's financial instruments are liquidity risk, foreign currency risk and credit risk. The directors regularly review and agree policies for managing each of these risks which are summarised below.

Market risk

Market risk encompasses three types of risk, being foreign currency exchange risk, price risk and fair value interest rate risk. The Group policies for managing fair value interest rate risk are considered along with those for managing cash flow interest rate risk and are set out in the subsection entitled ''interest rate risk'' below. The directors do not consider the Group's exposure to price risk to be significant. The Group's risk management is coordinated by the directors, and focuses on actively securing the Group's short to medium term cash flows by minimising the exposure to financial markets. The Group does not engage in the trading of financial assets for speculative purposes nor does it write options.

Credit risk

Credit risk is managed on a group basis. Credit risk arises principally from cash and cash equivalents and deposits with banks and financial institutions as well as credit exposure to customers including committed transactions and outstanding receivables. The group reviews its banking arrangements carefully to minimise such risks and currently has no customers and therefore this risk is viewed as minimal. Management monitor loans between members of the group as part of their internal reporting and assess outstanding receivables for ability to be repaid.

Liquidity risk

The group's policy is to regularly monitor current and expected liquidity requirements to ensure that it maintains sufficient reserves of cash to meet its liquidity requirements in the short and long term. The Group ordinarily finances its activities through cash generated from operating activities and private and public offerings of equity and debt securities.

Foreign currency risks

The group operates internationally although the majority of its operations are based in the United Kingdom and the majority of assets and liabilities denominated in British Pounds. It therefore is exposed to foreign exchange risk arising from exposure to various currencies primarily the Euro and US Dollar.

Due to the majority of assets being denominated in British Pounds the group has no formal policies for managing foreign currency risks.

Interest rate risk

The Group has limited exposure to interest-rate risk arising from its bank deposits. These deposit accounts are held at variable interest rates based on Allied Irish Bank base rate.

The directors do not consider the impact of possible interest rate changes based on current market conditions to be material to the net result for the year or the equity position at the year-end for either the year ended 31 December 2015 or 31 December 2016.

23. CAPITAL RISK MANAGEMENT

The Company's objectives when managing capital are to safeguard the Company's ability to continue as a going concern and to maximise shareholder value through the optimisation of the debt and equity balance.

The Group monitors its capital structure and makes adjustments, as and when it is deemed necessary and appropriate to do so, using such methods as the issuing of new shares. The capital structure of the Group has come from equity issues and the issue of convertible loan notes in the form of convertible equity instruments or convertible debt instruments.

The Company currently does not have any specific policies and processes for managing capital and is not subject to any externally imposed capital requirement other than requirements of the Companies Act 2006.

24. TRADE AND OTHER PAYABLES

	Six months to June 30 (Unaudited)	Year Ending December 31,	
Group	2017	2016	2015
	$000	$000	$000
Trade payables	2,368	1,496	463
Accruals	320	369	319
Convertible loan note liability	297	278	318
	2,985	2,143	1,100

25. RELATED PARTY TRANSACTIONS

Tiziana Pharma Limited is a wholly owned subsidiary of Tiziana Life Sciences plc. At year end, Tiziana Life Sciences plc had transferred £4,186,078 in total to Tiziana Pharma Limited during the year. Included within other debtors of Tiziana Life Sciences plc's company financial statements at the balance sheet date is $5,164,364 (2015: $3,603,797) owed by Tiziana Pharma Limited.

Tiziana Therapeutics Inc. is a wholly owned subsidiary of Tiziana Life Sciences plc. During the year, Tiziana Life Sciences plc transferred $1,181,525 (2015: $247,612) to Tiziana Therapeutics Inc. This balance is included within other debtors.

26. OPERATING LEASES

The Group leases number of office premises under operating lease. The future minimum rentals payable under non-cancellable operating leases as at 31 December are as follows:

	Six months to June 30 (Unaudited)	Year Ending December 31,	
	2017	2016	2015
	$000	$000	$000
Less than one year	231	266	-
Between one and five years	680	612	-
More than five years		-	-
Total	911	878	-

Lease expenses during the year to December 30, 2016 amount to $146,466 (2015: $7,373).

27. POST BALANCE SHEET EVENTS

On the 12th of July 2017, the Company announced a proposed restructuring of convertible loan notes ("CLN") an a proposed variation to the terms of warrants issued. The Company proposed that CLN Holders be offered an additional bonus coupon of 3 years of interest at the relevant applicable rate of return for agreeing to the immediate conversion of the CLN's into ordinary shares. If the CLN Holders agree to the proposal they will be subject to a restriction not to dispose of the relevant shares for a period of 12 months following conversion.

Furthermore, the Company has proposed to vary the terms of the warrants associated with the CLNs by extending the exercise period of these warrants to 31 December 2021. If the Warrant Holders agreement to the proposal, the ordinary shares they receive upon conversion of the warrants would also be subject to a restriction not to dispose of the relevant shares for a period of 12 months following such conversion.

On August 16 2017, the Company announces that further to the proposals announced on 12 July 2017, the holders of the Company's Convertible Loan Note ("CLN Holders") and the Company's Warrant Holders ("Warrant Holders") have passed the resolutions that were put to them to convert all of the loan notes and vary the terms of the warrants substantially prior to the intended deadline for consent. Accordingly the full $16,853,500 (at par value) of the CLNs have now been converted into ordinary shares (including accrued interest), resulting in the issue of 27,645,013 new ordinary shares in the Company. Therefore the fully diluted issued share capital of the Company is 138,216,920 ordinary shares (assuming all options and warrants, vested and unvested, exercised and exercisable, were converted).

On 19th of July 2017, the Company announced the enrollmement of its first patienet into the Phase IIa clinincal trial with Milciclib.

In July 2017, the Company announces publication of a research article in a prestigious journal, Clinical Immunology, entitled: "Oral treatment with foralumab, a fully human anti-CD3 monoclonal antibody, prevents skin xenograft rejection in humanized mice". This is the first-ever published report demonstrating the potential of oral therapy with foralumab (NI-0401) for inflammatory diseases such as non-alcoholic steatohepatitis (NASH). Tiziana's foralumab is the only fully human engineered anti-CD3 monoclonal antibody (mAb) in clinical development to date.

On August 11th 2017, the Company entered into a separation agreement with James Tripp, the former COO. James's employment with the Company was terminated in May 16th 2017. The Company has committed to paying a severance payment which is equivalent to nine months of his base compensation which was in effect as of the Separation Date. This amounts to approximately $168,750.

28. FINANCIAL COMMITMENTS

The Group's main financial commitments relate to the contractual payments in respect of its licensing agreements. Due to the uncertain nature of scientific research and development and the length of time required to reach commercialisation of the products of this research and development, pre-clinical, clinical and commercial milestone obligations are not detailed until there is a reasonable certainty that the obligation will become payable. Contractual commitments are detailed where amounts are known and certain.

- Milciclib project Research funding of approximately $2.0m has been committed to for 2017 and beyond. Other payments relate to the achievement of clinical milestones or the payment of royalties.

- Stemprinter – sponsored research funding of €150,000 in, 2017 subject to suitable progress of research (automatically renewed for up to 4 years if research milestones are achieved). Other payments relate to the achievement of clinical milestones or the payment of royalties.

- Foralumab project – license fees payable for the continued development of foralumab of $250,000 in 2017 and 2018 for a total fee payment of $750,000. Diligence obligations are payable to BMS / Medarex should the project continue and no Phase III clinical trial has been initiated by 15 December 2017. Other payments relate to the achievement of clinical milestones or the payment of royalties.

ITEM 19: EXHIBITS

Exhibit No.	Description
1.1*	Memorandum and Articles of Association of Tiziana Life Sciences PLC.
2.1*	Form of Deposit Agreement.
2.2*	Form of American Depositary Receipt.
4.1*†	Licence Agreement relating to Milciclib between Nerviana Medical Services S.r.l. and Tiziana Life Sciences PLC, dated January 2015.
4.2*†	Licence and Sublicence Agreement relating to CD3 (NI-0401) between Novimmune SA and Tiziana Life Sciences PLC, dated December 2014.
4.3*†	Licence and Sublicence Agreement relating to IL-6r (NI-1201) between Novimmune SA and Tiziana Life Sciences PLC, dated December 2016.
4.4*	Executive Director Service Agreement between Dr. Kunwar Shailubhai and Tiziana Life Sciences PLC, dated May 2017.
4.5*	Executive Director Service Agreement between Gabriele Marco Antonio Cerrone and Tiziana Life Sciences PLC, dated .
4.6*	Executive Director Service Agreement between Riccardo Dalla-Favera and Tiziana Life Sciences PLC, dated .
4.7*	Executive Director Service Agreement between Willy Simon and Tiziana Life Sciences PLC, dated January 2016.
4.8*	Senior Manager Employment Agreement between Tiziano Lazzaretti and Tiziana Life Sciences PLC, dated April 2016.
4.9*	Senior Manager Employment Agreement between Betty Liong Chu and Tiziana Life Sciences PLC, dated .
4.10*	Senior Manager Employment Agreement between Jules S. Jacob and Tiziana Life Sciences PLC, dated .
4.11*	Senior Manager Employment Agreement between Evangeline Priya Eddy and Tiziana Life Sciences PLC, dated .
4.12*	Senior Manager Employment Agreement between Vaseem A. Palejwala and Tiziana Life Sciences PLC, dated .
4.13*	Annual Lease for 55 Park Lane, Suite 14a, London W1K 1NA, United Kingdom, dated .
4.14*	Five-Year Lease for 420 Lexington Avenue, Suite 2525, New York, United States, dated .
4.15*	Annual Lease for 3085 Old Easton Road, Doylestown, Pennsylvania, United States, dated .
4.16*	2016 Equity Incentive Plan for Tiziana Life Sciences PLC, adopted by the Board on 23 May 2016 and approved by shareholders on 30 June 2016.
8.1*	List of Subsidiaries.

Exhibit No.	Description
15.1*	Consent of Mazars LLP, independent registered public accounting firm, regarding the financial statements of Tiziana Life Sciences PLC as of December 31, 2016 and 2015 and for each of the two years in the period ended December 31, 2016.

† Confidential treatment requested as to certain portions, which portions have been omitted and filed separately with the Securities and Exchange Commission

* To be filed by amendment

SIGNATURES

The Registrant hereby certifies that it meets all of the requirements for filing on Form 20-F and that it has duly caused and authorized the undersigned to sign this registration statement on its behalf.

TIZIANA LIFE SCIENCES plc

By: _____

Kunwar Shailubhai
Chief Executive Officer

Date: , 2018