Adaptimmune Therapeutics PLC
Form 20-F
October 13, 2015
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 20-F

o	**REGISTRATION STATEMENT PURSUANT TO SECTION 12(b) OR (g) OF THE SECURITIES EXCHANGE ACT OF 1934**
	OR
x	**ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934** **For the fiscal year ended June 30, 2015**
	OR
o	**TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
	OR
o	**SHELL COMPANY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

Commission File Number 001-37368

ADAPTIMMUNE THERAPEUTICS PLC

(Exact name of Registrant as specified in its charter)

England and Wales
(Jurisdiction of incorporation or organization)

101 Park Drive, Milton Park

Abingdon, Oxfordshire OX14 4RY

United Kingdom

(44) 1235 430000
(Address of principal executive offices)

ADAPTIMMUNE LLC

Two Commerce Square

Suite 1700, 2001 Market Street

Philadelphia, PA 19103

United States of America

(215) 825 9260
(Name, Address, Including Zip Code, and Telephone Number, Including Area Code, of Agent For Service)

James J. Noble, Chief Executive Officer

Adaptimmune Therapeutics Plc

101 Park Drive, Milton Park

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(Name, Telephone, E-mail and/or Facsimile number and Address of Company Contact Person)

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 6 Ordinary Shares, par value £0.001 per share	**The Nasdaq Stock Market LLC**

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

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

Indicate the number of outstanding shares of each of the issuer s classes of capital or common stock as of the close of the period covered by the annual report: 424,711,900 ordinary shares, par value £0.001 per share.

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. o Yes x 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. o Yes x 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. x Yes o 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). o Yes x No (not required)

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

Large accelerated filer o	Accelerated filer o	Non-accelerated filer x

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

U.S. GAAP o	International Financial Reporting Standards as issued by the International Accounting Standards Board x	Other o

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. o Item 17 o 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). o Yes x No

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GENERAL INFORMATION

In this annual report on Form 20-F (Annual Report), Adaptimmune, the Group, the company, we, us and our refer to Adaptimmune Th plc and its consolidated subsidiaries, except where the context otherwise requires. Adaptimmune® is a registered trademark of Adaptimmune.

PRESENTATION OF FINANCIAL AND OTHER DATA

The consolidated financial statement data as of June 30, 2015, 2014 and 2013 and for the years ended June 30, 2015, 2014 and 2013 have been derived from our consolidated financial statements, as presented elsewhere in this Annual Report, which have been prepared in accordance with International Financial Reporting Standards, or IFRS, as issued by the International Accounting Standards Board, or IASB, and as adopted by the European Union and audited in accordance with the standards of the Public Company Accounting Oversight Board (United States).

All references in this Annual Report to $ are to U.S. dollars, all references to £ are to pounds sterling and all references to are to Euros. Solely for the convenience of the reader, unless otherwise indicated, all pounds sterling amounts as of and for the year ended June 30, 2015 have been translated into U.S. dollars at the rate as of June 30, 2015, the last business day of our year ended June 30, 2015, of £1.00 to $1.5727. These translations should not be considered representations that any such amounts have been, could have been or could be converted into U.S. dollars at that or any other exchange rate as of that or any other date.

We have historically conducted our business through Adaptimmune Limited and its subsidiary, and therefore our historical financial statements present the consolidated results of operations of Adaptimmune Limited. Following the Corporate Reorganization, our financial statements present the consolidated results of Adaptimmune Therapeutics plc.

INFORMATION REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report contains forward-looking statements that are based on our current expectations, assumptions, estimates and projections about us and our industry. All statements other than statements of historical fact in this Annual Report are forward-looking statements.

These forward-looking statements are subject to known and unknown risks, uncertainties, assumptions and other factors that could cause our actual results of operations, financial condition, liquidity, performance, prospects, opportunities, achievements or industry results, as well as those of the markets we serve or intend to serve, to differ materially from those expressed in, or suggested by, these forward-looking statements. These forward-looking statements are based on assumptions regarding our present and future business strategies and the environment in which we expect to operate in the future. Important factors that could cause those differences include, but are not limited to:

- our ability to advance our NY-ESO TCR therapeutic candidate to a point where GlaxoSmithKline, or GSK, exercises the option to license the product;

- our ability to successfully advance our MAGE-A10 therapeutic candidate through clinical development;

- the success, cost and timing of our product development activities and clinical trials;

- our ability to successfully advance our technology platform to improve the safety and effectiveness of our existing TCR therapeutic candidates and to submit INDs for new TCR therapeutic candidates;

- the rate and degree of market acceptance of T-cell therapy generally and of our TCR therapeutic candidates;

- government regulation and approval, including, but not limited to, the expected regulatory approval timelines for TCR therapeutic candidates;

- patents, including, any legal challenges thereto or enforcement of patents against us;

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- the level of pricing and reimbursement for our TCR therapeutic candidates;

- general economic and business conditions or conditions affecting demand for our TCR therapeutic candidates in the markets in which we operate, both in the United States and internationally;

- volatility in equity markets in general and in the biopharmaceutical sector in particular;

- fluctuations in the price of raw materials and utilities;

- our relationships with suppliers and other third-party providers;

- increased competition from other companies in the biotechnology and pharmaceutical industries;

- claims for personal injury or death arising from the use of our TCR therapeutic candidates;

- changes in our business strategy or development plans, and our expected level of capital expenses;

- our ability to attract and retain qualified personnel;

- regulatory, environmental, legislative and judicial developments including a regulatory requirement to place any clinical trials on hold or to suspend any trials;

- a change in our status as an emerging growth company under the JOBS Act or a foreign private issuer; and

- additional factors that are not known to us at this time.

Additional factors that could cause actual results, financial condition, liquidity, performance, prospects, opportunities, achievements or industry results to differ materially include, but are not limited to, those discussed under Risk Factors in this Annual Report. Additional risks that we may currently deem immaterial or that are not presently known to us could also cause the forward-looking events discussed in this Annual Report not to occur. The words believe, may, will, estimate, continue, anticipate, intend, expect and similar words are intended to identify estimates and forward-looking statements. Estimates and forward-looking statements speak only at the date they were made, and we undertake no obligation to update or to review any estimate and/or forward-looking statement because of new information, future events or other factors. Estimates and forward-looking statements involve risks and uncertainties and are not guarantees of future performance. Our future results may differ materially from those expressed in these estimates and forward-looking statements. In light of the risks and uncertainties described above, the estimates and forward-looking statements discussed in this Annual Report might not occur, and our future results and our performance may differ materially from those expressed in these forward-looking statements due to, inclusive of, but not limited to, the factors mentioned above. Because of these uncertainties, you should not make any investment decision based on these estimates and forward-looking statements.

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PART I

Item 1. Identity of Directors, Senior Management and Advisers.

Not Applicable.

Item 2. Offer Statistics and Expected Timetable.

Not Applicable.

Item 3. Key Information.

A. Selected Financial Data.

The following table summarizes our consolidated financial data as at the dates and for the periods indicated. The consolidated financial statement data as at June 30, 2015, and 2014 and for the years ended June 30, 2015, 2014 and 2013 have been derived from our consolidated financial statements, as presented elsewhere in this Annual Report, which have been prepared in accordance with IFRS, as issued by the IASB, and as adopted by the European Union and audited in accordance with the standards of the Public Company Accounting Oversight Board (United States).

Our consolidated financial statements are prepared and presented in pounds sterling, our presentation currency. Solely for the convenience of the reader, unless otherwise indicated, all pounds sterling amounts as at and for the year ended June 30, 2015 have been translated into U.S. dollars at the rate at June 30, 2015, the last business day of our year ended June 30, 2015, of £1.00 to $1.5727.

Our historical results are not necessarily indicative of the results that may be expected in the future. The following selected consolidated financial data should be read in conjunction with our audited consolidated financial statements included elsewhere in this Annual Report and the related notes and Item 5, Operating and Financial Review and Prospects below.

	Year Ended June 30,		
2015 ($ 000)	2015 (£ 000)	2014 (£ 000)	2013 (£ 000)

Income Statement Data:				
Revenue	**10,723**	**6,818**	**355**	
Research and development expenses	(23,196)	(14,749)	(7,356)	(5,361)
General and administrative expenses	(11,325)	(7,201)	(1,602)	(797)
Other income	727	462	165	7
Operating loss	**(23,071)**	**(14,670)**	**(8,438)**	**(6,151)**
Finance income	506	322	2	9
Finance expense	(1,132)	(720)	(4)	(4)
Loss before tax	**(23,697)**	**(15,068)**	**(8,440)**	**(6,146)**
Taxation credit	2,105	1,339	982	578
Loss for the year	**(21,592)**	**(13,729)**	**(7,458)**	**(5,568)**
Basic and diluted per share	**$ (0.07)**	**£ (0.04)**	**£ (0.05)**	**£ (0.05)**
Weighted average number of shares outstanding	325,012,111	325,012,111	148,484,504	105,376,900

		As at June 30,	
	2015 ($ 000)	**2015 (£ 000)**	**2014 (£ 000)**
Balance Sheet Data:			
Cash and cash equivalents	229,089	145,666	30,105
Current asset investments	55,302	35,164	
Total assets	300,716	191,210	32,597
Total liabilities	41,074	26,117	31,182
Total equity/ Net assets	259,642	165,093	1,415

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On April 1, 2015, we completed a corporate reorganization. Pursuant to this reorganization, on February 23, 2015, all shareholders of Adaptimmune Limited exchanged each of the Series A preferred shares and ordinary shares held by them for newly issued Series A preferred shares and ordinary shares of Adaptimmune Therapeutics Limited on a one-for-100 basis, resulting in Adaptimmune Limited becoming a wholly-owned subsidiary of Adaptimmune Therapeutics Limited. On March 20, 2015, all holders of options over ordinary shares of Adaptimmune Limited exchanged each of their options for equivalent options over ordinary shares of Adaptimmune Therapeutics Limited. On April 1, 2015, pursuant to the final step in our corporate reorganization, Adaptimmune Therapeutics Limited re-registered as a public limited company with the name Adaptimmune Therapeutics plc.

The reorganization has been accounted for in accordance with the principles of reverse acquisition accounting. Accordingly, the historical consolidated financial statements of Adaptimmune Limited and subsidiary prior to the reorganization became those of Adaptimmune Therapeutics plc. For periods prior to the reorganization, the equity of Adaptimmune Therapeutics plc represents the historical equity of Adaptimmune Limited. No adjustments have been made to our consolidated financial statements in regard to the reorganization except for the share capital and that the calculation of basic and diluted loss per share shown on the face of the income statement and the weighted average number of shares outstanding gives effect to the reorganization by dividing the loss for the period by the weighted average number of shares outstanding as if the one-for-100 share exchange had been in effect throughout the period. Immediately prior to the admission to trading of our American Depositary Shares (ADSs) on the Nasdaq Global Select Market, all Series A preferred shares of Adaptimmune Therapeutics plc converted to ordinary shares on a one-for-one basis.

Exchange rate information

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 Annual Report.

		Noon Buying Rate		
	Period End	Average(1)	High	Low
		($ per £ 1.00)		
Year ended June 30,				
2011	1.5537	1.6105	1.6691	1.5358
2012	1.6262	1.5924	1.6275	1.5301
2013	1.6574	1.5668	1.6574	1.4837
2014	1.5578	1.6480	1.7165	1.5361
2015	1.5727	1.5754	1.7165	1.4648
Month:				
April 2015	1.5328	1.4968	1.5485	1.4648
May 2015	1.5286	1.5456	1.5772	1.5118
June 2015	1.5727	1.5576	1.5882	1.5187
July 2015	1.5634	1.5560	1.5634	1.5353
August 2015	1.5363	1.5578	1.5731	1.5362
September 2015	1.5116	1.5338	1.5573	1.5116
October 2015 (through to October 9)	1.5315	1.5245	1.5316	1.5162

(1) The average of the noon buying rate for pounds sterling on the last day of each full month during the relevant year or each business day during the relevant month indicated.

B. Capitalization and Indebtedness.

Not Applicable.

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C. Reasons for the Offer and Use of Proceeds.

Not Applicable.

D. Risk Factors.

Our business has significant risks. You should carefully consider the following risk factors as well as all other information contained in this Annual Report, including our consolidated financial statements and the related notes, before making an investment decision regarding our securities. The risks and uncertainties described below are those significant risk factors currently known and specific to us that we believe are relevant to our business, results of operations and financial condition. Additional risks and uncertainties not currently known to us or that we now deem immaterial may also impair our business, results of operations and financial condition.

Risks Related to Our Financial Condition and Capital Requirements

We are a clinical-stage biopharmaceutical company with no commercial products and prediction of future performance is very difficult.

We are a clinical-stage biopharmaceutical company focused on novel cancer immunotherapy products. We have no products or therapeutics approved for commercial sale and have not generated any revenue from product supplies or royalties. Our therapeutic candidates are based on engineered T-cell receptors, or TCRs, and are new and largely unproven. Our limited operating history, particularly in light of the rapidly evolving cancer immunotherapy field, may make it difficult to evaluate our current business and predict our future performance. Investment in biopharmaceutical product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate effect or an acceptable safety profile, gain regulatory approval and become commercially viable. Our inability to address these risks successfully would have a materially adverse effect on our business and prospects.

We have incurred net losses every year since our inception and expect to continue to incur net losses in the future.

We have generated losses since our inception in 2008, during which time we have devoted substantially all of our resources to research and development efforts relating to our TCR therapeutic candidates, including engaging in activities to manufacture and supply our TCR therapeutic candidates for clinical trials in compliance with current good manufacturing practices, or cGMP, conducting clinical trials of our TCR therapeutic candidates, providing general and administrative support for these operations and protecting our intellectual property. We do not have any products approved for sale and have not generated any revenue from product supplies or royalties. Based on our current plans, we do not expect to generate product or royalty revenues unless and until we obtain marketing approval for, and commercialize, any of our TCR therapeutic candidates.

For the years ended June 30, 2015, 2014 and 2013, we incurred net losses of £13.7 million, £7.5 million and £5.6 million, respectively. As of June 30, 2015, we had an accumulated deficit of £30.0 million. We expect to continue incurring significant losses as we continue with our research and development programs and to incur general and administrative costs associated with our operations. The extent of funding required to develop our product candidates is difficult to estimate given the novel nature of our TCR therapeutic candidates and their un-proven route to market. Our profitability is dependent upon the successful development, approval, and commercialization of our TCR therapeutic candidates, successfully achieving GSK milestones and achieving a level of revenues adequate to support our cost structure. We may never achieve profitability, and unless and until we do, we will continue to need to raise additional cash.

We have never generated any revenue from sales of our TCR therapeutic candidates and our ability to generate revenue from sales of our TCR therapeutic candidates and become profitable depends significantly on our success in a number of factors.

We have no TCR therapeutic candidates approved for commercial sale, have not generated any revenue from sales of our TCR therapeutic candidates, and do not anticipate generating any revenue from sales of our TCR therapeutic candidates until some time after we receive regulatory approval, if at all, for the commercial sale of a TCR therapeutic candidate. We intend to fund future operations through milestone payments under our collaboration and license agreement with GSK and through additional equity financings. Our ability to generate revenue and achieve profitability depends on our success in many factors, including:

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- completing research regarding, and preclinical and clinical development of, our TCR therapeutic candidates;

- obtaining regulatory approvals and marketing authorizations for our TCR therapeutic candidates for which we complete clinical trials;

- progressing our clinical trials within predicted timeframes and without any substantial delays, for example as may be caused by delays in patient recruitment, regulatory requirements to hold or suspend any clinical trials or delays in obtaining approvals required to conduct clinical trials;

- developing sustainable and scalable manufacturing and supply processes for our TCR therapeutic candidates, including establishing and maintaining commercially viable supply relationships with third parties and establishing our own commercial manufacturing capabilities and infrastructure;

- launching and commercializing TCR therapeutic candidates for which we obtain regulatory approvals and marketing authorizations, either directly or with a collaborator or distributor;

- obtaining market acceptance of our TCR therapeutic candidates as viable treatment options;

- addressing any competing technological and market developments;

- identifying, assessing, acquiring and/or developing new TCR therapeutic candidates;

- maintaining, protecting, and expanding our portfolio of intellectual property rights, including patents, trade secrets and know-how; and

- attracting, hiring and retaining qualified personnel.

Even if one or more of our TCR therapeutic candidates is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved TCR therapeutic candidate. Our expenses could increase beyond expectations if the U.S. Food and Drug Administration, or the FDA, or any other regulatory agency requires changes to our manufacturing processes or assays, or for us to perform preclinical programs and clinical or other types of trials in addition to those that we currently anticipate. If we are successful in obtaining regulatory approvals to market one or more of our TCR therapeutic candidates, our revenue will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval, the accepted price for the TCR therapeutic candidate, the ability to get reimbursement at any price, and whether we own the commercial rights for that territory. If the number of our addressable disease patients is not as significant as we estimate, the indication approved by regulatory authorities is narrower than we expect, or the reasonably accepted population for treatment is narrowed by competition, physician choice or treatment guidelines, we may not generate significant revenue from sales or supplies of such TCR therapeutic candidates, even if approved. If we are not able to generate revenue from the sale of any approved TCR therapeutic candidates, we may never become profitable.

If we fail to obtain additional financing, we may be unable to complete the development and commercialization of our TCR therapeutic candidates.

Our operations have required substantial amounts of cash since inception. We expect to continue to spend substantial amounts to continue the development of our TCR therapeutic candidates, including future clinical trials. If we receive approval for any of our TCR therapeutic candidates, we will require significant additional amounts in order to launch and commercialize these therapeutic candidates.

As of June 30, 2015, we had a total cash position of $284.3 million which comprised $229.1 million of cash and cash equivalents and $55.3 million of short-term deposits. We expect to use these funds to advance and accelerate the clinical development of our MAGE-A10 TCR therapeutic candidate, to further develop and enhance our manufacturing capabilities and secure a commercially viable manufacturing platform for all of our TCR therapeutic candidates, to advance additional TCR therapeutic candidates into preclinical testing and progress such TCR therapeutic candidates through to clinical trials as quickly as possible and to fund working capital, including other general corporate purposes. We believe that such proceeds, our existing cash, and cash equivalents together with milestone payments to us under the GSK collaboration and license agreement will be sufficient to fund our operations for the foreseeable future, including for at least the next 24 months. However, changing circumstances beyond our control may cause us to increase our spending significantly faster than we currently anticipate. We may require additional capital for the further development and commercialization of our TCR therapeutic candidates and may need to raise additional funds sooner if we choose to expand more rapidly than we presently anticipate.

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We cannot be certain that additional funding will be available on acceptable terms, or at all. We have no committed source of additional capital and if we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of our TCR therapeutic candidates or other research and development initiatives. Our license and supply agreements may also be terminated if we are unable to meet the payment obligations under these agreements. We could be required to seek collaborators for our TCR therapeutic candidates at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available or relinquish or license on unfavorable terms our rights to our TCR therapeutic candidates in markets where we otherwise would seek to pursue development or commercialization ourselves. Any of the above events could significantly harm our business, prospects, financial condition and results of operations and cause the price of our ADSs to decline.

Risks Related to the Development of Our TCR Therapeutic Candidates

Our business is highly dependent on our lead NY-ESO TCR therapeutic candidate, which will require significant additional clinical testing before we can seek regulatory approval and begin commercialization of any of our TCR therapeutic candidates.

There is no guarantee that any of our TCR therapeutic candidates will achieve regulatory approval or proceed to the next stage of clinical programs. The process for obtaining marketing approval for any candidate is very long and risky and there will be significant challenges for us to address in order to obtain marketing approval, if at all.

There is no guarantee that the results obtained in current clinical trials for our NY-ESO TCR therapeutic candidate will be sufficient to plan one or more pivotal clinical trials and obtain regulatory approval or marketing authorization. Negative results in this lead clinical program of our NY-ESO TCR therapeutic candidate or in other investigator-initiated clinical programs utilizing our NY-ESO therapeutic candidate may also impact our ability to obtain regulatory approval for other TCR therapeutic candidates, either at all or within anticipated timeframes because, although the TCR therapeutic candidate may target a different cancer peptide, the underlying technology platform, manufacturing process and development process is the same for all of our TCR therapeutic candidates. Accordingly, a failure in any one program may affect the ability to obtain regulatory approval to continue or conduct clinical programs for other TCR therapeutic candidates.

We may not be able to submit INDs, or the foreign equivalent outside of the United States, to commence additional clinical trials for other TCR therapeutic candidates on the timeframes we expect, and even if we are able to, the FDA or comparable foreign regulatory authorities may not permit us to proceed with planned clinical trials.

Progression of new TCR therapeutic candidates into clinical trials is inherently risky and dependent on the results obtained in preclinical programs, the results of other clinical programs and results of third-party programs that utilize common components, such as production of the lentiviral vector lot used for production and administration of our TCR therapeutic candidate. If results are not available when expected or problems are identified during therapy development, we may experience significant delays in development of pipeline products and in existing clinical programs, which may impact our ability to receive regulatory approval. This may also impact our ability to achieve certain financial milestones and the expected timeframes to market any of our TCR therapeutic candidate. Failure to submit further INDs or the foreign equivalent and commence additional clinical programs will significantly limit our opportunity to generate revenue.

We are currently in the process of completing preclinical development of our AFP therapeutic candidate. Our ability to submit an IND for our AFP therapeutic candidate will depend on the completion of that preclinical development and the development of a protocol for use of that AFP therapeutic candidate which is acceptable to the FDA or any foreign equivalent regulatory authority. Progression of our AFP therapeutic candidate into clinical programs will depend on our ability to find clinical sites able and willing to carry out such clinical programs and recruitment of patients into resulting clinical programs.

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Our TCR therapeutic candidates being developed may have potentially fatal cross-reactivity to other peptides or protein sequences within the body.

One of our prior TCR therapeutic candidates, designed to target a MAGE-A3 cancer-specific peptide, recognized another unrelated peptide from a protein called TITIN, expressed within normal cardiac and other muscle tissues in patients. As a result of this cross-reactivity to the TITIN protein in the heart, two patients died during our MAGE-A3 clinical program, the program was put on pause, then formally placed on hold by the FDA, after which we abandoned the program. We subsequently developed a preclinical safety testing program that identifies potential cross-reactivity risks that has not yet been used for our existing TCR therapeutic candidates, and accordingly, there may be gaps or other problems detected in the testing program at a later date. Even with the use of this testing program, there can be no guarantee that the FDA will permit us to begin clinical trials of any additional TCR therapeutic candidates or that other off-target cross-reactivity will not be identified or present in any patient group. Failure to develop an effective preclinical safety testing program will prevent or delay clinical trials of any TCR therapeutic candidate. Detection of any cross-reactivity will halt or delay any ongoing clinical trials for any TCR therapeutic candidate and prevent or delay regulatory approval. Given that the underlying technology platform, manufacturing process and development process is the same for all of our TCR therapies, issues pertaining to cross-reactivity for one TCR therapeutic candidate may impact our ability to obtain regulatory approval for other TCR therapeutic candidates undergoing development and clinical trials, which would significantly harm our business, prospects, financial condition and results of operations.

Cross-reactivity or allo-reactivity (binding to peptides presented on other Human Leukocyte Antigen, or HLA, types) could also occur where the affinity-enhanced engineered TCR resulting from administration of our TCR therapeutic candidate binds to peptides presented by HLAs other than the HLA type for which the relevant TCR was developed. We have also developed a preclinical screening process to identify allo-reactivity risk and have identified such allo-reactivity for one rare allele in the case of our MAGE-A10 TCR therapeutic candidate. Any allo- reactivity or other cross-reactivity that impacts patient safety could materially impact our ability to advance our TCR therapeutic candidates into clinical trials or to proceed to market approval and commercialization. In addition, there is no guarantee that exclusion of patients with the allo- reactive allele will successfully eliminate the risk of allo-reactivity, and serious side effects for patients may still exist. Given that the underlying technology platform, manufacturing process and development process are the same for all of our TCR therapeutic candidates, issues pertaining to allo-reactivity for one TCR therapeutic candidate may impact our ability to obtain regulatory approval for other TCR therapeutic candidates undergoing development and clinical trials, which would significantly harm our business, prospects, financial condition and results of operations.

Our T-cell therapy, which is a type of cell therapy that uses gene therapy technology, represents a novel approach to cancer treatment that could result in heightened regulatory scrutiny, delays in clinical development, or delays in or our inability to achieve regulatory approval or commercialization of our TCR therapeutic candidates.

Use of our TCR therapeutic candidates to treat a patient requires the use of gene therapy technology, which involves combining the patient s T cells with our lentiviral delivery vector containing the gene for our affinity-enhanced engineered TCR. This is a novel treatment approach that carries inherent development risks. We are therefore constantly evaluating and adapting our TCR therapeutic candidates following the results obtained during development work and the clinical programs. Further development, characterization and evaluation may be required, depending on the results obtained, in particular where such results suggest any potential safety risk for patients. The need to develop further assays, or to modify in any way the protocols related to our TCR therapeutic candidates to improve safety or effectiveness, may delay the clinical program, regulatory approval or commercialization, if approved at all, of any TCR therapeutic candidate. Consequently, this may have a material impact on our ability to receive milestone payments and/or generate revenues from our TCR therapeutic candidates.

In addition, given the novelty of our TCR therapeutic candidates, the end users and medical personnel require a substantial amount of education and training in their administration of our TCR therapeutic candidates. Regulatory authorities have very limited experience with commercial

engineered cell therapies and TCR therapeutic candidates for the treatment of cancer. As a result, regulators may be more risk adverse or require substantial dialogue and education as part of the normal regulatory approval process for each stage of development of any TCR therapeutic candidate. To date, no gene therapy products have been approved in the United States and only one has been approved in the European Union under exceptional circumstances. Consequently, it is difficult to predict and evaluate what additional regulatory hurdles may apply to the development of our TCR therapeutic candidates and whether additional investment, time or resources will be required to overcome any such hurdles.

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Additionally, because our technology involves the genetic modification of patient cells *ex-vivo* using a viral vector, we are subject to many of the challenges and risks of gene therapy, including the following challenges:

- Regulatory requirements governing gene and cell therapy products have changed frequently and may continue to change in the future. To date, no products that involve the genetic modification of patient cells have been approved in the United States and only one has been approved in the European Union, or EU.

- Random gene insertion associated with retrovirus-mediated genetically modified products, known as insertional oncogenesis, could lead to lymphoma, leukemia or other cancers, or other aberrantly functioning cells. Insertional oncogenesis was seen in early gene therapy studies conducted outside of the United States in 2003. In those studies, insertional oncogenesis resulted in patients developing leukemia following treatment with the relevant gene therapy, with one patient dying. As a result of the data from those studies, the FDA temporarily halted gene therapy trials in the United States. The previous trials involved modification of stem cells rather than T cells and utilized a murine gamma-retroviral vector rather than a lentiviral vector. We cannot guarantee that insertional oncogenesis resulting from administration of our TCR therapeutic candidates will not occur.

- Although our viral vectors are not able to replicate, there may be a risk with the use of retroviral or lentiviral vectors that they could undergo recombination and lead to new or reactivated pathogenic strains of virus or other infectious diseases.

- There is the potential for delayed adverse events following exposure to gene therapy products due to persistent biological activity of the genetic material or other components of products used to carry the genetic material. In part for this reason, the FDA recommends a 15-year follow-up observation period for all surviving patients who receive treatment using gene therapies in clinical trials. We may need to adopt such an observation period for our therapeutic candidates; however, the FDA does not require that the tracking be complete prior to its review of the Biologics License Application, or BLA.

- Clinical trials using genetically modified cells conducted at institutions that receive funding for recombinant DNA research from the U.S. National Institutes of Health, or NIH, are subject to review by the NIH Office of Biotechnology Activities Recombinant DNA Advisory Committee, or RAC. Although the FDA decides whether individual protocols may proceed, the RAC review process can delay or impede the initiation of a clinical trial, even if the FDA has reviewed the study and approved its initiation.

If adverse events of the type described above were to occur, further advancement of our clinical trials could be halted or delayed, which would have a material adverse effect on our business and operations. In addition, heightened regulatory scrutiny of gene therapy product candidates may result in delays and increased costs in bringing a product candidate to market, if at all. Delay or failure to obtain, or unexpected costs in

obtaining, the regulatory approval necessary to bring a potential product to market could decrease our ability to generate revenue in the future.

T-cell therapy is a novel approach to cancer treatment that creates significant increased risk in terms of side-effect profile, ability to satisfy regulatory requirements associated with clinical trials and the long- term viability of administered TCR therapeutic candidates.

Development of a pharmaceutical or biologic therapy or product has inherent risks based on differences in patient population and responses to therapy and treatment. The mechanism of action and impact on other systems and tissues within the human body following administration of our TCR therapeutic candidate is not completely understood, which means that we cannot predict the long-term effects of treatment with our TCR therapeutic candidates.

We are aware that certain patients do not respond to our TCR therapeutic candidates and that other patients may relapse or cease to present the peptide being targeted by such TCR therapeutic candidates. The percentage of the patient population in which these events may occur is unknown, but the inability of patients to respond and the possibility of relapse may impact our ability to conduct clinical trials, to obtain regulatory approvals, if at all, and to successfully commercialize any TCR therapeutic candidate.

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Our clinical trials and the investigator-initiated clinical trials using our NY-ESO TCR therapeutic are still in the early stages, and it is difficult to predict the results that will be obtained in ongoing clinical trials or the next phase or phases of any clinical program.

There is a significant risk at each stage of any clinical program that serious adverse events or low efficacy, as well as less favorable safety profiles, will prevent our TCR therapeutic candidates from proceeding further or will result in those programs being suspended or being placed on hold (whether voluntarily or as a result of a regulatory authority requirement). For example, there is a risk that the target peptide to which any TCR therapeutic candidate is directed may be present in both cancer cells and other non-cancer patient cells and tissues. Should this be the case patients may suffer a range of side effects associated with the TCR therapeutic candidate binding to both the cancer cells and other cells and tissues. The extent of such side effects will depend on the levels of the target peptide in each patient s cells and tissues and the nature of their cells and tissues.

In our NY-ESO TCR therapeutic candidate trials, adverse events that have been reported in more than 15% of patients and considered at least possibly related to our NY-ESO TCR therapeutic candidate include diarrhea, rash, fever, fatigue, disturbed liver function tests, low neutrophil or lymphocyte count, nausea and anemia. Several events in our U.S. clinical trials have been classified as serious adverse events. Related serious adverse events seen in our sponsored clinical programs and occurring in more than one patient include neutropenia, pyrexia, Cytokine-Release Syndrome, Graft Versus Host Disease, or GVHD, and dehydration. GVHD, impacting the skin and gastrointestinal tract, has only been reported in our myeloma transplant study involving autologous stem cell, or auto-SCT. To date, we have also seen a suspected unexpected serious adverse reaction of grade 4 supraventricular tachycardia, or SVT, in one patient and grade 4 respiratory failure with grade 4 febrile neutropenia in a second patient in our sponsored trials.

In addition to our sponsored clinical programs, our NY-ESO TCR therapeutic is being used in an investigator-initiated clinical program in Europe. The clinical program forms part of a European Framework grant collaboration program known as ATTACK 2 (Adoptive engineered T-cell Targeting to Activate Cancer Killing) which is led by the University of Manchester. This clinical program currently uses a different protocol with a different pre-conditioning regimen and includes the use of Interleukin-2 (IL-2). To date, two patients have been treated in this program, one of whom passed away 46 days after T-cell infusion. The underlying cause of death is under investigation by the ATTACK consortium and Adaptimmune. Enrollment in this study has been placed on hold by the study sponsor pending the results of this investigation. The enrollment of patients in our own clinical trials using our NY-ESO TCR therapeutic candidate have so far not been affected, although regulatory authorities in the United Kingdom and United States have been informed of the event. Whether our clinical trials are affected will depend on the results of the investigation. Should these investigations identify any safety risk to patients caused by our NY-ESO TCR therapeutic candidate, our clinical programs could be placed on hold.

Because administration of our TCR therapeutic candidates is patient-specific, the process requires careful handling of patient-specific products and fail-safe tracking, namely the need to ensure that the tracking process is without error and that patient samples are tracked from patient removal, through manufacturing and re-administration to the same patient. It is difficult to predict the investment in appropriate mechanisms and systems that will be required to ensure such fail-safe tracking and there is always a risk of a failure in any such system. Inability to develop or adopt an acceptable fail-safe tracking methodology and handling regime may delay or prevent us from receiving regulatory approval. This risk may be increased where our TCR therapeutic candidates are used in clinical programs that we do not control or sponsor and, should an error be made in the administration of our TCR therapeutic candidates in such clinical programs, this could affect the steps required in our own clinical programs and manufacturing process requiring the addition of further tracking mechanisms to ensure fail-safe tracking.

Validation of our TCR therapeutic candidates requires access to human samples but there is no guarantee that such samples can be obtained or, if they can be obtained, that the terms under which they are provided will be favorable to us.

Certain of the steps involved in validating and carrying out safety testing in relation to our TCR therapeutic candidates require access to samples (e.g., tissues samples or cell samples) from third parties. Such samples may be obtained from universities or research institutions and will often be provided, subject to satisfaction of certain terms and conditions. There can be no guarantee that we will be able to obtain samples in sufficient quantities to enable development of and use of the full preclinical safety testing program for all TCR therapeutic candidates undergoing development. In addition, the terms under which such samples are available may not be acceptable to us or may restrict our use of any generated results or require us to make payments to the third parties.

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Our TCR therapeutic candidates and their application are not fully scientifically understood and are still undergoing validation and investigation.

Our TCR therapeutic candidates and their potential associated risks are still under investigation. For example, there is a potential risk that, given that the TCR chains are produced separately and then assembled within patient T cells into full TCRs, the TCR chains from both transduced and naturally occurring T cells could be assembled into an unintended end TCR due to mis-pairing of TCR chains, which could create unknown recognition and cross-reactivity problems within patients. Although this phenomenon has not been reported in humans, it remains a theoretical risk for our TCR therapeutic candidates and is still being studied and investigated. This could delay regulatory approval, if any, for the relevant TCR therapeutic candidates. To the extent that any mis-pairing of TCR chains is identified, either in our or our competitors clinical trials, additional investment may be required in order to modify relevant TCR therapeutic candidates and to further assess and validate the risk of such mis-pairing to patients. There is also no guarantee that following modification of the relevant TCR therapeutic candidate, such modified TCR therapeutic candidate will remain suitable for patient treatment, that it will eliminate the risk of mis-pairing of TCR chains or that regulatory approval will be obtained at all or on a timely basis in relation to such modified TCR therapeutic candidates. The occurrence of such events could significantly harm our business, prospects, financial condition and results of operations.

We may not be able to identify and validate additional target peptides or isolate and develop affinity-enhanced TCRs that are suitable for validation and further development.

The success of our TCR therapeutic candidates depends on both the identification of target peptides presented on cancer cells, which can be bound by TCRs, and isolation and affinity enhancement of TCRs, which can be used to treat patients if regulatory approval is obtained. There is an inherent risk that the number of target peptides that can be identified and/or our ability to develop and isolate suitable TCRs for affinity enhancement could be significantly lower than projected or that no additional TCR therapeutic candidates suitable for further development can be identified. Any failure to identify and validate further target peptides will reduce the number of potential TCR therapeutic candidates that we can successfully develop, which in turn will reduce the commercial opportunities available to us and increase our reliance on our NY-ESO TCR therapeutic candidate.

In addition, there is no guarantee that our attempts to develop further TCR therapeutic candidates will result in candidates for which the safety and efficacy profiles enable progression to and through preclinical testing. Failure to identify further candidates for progression into preclinical testing and clinical programs will significantly impact our commercial returns, increase our reliance on the success of our existing NY-ESO and MAGE-A10 TCR therapeutic candidate programs and may significantly harm our business, prospects, financial condition and results of operations. If resources become limited or if we fail to identify suitable target peptides, naturally occurring TCRs or affinity-enhanced TCRs, our ability to submit INDs for further TCR therapeutic candidates may be delayed or never realized, which would have a materially adverse effect on our business.

We may encounter substantial delays in our clinical trials or may not be able to conduct our trials on the timelines we expect.

Conduct of clinical trials is dependent on finding clinical sites prepared to carry out the relevant clinical trials, recruitment of patients both in terms of number and type of patients and general performance of the relevant clinical site. It is difficult to predict how quickly we will be able to recruit suitable patients, find suitable sites, begin clinical programs and administer our TCR therapeutic candidates.

In addition, our clinical trials will compete with other clinical trials for TCR therapeutic candidates that are in the same therapeutic areas as our TCR therapeutic candidates, which will reduce the number and types of patients available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Because the number of qualified clinical investigators is limited, we currently, and expect to continue to, conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials at such clinical trial sites. Moreover, because our TCR therapeutic candidates represent a departure from more commonly used methods for cancer treatment, potential patients and their physicians may opt to use conventional therapies, such as chemotherapy and hematopoietic cell transplantation, rather than enrollment in any of our current or future clinical trials.

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Even if we are able to enroll a sufficient number of patients in our clinical trials, delays in patient enrollment may result in increased costs or may affect the timing or outcome of the planned clinical trials, which could prevent completion of these trials and adversely affect our ability to advance the development of our TCR therapeutic candidates.

We may not be able to develop or obtain approval for the analytical assays and companion diagnostics required for commercialization of our TCR therapeutic candidates.

Administration of our TCR therapeutic candidates requires the use of an immuno- chemistry screening assay in which patients are screened for the presence of the cancer peptide targeted by our TCR therapeutic candidates. This assay requires the identification of suitable antibodies which can be used to identify the presence of the relevant target cancer peptide.

If safe and effective use of a biologic product depends on an *in vitro* diagnostic, such as a test to detect patients with HLA type A2, then the FDA generally requires approval or clearance of the diagnostic, known as a companion diagnostic, concurrently with approval of the therapeutic product. To date, the FDA has generally required *in vitro* companion diagnostics intended to select the patients who will respond to cancer treatment to obtain a pre-market approval, or PMA, which can take up to several years, for that diagnostic simultaneously with approval of the biologic product.

We expect that, for our NY-ESO TCR therapeutic candidate, the FDA and similar regulatory authorities outside of the United States will require the development and regulatory approval of a companion diagnostic assay as a condition to approval. We also expect that the FDA may require PMA supplemental approvals for use of that same companion diagnostic as a condition of approval of additional TCR therapeutic candidates. We do not have experience or capabilities in developing or commercializing these companion diagnostics and plan to rely in large part on third parties to perform these functions. Companion diagnostic assays are subject to regulation by the FDA and similar regulatory authorities outside of the United States as medical devices and require separate regulatory approval prior to the use of such diagnostic assays with our TCR therapeutic candidates.

If we, or any third parties that we engage to assist us, are unable to successfully develop companion diagnostic assays for use with our TCR therapeutic candidates, or are unable to obtain regulatory approval or experience delays in either development or obtaining regulatory approval, we may be unable to identify patients with the specific profile targeted by our TCR therapeutic candidates for enrollment in our clinical trials. Accordingly, further investment may be required to further develop or obtain the required regulatory approval for the relevant companion diagnostic assay, which would delay or substantially impact our ability to conduct further clinical trials or obtain regulatory approval.

Manufacturing and administering our TCR therapeutic candidates is complex and we may encounter difficulties in production, particularly with respect to process development or scaling up of our manufacturing capabilities. If we encounter such difficulties, our ability to provide supply of our TCR therapeutic candidates for clinical trials or for commercial purposes could be delayed or stopped.

The process of manufacturing and administering our TCR therapeutic candidates is complex and highly regulated. The manufacture of our TCR therapeutic candidates involves complex processes, including manufacture of a lentiviral delivery vector containing the gene for our affinity-enhanced engineered TCR. Administration of our TCR therapeutic candidates includes harvesting white blood cells from the patient, isolating certain T cells from the white blood cells, combining patient T cells with our lentiviral delivery vector through a process known as

transduction, expanding the transduced T cells to obtain the desired dose, and ultimately infusing the modified T cells back into the patient s body. As a result of the complexities, our manufacturing and supply costs are likely to be higher than those at more traditional manufacturing processes and the manufacturing process is less reliable and more difficult to reproduce. Our manufacturing process is and will be susceptible to product loss or failure due to logistical issues, including manufacturing issues associated with the differences in patients white blood cells, interruptions in the manufacturing process, contamination, equipment or reagent failure, supplier error and variability in TCR therapeutic candidate and patient characteristics. Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects, and other supply disruptions.

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If for any reason we (or any other manufacturer of our therapy) lose a patient s white blood cells or such material gets contaminated or later processing steps fail at any point, the manufacturing process of the TCR therapeutic candidate for that patient will need to be completely restarted and the resulting delay may adversely affect that patient s outcome. If microbial, viral or other contaminations are discovered in our TCR therapeutic candidates or in the manufacturing facilities in which our TCR therapeutic candidates are made or administered, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination.

As our TCR therapeutic candidates progress through preclinical programs and clinical trials towards approval and commercialization, it is expected that various aspects of the manufacturing and administration process will be altered in an effort to optimize processes and results. We have already identified some improvements to our manufacturing and administration processes, but these changes may not achieve the intended objectives, and could cause our TCR therapeutic candidates to perform differently and affect the results of planned clinical trials or other future clinical trials. In addition, such changes may require amendments to be made to regulatory applications which may further delay the timeframes under which modified manufacturing processes can be used for any TCR therapeutic candidate. For example, we are planning to make changes to the manufacturing process for cell products and vector material used in our NY-ESO TCR therapeutic candidate for which we are likely to need to conduct small clinical trials to gather safety data for each of the different indications for which larger clinical trials are planned. If our NY-ESO TCR therapeutic candidate manufactured under the new process has a worse safety or efficacy profile than the prior investigational product, we may need to re-evaluate the use of that manufacturing process, which could significantly delay or even terminate the progress of our clinical trials.

Developing a commercially viable process is a difficult and uncertain task, and there are risks associated with scaling to the level required for advanced clinical trials or commercialization, including, among others, increased costs, potential problems with process scale-out, process reproducibility, stability issues, lot consistency, and timely availability of reagents or raw materials. We may ultimately be unable to reduce the expenses associated with our TCR therapeutic candidates to levels that will allow us to achieve a profitable return on investment.

We are in the process of developing and transferring new processes to facilitate such manufacture into third-party contract suppliers. Such process scale-up and transfer will require a demonstration of comparability between the product used in clinical trials and the potential commercial product manufactured by the new process at the new facility. If we are unable to demonstrate that our commercial scale product is comparable to the product used in clinical trials, we may not receive regulatory approval for that product without additional clinical trials. We cannot guarantee that we will be able to make the required modifications within currently anticipated timeframes or that such modifications, when made, will obtain regulatory approval or that the new processes or modified processes will successfully be transferred to the third party contract suppliers within currently anticipated timeframes. Any delay or failure in obtaining approval will impact our ability to commercialize and obtain marketing approval for our TCR therapeutic candidates. Such failure may also impact our collaboration with GSK and result in GSK not exercising options or not developing any of our additional TCR therapeutic candidates. Even if we are successful, our manufacturing capabilities could be affected by increased costs, unexpected delays, equipment failures, labor shortages, natural disasters, power failures and numerous other factors that could prevent us from realizing the intended benefits of our manufacturing strategy, which in turn could have a material adverse effect on our business. We have insurance to cover certain business interruption events, particularly research and development expenditure (capped at £10 million) and committed costs (capped at £250,000). However, because our level of insurance is capped, it may be insufficient to fully compensate us if any of these events were to occur in the future.

Our manufacturing process needs to comply with FDA regulations and foreign regulations relating to the quality and reliability of such processes. Any failure to comply with relevant regulations could result in delays in or termination of our clinical programs and suspension or withdrawal of any regulatory approvals.

In order to commercially produce our products, we will need to comply with the FDA s cGMP regulations and guidelines. We may encounter difficulties in achieving quality control and quality assurance and may experience shortages in qualified personnel. We are subject to inspections

by the FDA and comparable agencies in other jurisdictions to confirm compliance with applicable regulatory requirements. Any failure to follow cGMP or other regulatory requirements or delay, interruption or other issues that arise in the manufacture, fill- finish, packaging, or storage of our TCR therapeutic candidates as a result of a failure of our facilities or the facilities or operations of third parties to comply with regulatory requirements or pass any regulatory authority inspection could significantly impair our ability to develop and commercialize our TCR therapeutic candidates, including leading to significant delays in the availability of our TCR therapeutic candidates for our clinical trials or the termination of or suspension of a clinical trial, or the delay or prevention of a filing or approval of marketing applications for our TCR therapeutic candidates. Significant non-compliance could also result in the imposition of sanctions, including warning or untitled letters, fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approvals for our TCR therapeutic candidates, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of products, operating restrictions and criminal prosecutions, any of which could damage our reputation and our business.

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The outcome of clinical trials is uncertain and our clinical trials may fail to demonstrate adequately the safety and efficacy of any of our TCR therapeutic candidates which would prevent or delay regulatory approval and commercialization.

There is a risk in any clinical trial (whether sponsored by us or investigator-initiated) that side effects from our TCR therapeutic candidates will require a hold on, or termination of, our clinical programs or further adjustments to our clinical programs in order to progress our TCR therapeutic candidate. Our TCR therapeutic candidates are novel and unproven and regulators will therefore require evidence that the TCR therapeutic candidates are safe before permitting clinical trials to commence and evidence that the TCR therapeutic candidates are safe and effective before granting any regulatory approval. In particular, because our TCR therapeutic candidates are subject to regulation as biological products, we will need to demonstrate that they are safe, pure and potent for use in each target indication. The TCR therapeutic candidate must demonstrate an acceptable risk versus benefit profile in its intended patient population and for its intended use. The risk/benefit profile required for product licensure will vary depending on these factors and may include not only the ability to show tumor shrinkage, but also adequate duration of response, a delay in the progression of the disease and/or an improvement in survival. For example, response rates from the use of our TCR therapeutic candidates will not be sufficient to obtain regulatory approval unless we can also show an adequate duration of response.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. Success in preclinical programs and early clinical trials does not ensure that later clinical trials will be successful. Moreover, the results of preclinical programs and early clinical trials of our TCR therapeutic candidates may not be predictive of the results of later-stage clinical trials. To date, we have only obtained interim results from Phase 1/2 clinical trials that are uncontrolled, involve small sample sizes and are of shorter duration than would be required for regulatory approval. There may be other reasons why our early clinical trials are not predictive of later clinical trials. In addition, the results of trials in one set of patients or line of treatment may not be predictive of those obtained in another and protocols may need to be revised based on unexpected early results. For example, in our ovarian cancer trial with our NY-ESO TCR therapeutic candidate, the first patient treated experienced a grade 3 Cytokine-Release Syndrome at day seven post-infusion, concomitant with a significant proliferation of the engineered T cells that constituted about 100% of the peripheral blood at day 14. This level of Cytokine-Release Syndrome had not been seen in previous results from trials using our NY-ESO TCR therapeutic candidate. The patient s tumor markers were also falling during this time. To manage the Cytokine-Release Syndrome, the patient was treated with high dose steroids that abrogated the engineered T-cell function. The protocol was then modified to allow for use of the anti-IL6R antibody, tocilizumab, for treatment of Cytokine-Release Syndrome in future patients, which has been shown to control Cytokine-Release Syndrome without abrogating the anti-tumor response. As another example, in the European investigator-initiated clinical program in gastro-esophageal cancer there has been one patient death. The underlying cause of death is under investigation.

We expect there may be greater variability in results for our TCR therapeutic candidates which are administered on a patient-by-patient basis than for off-the-shelf products, like many other biologics. There is typically an extremely high rate of attrition from the failure of TCR therapeutic candidates proceeding through clinical trials. TCR therapeutic candidates in later stages of clinical trials may fail to show the desired safety and efficacy profile despite having progressed through preclinical programs and initial clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or unacceptable safety issues, notwithstanding promising results in earlier trials. Most biologic candidates that begin clinical trials are never approved by regulatory authorities for commercialization. We cannot therefore guarantee that we will be successful in obtaining the required efficacy and safety profile from the performance of any of our clinical programs.

In addition, even if such trials are successfully completed, we cannot guarantee that the FDA or foreign regulatory authorities will interpret the results as we do. Accordingly, more trials may be required before we can submit our TCR therapeutic candidate for regulatory approval. To the extent that the results of the trials are not satisfactory to the FDA or foreign regulatory authorities for support of a marketing application, we may be required to expend significant resources, which may not be available to us, to conduct additional trials in support of potential approval of our TCR therapeutic candidates. We cannot predict whether any of our TCR therapeutic candidates will satisfy regulatory requirements at all or for indications in which such TCR therapeutic candidates are currently being evaluated as part of any clinical programs.

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We have limited experience conducting clinical trials which may cause a delay in any clinical program and in the obtaining of regulatory approvals.

Although we have recruited a team that has significant experience with clinical trials, as a company we have limited experience in conducting clinical trials and no experience in conducting clinical trials through to regulatory approval of any TCR therapeutic candidate. In part because of this lack of experience, we cannot be certain that planned clinical trials will begin or be completed on time, if at all. Large-scale trials would require significant additional financial and management resources, and reliance on third-party clinical investigators, contract research organizations, or CROs, or consultants. Relying on third-party clinical investigators, consultants or CROs may force us to encounter delays that are outside of our control. Our NY-ESO TCR therapeutic candidate is being used in investigator-initiated clinical programs in gastro esophageal cancer patients. We are not sponsoring these clinical programs and have limited control over clinical decisions taken in such clinical programs including the methodology of patient treatment, timescales of treatment or when additional sites may be initiated and start enrolling patients.

Our TCR therapeutic candidates may have undesirable side effects or have other properties that could halt their clinical development, prevent their regulatory approval, limit their commercial potential or otherwise result in significant negative consequences.

Where any TCR therapeutic candidate has undesirable side effects, regulatory approval for such therapeutic may be delayed or suspended, or alternatively may be restricted to particular disease indications or states that are more limited than desirable. This could result in the failure of our products reaching the market or a reduction in the patient population for which any TCR therapeutic candidate can be used. Events that have been reported in more than 15% of patients and considered at least possibly related to our NY-ESO TCR therapeutic candidate include diarrhea, rash, fever, fatigue, disturbed liver function tests, low neutrophil or lymphocyte count, nausea and anemia. Several events in our U.S. clinical trials have been classified as serious adverse events. Related serious adverse events seen in our sponsored clinical programs and occurring in more than one patient include neutropenia, pyrexia, Cytokine-Release Syndrome, Graft Versus Host Disease (GVHD) and dehydration. GVHD impacting the skin and gastrointestinal tract, has only been reported in our myeloma transplant study involving auto-SCT. To date, we have also seen a suspected unexpected serious adverse reaction of grade 4 supraventricular tachycardia, or SVT, in one patient and grade 4 respiratory failure and grade 4 febrile neutropenia in a second patient in our sponsored trials.

Any unacceptable toxicities arising in ongoing clinical programs could result in suspension or termination of those clinical programs. Any suspension or termination will affect other TCR therapeutic candidates and thereby impact our ability to recognize any product revenues. Any side effects may also result in the need to perform additional trials, which will delay regulatory approval for such TCR therapeutic candidate, if at all, and require additional resources and financial investment to bring the relevant TCR therapeutic candidate to market.

In addition, the impact of TCR therapeutic candidates may vary from patient to patient and this may affect the number of patients who can be successfully treated with our TCR therapeutic candidates. Depending on the nature of the indication, certain patients may need to be excluded from treatment, which could also impact our ability to recruit patients to utilize such therapies or to recruit patients to conduct clinical trials in general for our TCR therapeutic candidates.

Clinical trials are expensive, time-consuming and difficult to implement.

Clinical trials, depending on the stage, can be costly as well as difficult to implement and define, particularly with technologies that are not tried and tested, such as our TCR therapeutic candidates. These factors can lead to a longer clinical development timeline and regulatory approval process, including a requirement to conduct further or more complex clinical trials in order to obtain regulatory approval. Regulatory authorities may disagree with the design of any clinical program, and designing an acceptable program could lead to increased timeframes for obtaining of approvals, if any. In addition, progression of clinical trials depends the on ability to recruit suitable patients to those trials and delay in recruiting will impact the timeframes of such clinical trials and as a result the timeframes for obtaining regulatory approval, if any, for the relevant TCR therapeutic candidates.

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In particular, eligible patients must be screened for the target peptide and HLA type, which may reduce the number of patients who can be recruited for any clinical program. The ability to administer our TCR therapeutic candidates to patients in accordance with set protocols for the clinical trials and the results obtained depends on patient participation for the duration of the clinical trial, which many of these patients are unable to do because of their late-stage cancer and low or limited life expectancy.

Although the initial results in our clinical trials to date may suggest a promising tolerability profile, these results may not be indicative of results obtained in later and larger clinical trials. Long-term follow-up of patients from earlier trials may also result in detection of additional side effects or identification of other safety issues. There is no guarantee of success in any clinical trial and there is a very high attrition rate for pharmaceutical or biological compounds entering clinical trials. Any side effects or negative safety issues identified at any stage of clinical development will require additional investigation and assessment which can result in additional costs and resource requirements that could delay or potentially terminate our clinical trials.

We may face difficulty in enrolling patients in our clinical trials.

We may find it difficult to enroll patients in our clinical trials. For example, in our Phase 1/2 melanoma trial with our NY-ESO TCR therapeutic candidate, there was a delay in enrollment as a result of competition from other emerging therapies. Identifying and qualifying patients, including testing of patients for appropriate target peptides or HLA type, to participate in clinical trials of our TCR therapeutic candidates are critical to our success. The timing of our clinical trials depends on the speed at which we can recruit patients to participate in testing our TCR therapeutic candidates. If patients are unwilling to participate in our trials because of negative publicity from adverse events or for other reasons, including competitive clinical trials for similar patient populations, the timeline for recruiting patients, conducting trials and obtaining regulatory approval of potential products may be delayed or prevented. These delays could result in increased costs, delays in advancing our product development, delays in testing the effectiveness of our technology or termination of the clinical trials altogether. We may not be able to identify, recruit and enroll a sufficient number of patients, or those with required or desired characteristics to achieve sufficient diversity in a given trial in order to complete our clinical trials in a timely manner. Patient enrollment is affected by factors including:

- eligibility criteria for the trial in question, in particular, presenting the correct HLA type and target antigen;
- severity of the disease under investigation;
- design of the trial protocol;
- size of the patient population;
- perceived risks and benefits of the TCR therapeutic candidate under trial;

- novelty of the TCR therapeutic candidate and acceptance by oncologists;
- proximity and availability of clinical trial sites for prospective patients;
- availability of competing therapies and clinical trials;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians; and
- ability to monitor patients adequately during and after treatment.

If we have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay, limit or terminate ongoing or planned clinical trials, any of which would have an adverse effect on our business.

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Our TCR therapeutic candidates for which we intend to seek approval as biologic products may face competition sooner than anticipated.

The enactment of the Biologics Price Competition and Innovation Act of 2009, or BPCIA, created an abbreviated pathway for the approval of biosimilar and interchangeable biological products. The abbreviated regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as interchangeable based on its similarity to an existing reference product. Under the BPCIA, an application for a biosimilar product cannot be approved by the FDA until 12 years after the original branded product is approved under a BLA. On March 6, 2015, the FDA approved the first biosimilar product under the BPCIA. However, the law is complex and is still being interpreted and implemented by the FDA and as a result, its ultimate impact, implementation and meaning are subject to uncertainty. While it is uncertain when such processes intended to implement BPCIA may be fully adopted by the FDA, any such processes could have a material adverse effect on the future commercial prospects for our biological products.

We believe that if our NY-ESO TCR therapeutic candidate is approved as a biological product under a BLA it should qualify for the 12-year period of exclusivity. However, there is a risk that the FDA will not consider our NY-ESO TCR therapeutic candidate or any additional TCR therapeutic candidates to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Additionally, this period of regulatory exclusivity does not apply to companies pursuing regulatory approval via their own traditional BLA, rather than via the abbreviated pathway. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

Foreign countries also have abbreviated regulatory pathways for biosimilars and hence even where the FDA does not approve a biosimilar biologic, a biosimilar could be approved using an abbreviated regulatory pathway in other markets where our TCR therapeutic candidates are approved and marketed.

Risks Related to Government Regulation

The FDA regulatory approval process is lengthy and time- consuming, and we may experience significant delays in the clinical development and regulatory approval of our TCR therapeutic candidates.

We have not previously submitted a BLA to the FDA, or similar approval submissions to comparable foreign authorities. A BLA must include extensive preclinical and clinical data and supporting information to establish the TCR therapeutic candidate s safety and effectiveness for each desired indication. The BLA must also include significant information regarding the chemistry, manufacturing and controls for the product. We expect the novel nature of our TCR therapeutic candidates to create additional challenges in obtaining regulatory approval, if at all. For example, the FDA has limited experience with commercial development of T-cell therapies for cancer. Accordingly, the regulatory approval pathway for our TCR therapeutic candidates may be uncertain, complex, expensive and lengthy, and approval may not be obtained.

We could also encounter delays if physicians encounter unresolved ethical issues associated with enrolling patients in clinical trials of our TCR therapeutic candidates in lieu of prescribing existing treatments that have established safety and efficacy profiles. Further, a clinical trial may be suspended or terminated by us, the sponsor of an investigator-initiated trial, the Institutional Review Boards, or IRBs, for the institutions in which such trials are being conducted, the Data Monitoring Committee for such trial, or by the FDA or other regulatory authorities due to a

number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a TCR therapeutic candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. If we experience termination of, or delays in the completion of, any clinical trial of our TCR therapeutic candidates, the commercial prospects for our TCR therapeutic candidates will be harmed, and our ability to generate product revenue will be delayed. In addition, any delays in completing our clinical trials will increase our costs, slow our product development and approval process and jeopardize our ability to commence product sales and generate revenue.

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GSK may also experience similar difficulties in conducting future clinical trials of licensed TCR therapeutic candidates. Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may ultimately lead to the denial of regulatory approval of our TCR therapeutic candidates.

The FDA regulatory process can be difficult to predict, in particular whether for example accelerated approval processes are available or further unanticipated clinical trials are required will depend on the data obtained in our ongoing clinical trials.

The regulatory approval process and the amount of time it takes us to obtain regulatory approvals for our TCR therapeutic candidates will depend on the data that are obtained in our ongoing clinical trials and in one or more future registrational or pivotal clinical trials. We may attempt to seek approval on a per indication basis for our TCR therapeutic candidates on the basis of a single pivotal trial. While the FDA requires in most cases two adequate and well-controlled pivotal clinical trials to demonstrate the efficacy of a product candidate, a single pivotal trial with other confirmatory evidence may be sufficient in rare instances where the trial is a large multicenter trial demonstrating internal consistency and a statistically very persuasive finding of a clinically meaningful effect on mortality, irreversible morbidity or prevention of a disease with a potentially serious outcome and confirmation of the result in a second trial would be practically or ethically impossible. Depending on the data we obtain, the FDA or other regulatory authorities may require additional clinical trials to be carried out or further patients to be treated prior to the granting of any regulatory approval for marketing of our TCR therapeutic candidates. It is difficult for us to predict with such a novel technology exactly what will be required by the regulatory authorities in order to take our TCR therapeutic candidates to market or the timeframes under which the relevant regulatory approvals can be obtained.

In addition, depending on the data that are obtained by us in our current and future clinical trials, we may seek breakthrough therapy or fast track designation or accelerated approval from the FDA for our TCR therapeutic candidates and equivalent accelerated approval procedures in other countries. However, given the novel nature of our TCR therapeutic candidates, it is difficult for us to predict or guarantee whether the FDA or other regulatory authorities will approve such requests or what further clinical or other data may be required to support an application for such accelerated approval procedures.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the TCR therapeutic candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. The FDA and foreign regulatory authorities also have substantial discretion in the drug and biologics approval process. The number and types of preclinical programs and clinical trials that will be required for regulatory approval varies depending on the TCR therapeutic candidate, the disease or condition that the TCR therapeutic candidate is designed to address, and the regulations applicable to any particular TCR therapeutic candidate. Approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a TCR therapeutic candidate s clinical development and may vary among jurisdictions, and there may be varying interpretations of data obtained from preclinical programs or clinical trials, either of which may cause delays or limitations in the approval or the decision not to approve an application. In addition, approval of our TCR therapeutic candidates could be delayed or refused for many reasons, including the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;

- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that our TCR therapeutic candidates are safe and effective for any of their proposed indications;

- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;

- we may be unable to demonstrate that our TCR therapeutic candidates clinical and other benefits outweigh their safety risks;

- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical programs or clinical trials;

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- the data collected from clinical trials of our TCR therapeutic candidates may not be sufficient to the satisfaction of the FDA or comparable foreign regulatory authorities to support the submission of a BLA or other comparable submission in foreign jurisdictions or to obtain regulatory approval in the United States or elsewhere;

- our manufacturing processes or facilities or those of the third-party manufacturers with which we may not be adequate to support approval of our TCR therapeutic candidates; and

- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

It is possible that none of our TCR therapeutic candidates will ever obtain the appropriate regulatory approvals necessary to commercialize the TCR therapeutics. Any delay in obtaining, or failure to obtain, required approvals would materially adversely affect our ability to generate revenue from the particular TCR therapeutic candidate, which would result in significant harm to our business.

Obtaining and maintaining regulatory approval of our TCR therapeutic candidates in one jurisdiction does not mean that we will be successful in obtaining regulatory approval of our TCR therapeutic candidates in other jurisdictions.

Obtaining and maintaining regulatory approval of our TCR therapeutic candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction, while a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. For example, even if the FDA grants marketing approval of a TCR therapeutic candidate, comparable regulatory authorities in foreign jurisdictions must also approve the manufacturing, marketing and promotion of the TCR therapeutic candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and greater than, those in the United States, including additional preclinical programs or clinical trials as clinical trials conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the United States, a TCR therapeutic 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 TCR therapeutic candidates is also subject to approval.

We may also submit marketing applications in other countries. Regulatory authorities in jurisdictions outside of the United States have requirements for approval of TCR therapeutic candidates with which we must comply prior to marketing in those jurisdictions. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our TCR therapeutic candidates in certain countries. If we fail to comply with the regulatory requirements in international markets and/or receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our TCR therapeutic candidates will be harmed.

We plan to seek breakthrough therapy or fast track designations and may pursue accelerated approval for some or all of our current TCR therapeutic candidates, but we may be unable to obtain such designations or, obtain or maintain the benefits associated with such designations.

We may seek breakthrough therapy or fast track designations for our TCR therapeutic candidates in the United States or equivalent regulations elsewhere in the world. In 2012, the FDA established a breakthrough therapy designation which is intended to expedite the development and review of products that treat serious or life-threatening diseases when preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation of a TCR therapeutic candidate as a breakthrough therapy provides potential benefits that include more frequent meetings with the FDA to discuss the development plan for the TCR therapeutic candidate and ensure collection of appropriate data needed to support approval; more frequent written correspondence from the FDA about things such as the design of the proposed clinical trials and use of biomarkers; intensive guidance on an efficient drug development program, beginning as early as Phase 1; organizational commitment involving senior managers; and eligibility for rolling review and priority review.

Breakthrough therapy designation does not change the standards for product approval. We intend to seek breakthrough therapy designation for some or all of our TCR therapeutic candidates, but there can be no assurance that we will receive breakthrough therapy designation. Additionally, other treatments from competing companies may obtain the designations and impact our ability to develop and commercialize our TCR therapeutic candidates, which may adversely impact our business, financial condition or results of operation.

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We may also seek fast track designation. If a drug or biologic candidate is intended for the treatment of a serious or life-threatening condition or disease and the drug demonstrates the potential to address unmet medical needs for the condition, the sponsor may apply for fast track designation. Under the fast track program, the sponsor of a new drug or biologic candidate may request that the FDA designate the candidate for a specific indication as a fast track drug or biologic concurrent with, or after, the submission of the IND for the candidate. The FDA must determine if the drug or biologic candidate qualifies for fast track designation within 60 days of receipt of the sponsor s request. Even if we do apply for and receive fast track designation, we may not experience a faster development, review or approval process compared to conventional FDA procedures. The FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program.

We may also seek accelerated approval for products that have obtained fast track designation. Under the FDA s fast track and accelerated approval programs, the FDA may approve a drug or biologic for a serious or life-threatening illness that provides meaningful therapeutic benefit to patients over existing treatments based upon a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. For drugs granted accelerated approval, post-marketing confirmatory trials have been required to describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. These confirmatory trials must be completed with due diligence. Moreover, the FDA may withdraw approval of our TCR therapeutic candidate or indication approved under the accelerated approval pathway if, for example:

- the trial or trials required to verify the predicted clinical benefit of our TCR therapeutic candidate fail to verify such benefit or do not demonstrate sufficient clinical benefit to justify the risks associated with the drug;

- other evidence demonstrates that our TCR therapeutic candidate is not shown to be safe or effective under the conditions of use;

- we fail to conduct any required post approval trial of our TCR therapeutic candidate with due diligence; or

- we disseminate false or misleading promotional materials relating to the relevant TCR therapeutic candidate.

Even if we receive regulatory approval of our TCR therapeutic candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense as well as significant penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our TCR therapeutic candidates.

Any regulatory approvals that we receive for our TCR therapeutic candidates will require surveillance to monitor the safety and efficacy of the TCR therapeutic candidate. The FDA may also require a risk evaluation and mitigation strategy in order to approve our TCR therapeutic candidates, which could entail requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or a comparable foreign regulatory authority approves our TCR therapeutic candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export and recordkeeping for our TCR therapeutic candidates will be subject to extensive and

ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration and listing, as well as continued compliance with cGMPs and current good clinical practices, or cGCPs, for any clinical trials that we conduct post-approval. We and our contract manufacturers will be subject to periodic unannounced inspections by the FDA to monitor and ensure compliance with cGMPs. We must also comply with requirements concerning advertising and promotion for any TCR therapeutic candidates for which we obtain marketing approval. Promotional communications with respect to prescription drugs, including biologics, are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product s approved labeling. Thus, we will not be able to promote any TCR therapeutic candidates we develop for indications or uses for which they are not approved. Later discovery of previously unknown problems with our TCR therapeutic candidates, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

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- restrictions on our ability to conduct clinical trials, including full or partial clinical holds on ongoing or planned trials;

- restrictions on such products manufacturing processes;

- restrictions on the marketing of a product;

- restrictions on product distribution;

- requirements to conduct post-marketing clinical trials;

- untitled or warning letters;

- withdrawal of the products from the market;

- refusal to approve pending applications or supplements to approved applications that we submit;

- recall of products;

- fines, restitution or disgorgement of profits or revenue;

- suspension or withdrawal of regulatory approvals;

- refusal to permit the import or export of our products;

- product seizure;
- injunctions;
- imposition of civil penalties; or
- criminal prosecution.

The FDA s and other regulatory authorities policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our TCR therapeutic 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.

In addition, if following a pivotal clinical trial we were able to obtain accelerated approval of our NY-ESO TCR therapeutic candidate, the FDA will require us to conduct a confirmatory trial or trials to verify the predicted clinical benefit and additional safety studies. The results from the confirmatory trial or trials may not support the clinical benefit, which would result in the approval being withdrawn.

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

As part of its marketing authorization process, the European Medicines Agency, or 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 diseases or life-threatening diseases and those designated as orphan medicinal products.

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A conditional marketing authorization may be granted when the CHMP finds that, although comprehensive clinical data referring to the safety and efficacy 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 are 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 are generated, submitted, assessed and acted upon. Although we may seek a conditional marketing authorization for one or more of our TCR therapeutic candidates by the EMA, the EMA or CHMP may ultimately not agree that the requirements for such conditional marketing authorization have been satisfied and hence delay the commercialization of our TCR therapeutic candidates.

We may not be able to obtain or maintain orphan drug exclusivity for our TCR therapeutic candidates.

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs or biologics for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug or biologic intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals in the United States.

Generally, if a product with an orphan drug designation subsequently 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 EMA or the FDA from approving another

marketing application for the same drug for that time period. The applicable period is seven years in the United States and 10 years in Europe. The European exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

Some of our TCR therapeutic candidates may be eligible for orphan drug designation. In the United States, under the Orphan Drug Act, the FDA may grant orphan designation to a drug intended to treat a rare disease or condition. Such diseases and conditions are those that affect fewer than 200,000 individuals in the United States or, if they affect more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and making a drug product available in the United States for these types of diseases or conditions will be recovered from sales of the product. If the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by that agency. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process, but it can lead to financial incentives, such as opportunities for grant funding toward clinical trial costs, tax advantages in-lieu of R&D tax credits and user-fee waivers. If a product that has orphan drug designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan drug marketing exclusivity for a period of seven years. Orphan drug marketing exclusivity generally prevents the FDA from approving another application, including a full BLA, to market the same drug for the same indication for seven years, except in limited circumstances, including if the FDA concludes that the later drug is clinically superior to the approved drug.

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A drug is clinically superior if it is safer, more effective or makes a major contribution to patient care. Orphan drug marketing exclusivity rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition. There can be no assurance that any TCR therapeutic candidate will be eligible for orphan drug designation in the United States or in other jurisdictions or that it will obtain orphan drug marketing exclusivity upon approval. Inability to obtain orphan drug designation for a specific TCR therapeutic candidate in the future would prevent us from taking advantage of the financial benefits associated with orphan drug designation and would preclude us from obtaining marketing exclusivity upon approval, if any. Even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve another drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

Any failure by us to comply with existing regulations could harm our reputation and operating results.

The production of our TCR therapeutic candidates is highly regulated and subject to constant inspection. The regulatory environment may also change from time to time. Any failure to comply with regulatory requirements, whether in the United States or in other countries in which our TCR therapeutic candidates are supplied, may result in investigation by regulatory authorities, suspension of regulatory authorizations and, as a result, suspension of clinical programs or ability to supply any of our TCR therapeutic candidates and potentially significant fines or other penalties being imposed in relation to any breach. Any failure may also harm our reputation and impact our ability going forward to obtain regulatory approvals for other TCR therapeutic candidates or require us to undertake additional organizational changes to minimize the risk of further breach.

Our research and development activities utilize hazardous, radioactive and biological materials. Should such materials cause injury or be used other than in accordance with applicable laws and regulations, we may be liable for damages.

We use radioactive, hazardous and biological reagents and materials in our research and development at our U.K. site. We have obtained the appropriate certification required for the use of these reagents but our use is subject to compliance with applicable laws and there is a risk that should any third party or employee suffer injury or damage from radioactive, hazardous or biological reagents that we may incur liability or obligations to compensate such third parties or employees. We have employers liability insurance capped at £10.0 million per occurrence and public liability insurance capped at £3.0 million per occurrence, however, these amounts may be insufficient to compensate us if these events actually occur in the future.

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

Our operations are subject to anti-corruption laws, including the U.K. Bribery Act 2010, or Bribery Act, the U.S. Foreign Corrupt Practices Act, or FCPA, 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 bribing, being bribed or making other prohibited payments to government officials or other persons to obtain or retain business or gain some other business advantage. 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 actions, if non-compliant, could potentially subject us to liability under the Bribery Act, FCPA or local anti-corruption laws. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in 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 on countries and persons, anti-money laundering laws, customs requirements and currency exchange regulations, collectively referred to as the Trade Control laws.

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However, 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 U.K., U.S. or other authorities could also have an adverse impact on our reputation, our business, results of operations and financial condition.

If we are found in violation of federal or state fraud and abuse or other health care laws, we may be required to pay a penalty and/or be suspended from participation in federal or state health care programs, which may adversely affect our business, financial condition and results of operations.

After we obtain marketing approval for our products in the United States, if any, we will be subject to various federal and state health care fraud and abuse and other health care laws. Healthcare providers, physicians and third-party payors play a primary role in the recommendation and use of pharmaceutical products that are granted marketing approval. Accordingly, arrangements with third-party payors, existing or potential customers and referral sources are subject to broadly applicable fraud and abuse and other healthcare laws and regulations, and these laws and regulations may constrain the business or financial arrangements and relationships through which manufacturers market, sell and distribute the products for which they obtain marketing approval.

Such restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in cash or kind, in exchange for, or to induce, either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federal healthcare programs 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. Cases have been brought under false claims laws alleging that off-label promotion of pharmaceutical products or the provision of kickbacks has resulted in the submission of false claims to governmental health care programs. The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively, the Healthcare Reform Act, amended the intent requirement of the federal Anti-Kickback Statute. A person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it. Under federal government regulations, some arrangements, known as safe harbors, are deemed not to violate the federal Anti-Kickback Statute and analogous state law requirements;

- the federal False Claims Act or FCA, which prohibits, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid or other third-party payors that are false or fraudulent. Federal Anti-Kickback Statute violations and certain marketing practices, including off-label promotion, also may implicate the FCA. In addition, private individuals have the ability to bring actions on behalf of the government under the federal False Claims Act and under the false claims laws of several states;

- federal criminal laws that prohibit executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

- the federal Physician Payment Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, information related to payments and other transfers of value to physicians, other healthcare providers and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members. The CMS publishes the reported data in a searchable form on an annual basis;

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- The Health Insurance Portability and Accountability Act of 1996 (HIPAA) imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, which governs the conduct of certain electronic healthcare transactions and protects the security and privacy of protected health information; and

- state and foreign law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to: items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry s voluntary compliance guidelines and the relevant compliance guidance issued by the federal government or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state 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. California and a few other states have passed laws that require pharmaceutical companies to comply with the April 2003 Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers and/or the Pharmaceutical Research and Manufacturers of America Code on Interactions with Healthcare Professionals. In addition, several states impose other marketing restrictions or require pharmaceutical companies to make marketing or price disclosures to the state. There are ambiguities as to what is required to comply with these state requirements and if we fail to comply with an applicable state law requirement we could be subject to penalties.

Neither the government nor the courts have provided definitive guidance on the application of fraud and abuse laws to our business. Law enforcement authorities are increasingly focused on enforcing these laws. Although we seek to structure our business arrangements in compliance with all applicable requirements, these laws are broadly written, and it is often difficult to determine precisely how the law will be applied in specific circumstances. Accordingly, and it is possible that, once we begin marketing our product(s) some of our practices may be challenged under these laws. While we intend to structure our business arrangements to comply with these laws, it is possible that the government could allege violations of, or convict us of violating, these laws. Violation of any of the laws described above or any other governmental laws and regulations may result in penalties, including civil and criminal penalties, damages, fines, the curtailment or restructuring of operations, the exclusion from participation in federal and state healthcare programs and imprisonment. Furthermore, efforts to ensure that business activities and business arrangements comply with applicable healthcare laws and regulations can be costly for manufacturers of branded prescription products. Additionally, if we are found in violation of one or more of these laws our business, results of operations and financial condition may be adversely affected.

Our current cash projections include reliance on the ability to obtain certain tax credits and the operation of certain tax regimes with in the United Kingdom. Should these cease to be available, this could impact our ongoing requirement for investment and the timeframes within which additional investment is required.

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 our principal research subsidiary company, Adaptimmune Limited, is able to surrender the trading losses that arise from its research and development activities for a payable tax credit of up to 33.4% 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. Subcontracted research expenditures are eligible for a cash rebate of up to 21.7%. The majority of our pipeline research, clinical trials management and manufacturing development activities, all of which are being carried out by Adaptimmune Limited, are eligible for inclusion within these tax credit cash rebate claims.

We may not be able to continue to claim research and development tax credits (R&D tax credits) in the future as we increase our personnel and expand our business because we may no longer qualify as an SME (small or medium-sized enterprise). In order to qualify as an SME for R&D tax credits, we must continue to be a company with fewer than 500 employees and also have either an annual turnover not exceeding 100 million or a balance sheet not exceeding 86 million.

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We may also benefit in the future from the United Kingdom s patent box regime, which would allow certain profits attributable to revenues from patented products to be taxed at a rate that over time will be reduced to 10%. As we have many different patents covering our products, future upfront fees, milestone fees, product revenues, and royalties could be taxed at this favorably low 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 United Kingdom research and development tax credit regime or the patent box regime, or we are unable to qualify for such advantageous tax legislation, our business, results of operations and financial condition may be adversely affected.

Risks Related to the Commercialization of Our TCR Therapeutic Candidates

The market opportunities for our TCR therapeutic candidates may be limited to those patients who have failed prior treatments.

Initial approval of new cancer therapies may be limited to what is referred to as third-line use. Third-line treatment is the third type of treatment following initial, or first-line, treatment and second-line treatment, which is given when first-line treatment does not work or ceases working. However, cancer therapies may be used from the point at which cancer is detected in its early stages (first line) onward. Whenever the first-line therapy fails or the process is unsuccessful, second-line therapy may be administered, such as additional rounds of chemotherapy, radiation and antibody drugs or a combination of these treatments. If second-line therapies fail, patients are generally given the opportunity to receive third-line therapies, which tend to be more novel therapies. Our current clinical trials generally require that patients have received chemotherapy prior to enrollment. Depending upon the outcome of our current trials, we may conduct future clinical trials using our TCR therapeutic candidates for first-line therapy, but there can be no guarantee that clinical trials will be approved or that if approved such trials will lead to regulatory approval. If our TCR therapeutic candidates only receive third-line or second-line approval, the patient population to which we can supply our TCR therapeutic candidates will be significantly reduced, which may limit our commercial opportunities.

Our estimates of the patient population that may be treated by our TCR therapeutic candidates is based on published information. This information may not be accurate in relation to our TCR therapeutic candidates and our estimates of potential patient populations could therefore be much higher than those that are actually available or possible for commercialization.

In addition, these estimates are based on assumptions about the number of eligible patients which have the peptide and HLA type targeted by our TCR therapeutic candidates. Different patient populations will present different peptides according to their specific HLA type. HLA types vary across the patient population and, due to this variability, any therapy will initially only be suitable for treatment of patients expressing the particular HLA type presenting the relevant peptide. For example, approximately 50% of the U.S. Caucasian population expresses HLA A2, which contains the peptide used in our NY-ESO TCR therapeutic candidate program. Our current TCR therapeutic candidates have been developed for patients with HLA A2 which may reduce the size of the patient population that can be treated unless we develop and receive regulatory approval for TCR therapeutic candidates approved for additional HLA peptides.

We currently have no marketing and sales organization and have no experience in marketing products. If we are unable to establish marketing and sales capabilities or enter into agreements with third parties to market and sell our TCR therapeutic candidates, we may not be able to generate product revenue.

As an organization, we have never marketed or supplied commercial pharmaceutical or biologic products or therapies. We do not currently have a dedicated sales force and will need to grow and develop the sales function and associated support network if we are to supply TCR therapeutic candidates on a commercial basis. As our TCR therapeutic candidates proceed through clinical programs, we intend to develop an in-house marketing organization and sales force, which will require significant capital expenditures, management resources, and time. We will have to compete with other pharmaceutical and biotechnology companies to recruit, hire, train, and retain marketing and sales personnel. This process may result in additional delays in bringing our TCR product candidate to market or in certain cases require us to enter into alliances with third parties in order to do so. However, there can be no assurance that we will be able to establish or maintain such collaborative arrangements, or even if we are able to do so, that they will result in effective sales forces. Any revenue we receive will depend upon the efforts of such third parties, which may not be successful. We may have little or no control over the marketing and sales efforts of such third parties, and our revenue from TCR therapeutic candidate sales may be lower than if we had commercialized our TCR therapeutic candidates ourselves. We also face significant competition in our search for third parties to assist us with the sales and marketing efforts of our TCR therapeutic candidates. Such competition may also result in delay or inability to supply TCR therapeutic candidates to particular countries or territories in the world which in turn will restrict the revenue that can be obtained from any TCR therapeutic candidate. Any inability on our part to develop in-house sales and commercial distribution capabilities or to establish and maintain relationships with third-party collaborators that can successfully commercialize any TCR therapeutic candidate in the United States or elsewhere will have a materially adverse effect on our business and results of operations.

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If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our TCR therapeutic candidates.

We face an inherent risk of product liability as a result of the clinical testing of our TCR therapeutic candidates and will face an even greater risk upon any commercialization. For example, we may be sued if any of our TCR therapeutic candidates causes or is perceived to cause injury or is 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 may incur substantial liabilities or be required to limit commercialization of our TCR therapeutic candidate. Even a successful defense would require significant financial and management resources and, regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our TCR therapeutic candidates;
- injury to our reputation;
- withdrawal of clinical trial participants;
- initiation of investigations by regulators;
- costs to defend the related litigation;
- a diversion of management s time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue;

- exhaustion of any available insurance and our capital resources;

- the inability to commercialize TCR therapeutic candidate; and

- a decline in our share price.

Our inability to obtain sufficient product liability insurance at an acceptable price to protect against potential product liability claims could also prevent or inhibit the commercialization of our TCR therapeutic candidates. We currently hold £15.0 million in clinical trial insurance coverage in the aggregate per year, with a per trial limit of £3.0 million. We also hold products and services liability insurance capped at £3.0 million in the aggregate and public liability insurance capped at £3.0 million per occurrence. These levels may not be adequate to cover all liabilities that we may incur. We may also need to increase our insurance coverage as we expand the scope of our clinical trials and commercialize any of our product TCR therapeutic candidates. In addition, 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.

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Even if we obtain regulatory approval of our TCR therapeutic candidates, they may not gain market acceptance among physicians, patients, hospitals, cancer treatment centers and others in the medical community.

The use of engineered T cells as a potential cancer treatment is a recent development and may not become broadly accepted by physicians, patients, hospitals, cancer treatment centers and others in the medical community. Additional factors will influence whether our TCR therapeutic candidates are accepted in the market, including:

- the clinical indications for which our TCR therapeutic candidates are approved;
- physicians, hospitals, cancer treatment centers and patients considering our TCR therapeutic candidates as a safe and effective treatment;
- the potential and perceived advantages of our TCR therapeutic candidates over alternative treatments;
- the prevalence and severity of any side effects;
- product labeling or prescribing information requirements of the FDA or other regulatory authorities;
- limitations or warnings contained in the labeling approved by the FDA;
- the timing of market introduction of our TCR therapeutic candidates as well as competitive products;
- the cost of treatment in relation to alternative treatments;
- the availability of coverage, adequate reimbursement and pricing by third-party payors and government authorities;

- the willingness of patients to pay for our TCR therapeutic candidate on an out-of-pocket basis in the absence of coverage by third-party payors and government authorities;

- relative convenience and ease of administration as compared to alternative treatments and competitive therapies; and

- the effectiveness of our sales and marketing efforts.

In addition, although we are not utilizing embryonic stem cells or replication competent vectors, adverse publicity due to the ethical and social controversies surrounding the therapeutic use of such technologies, and reported side effects from any clinical trials using these technologies or the failure of such trials to demonstrate that these therapies are safe and effective may limit market acceptance of our TCR therapeutic candidates. If our TCR therapeutic candidates are approved but fail to achieve market acceptance among physicians, patients, hospitals, cancer treatment centers or others in the medical community, we will not be able to generate significant revenue.

Even if our TCR therapeutic candidates achieve market acceptance, we may not be able to maintain that market acceptance over time if new products or technologies are introduced that are more favorably received than our TCR therapeutic candidates, are more cost effective or render our TCR therapeutic candidates obsolete.

Coverage and reimbursement may be limited or unavailable in certain market segments for our TCR therapeutic candidates, which could make it difficult for us to sell our TCR therapeutic candidates profitably.

Successful sales of our TCR therapeutic candidates, if approved, depend on the availability of coverage and adequate reimbursement from third-party payors. In addition, because our TCR therapeutic candidates represent new approaches to the treatment of cancer, we cannot accurately estimate the potential revenue from our TCR therapeutic candidates.

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Patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Obtaining coverage and adequate reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance.

Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which drugs and treatments they will cover and the amount of reimbursement. Reimbursement by a third-party payor may depend upon a number of factors, including, but not limited to, 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 approval of a TCR therapeutic candidate from a government or other third-party payor is a time-consuming and costly process which likely could require us to provide to the payor supporting scientific, clinical and cost-effectiveness data for the use of our products. Even if we obtain coverage for a given TCR therapeutic candidate, the resulting reimbursement payment rates might not be adequate for us to achieve or sustain profitability or may require co-payments that patients find unacceptably high. Patients are unlikely to use our TCR therapeutic candidates unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our TCR therapeutic candidates.

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. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our TCR therapeutic candidates to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained.

We intend to seek approval to market our TCR therapeutic candidates in both the United States and in selected jurisdictions. If we obtain approval in one or more foreign jurisdictions for our TCR therapeutic candidates, we will be subject to rules and regulations in those jurisdictions. In some foreign countries, particularly those in the EU, the pricing of biologics is subject to governmental control. In these

countries, pricing negotiations with governmental authorities can take considerable time after obtaining marketing approval of a TCR therapeutic candidate. In addition, market acceptance and sales of our TCR therapeutic candidates will depend significantly on the availability of coverage and adequate reimbursement from third-party payors for our TCR therapeutic candidates and may be affected by existing and future health care reform measures.

Third-party payors, whether domestic or foreign, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. In both the United States and certain foreign jurisdictions, there have been a number of legislative and regulatory changes to the health care system that could impact our ability to sell our products profitably. In particular, the recently enacted U.S. Healthcare Reform Act and its implementing regulations, among other things, revised the methodology by which rebates owed by manufacturers to the state and federal government for covered outpatient drugs and certain biologics, including our TCR therapeutic candidates, under the Medicaid Drug Rebate Program are calculated, increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program, extended the Medicaid Drug Rebate program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations, subjected manufacturers to new annual fees and taxes for certain branded prescription drugs, and provided incentives to programs that increase the federal government s comparative effectiveness research.

Other legislative changes have been proposed and adopted in the United States since the Healthcare Reform Act was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation s automatic reduction to several government programs.

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This includes aggregate reductions of Medicare payments to providers up to two percent per fiscal year, which went into effect on April 1, 2013 and will remain in effect until 2024, unless additional congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, or the ATRA, which, among other things, reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. We cannot predict the initiatives that may be adopted in the future. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare and/or impose price controls may adversely affect:

- the demand for our TCR therapeutic candidates, if we obtain regulatory approval;
- our ability to set a price that we believe is fair for our TCR therapeutic candidates;
- our ability to generate revenue and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors, which may adversely affect our future profitability.

Risks Related to Our Reliance Upon Third Parties

We rely heavily on GSK for our NY-ESO TCR therapeutic candidate clinical program, which may also affect other TCR therapeutic candidates.

Our ability to commercialize our NY-ESO TCR therapeutic candidate and our other TCR therapeutic candidates depends heavily on the ongoing collaboration with GSK and payments made by GSK to us upon achievement of specified milestones. GSK has the right to nominate four target

programs in addition to the NY-ESO TCR therapeutic candidate program under the collaboration arrangements. We have no control over whether GSK will elect to progress additional targets under the collaboration arrangements and therefore trigger additional investment from GSK in our TCR therapeutic candidates. If GSK does not elect to do so, we may require additional capital or investment or need to enter into alternative strategic alliances. In addition, GSK has a right to terminate the collaboration and license agreement or any specific license under the collaboration and license agreement for any reason on provision of sixty days notice. Termination may impact not only our requirement for additional investment or capital but also the timeframes within which current clinical programs can be performed and the development of a suitable commercial-scale manufacturing process for any of our TCR therapeutic candidates. In addition, GSK has an option to obtain an exclusive worldwide license to our NY-ESO TCR therapeutic candidate program, which is exercisable during specified time periods. If the option is exercised, GSK will assume full responsibility for our NY-ESO TCR therapeutic candidate program.

The current development plan or any future development plan agreed upon between GSK and us may be unsuccessful or fail to result in candidate therapies that are feasible for further development or commercialization. There is therefore no guarantee that any payments due on commercialization of products under the agreement between GSK and us will be due or payable by GSK at any time or on the timeframes currently expected. In addition, milestone payments may not be paid where any development plan is terminated prior to completion for lack of feasibility or lack of identification of any suitable candidates that meet the required criteria for progression to the next stage of development.

In addition, the development plan agreed upon with GSK and any future development plans will be subject to change as a result of risks inherent with the development of any pharmaceutical, biological or gene therapy product. Changes to the development plan may impact the timing and extent of milestone payments made by GSK to us.

GSK has the ability to influence or control certain decisions relating to the development of therapies covered by our collaboration and license agreement with GSK. This ability could result in delays to the clinical programs covered by the collaboration or changes to the scope of those clinical programs, including the disease indications relevant to such clinical programs. Under the agreement, we are also prohibited from independently developing or commercializing therapies directed at the targets subject to outstanding options granted to GSK. In addition, GSK may have competing internal or commercial interests including its independent collaboration with Immunocore Limited, or Immunocore, any of which could impact our collaboration or the ability of GSK to take any clinical programs forward to the next stage following the exercise of their option.

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GSK and Novartis have publicly announced that Novartis has opt-in rights over GSK s current and future oncology research and development pipeline. As part of that announced transaction, GSK has sold the rights to GSK s marketed oncology portfolio, related R&D activities and the AKT Inhibitors currently in development. GSK has also agreed to grant Novartis preferred partner rights for co-development and commercialization of GSK s current and future oncology pipeline products for a period of 12.5 years from completion of the applicable transactions between GSK and Novartis. The relevant agreement grants Novartis a right of first negotiation over the co-development or commercialisation of any GSK Relevant Development Product in a major market. A Relevant Development Product as defined in the public announcement is a product in development for the treatment, palliation, diagnosis or prevention of all cancers, including immunology, epigenetics and treatment of solid or hematologic tumors (excluding in all cases, vaccines). The right of first negotiation also lasts for 12.5 years from completion of the applicable transactions between GSK and Novartis and according to the public announcement applies where GSK decides to seek a third party partner for co-development or commercialization of, or to whom to divest rights to, a Relevant Development Product in a global or major market or where GSK proposes to seek a marketing authorization for a Relevant Development Product in a major market.

The existence of these opt-in rights could impact GSK s decision whether to exercise any option under our collaboration or the ability of GSK to take any clinical programs forward to the next stage, following the exercise of its option.

The relationship with GSK could also result in disputes arising between us and GSK which could result in costly arbitration or litigation and could impact the ongoing clinical programs or progress of such clinical programs. All intellectual property rights arising from the performance of the collaboration and license agreement will be jointly owned apart from intellectual property rights that we solely create. Both GSK and we have freedom to use jointly owned intellectual property rights.

Further development of our TCR therapeutic candidates is also dependent on the work currently planned to be carried out under the agreement with GSK and any delay in such work or termination by GSK of any development program or agreement, may result in substantial delays in the development of our TCR therapeutic candidates and ability to bring our TCR therapeutic candidates to market. Such termination or delays may also result in the need for further investment to replace revenue expected to be earned under the GSK collaboration and license agreement.

The GSK collaboration programs relate to specific TCR therapeutic candidates directed to nominated targets. Should any of these programs not be successful or resulting clinical programs show a lack of efficacy or problems with safety, tolerability or durability of response, GSK may decide not to proceed further with such collaboration programs and our ability to obtain other partners for further development of such candidates or of new TCR therapeutic candidates could be significantly compromised.

We rely heavily on Thermo Fisher Scientific Inc., or ThermoFisher, and the technology that we license from them.

The ability to use the ThermoFisher Dynabeads® CD3/CD28 technology to isolate, activate and expand T cells is important to our ongoing ability to offer TCR therapeutic candidates. In December 2012, we entered into a series of license and sub-license agreements with Life Technologies Corporation (now part of ThermoFisher) . These agreements provide us with a field-based exclusive license under certain intellectual property rights owned or controlled by ThermoFisher

in relation to the methods of use of the ThermoFisher Dynabeads® CD3/CD28 technology to isolate, activate and expand T-cells and enable transfection of the T-cells with any TCR genes to manufacture our TCR products and use and sell those TCR products to treat cancer, infectious disease and/or autoimmune disease. We also have a field-based exclusive sub-license under certain other patents which cover the method of use of the Dynabeads® CD3/CD28 and are controlled by ThermoFisher under a head-license from the University of Michigan, the United States Navy and the Dana-Farber Cancer Institute.

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We have a research supply agreement for the Dynabeads® CD3/CD28 CTS, which currently runs for a period of three years beginning June 2013. We are in the process of negotiating a new supply agreement; however there is no certainty that a re-negotiation will be possible on commercially acceptable terms, which could impact the supply of TCR therapeutic candidates for clinical trials and require us to obtain an alternative source of these beads, which may not be available to us on reasonable terms or at all, and may be subject to the requirement for additional regulatory approval.

ThermoFisher has the right to terminate the above described agreements for material breach or insolvency. If ThermoFisher terminates the exclusive license, sub-license and supply agreements or otherwise refuses to supply the Dynabeads® product, we will have to seek an alternative source of the beads or develop an alternative process methodology to enable supply of our TCR therapeutic candidates. An alternative source may be difficult to find or more expensive, which may delay timeframes either for clinical programs or ultimately commercial supply of our TCR therapeutic candidates. A requirement to identify an alternative source may also require a change in our regulatory application or additional regulatory testing to ensure that any alternative source is comparable and does not present any additional risk which could also result in our program experiencing delays and increased costs.

The sub-license agreement, in addition to having the same relevant exclusivity scope and field-based restrictions and many of the terms being equivalent to those set out in the main license agreement with ThermoFisher, also includes additional requirements that any manufacture of engineered TCR products for sale in the United States must occur in the United States and reserves rights for the United States government to use the technology in accordance with 35 U.S.C. § 200 et seq. and for the University of Michigan and Dana-Farber Cancer Institute to use the technology for non-commercial research purposes.

We rely on third parties to manufacture and supply our TCR therapeutic candidates, and we may have to rely on third parties to produce and process our TCR therapeutic candidates, if approved.

We currently rely on outside contract manufacturing organizations (CMOs) to manufacture, supply and process our TCR therapeutic candidates. If one or more of these CMOs become unable or unwilling to continue to manufacture our engineered TCR therapeutic candidates in the future, we may be forced to find an alternative third-party manufacturer, which we may not be able to do on commercially reasonable terms, if at all. Failure to identify a suitable alternative manufacturer could impact our business, financial condition or results of operations.

We rely on a limited number of third-party manufacturers for clinical trial product supplies, and if we are unable to develop our own commercial manufacturing facility for any commercial product supplies, we will be exposed to the following risks:

- We may be unable to contract with manufacturers on commercially acceptable terms or at all because the number of potential manufacturers is limited and the FDA, EMA and other comparable foreign regulators must approve any replacement manufacturer, which would require new testing and compliance inspections. In addition, a new manufacturer would have to be educated in, and develop substantially equivalent processes for, production of our TCR therapeutic candidates after receipt of any applicable regulatory approval.

- Our third-party manufacturers might be unable to timely formulate and manufacture our TCR therapeutic candidates or produce the quantity and quality required to meet our clinical trial and commercial needs, if any.

- Contract manufacturers may not be able to execute our manufacturing procedures appropriately.

- Our future contract manufacturers may not perform as agreed or may not remain in the contract manufacturing business for the time required to supply our clinical trials or to successfully produce, store and distribute our TCR therapeutic candidates.

- Manufacturers are subject to ongoing periodic unannounced inspection by the FDA, EMA, and other comparable foreign regulators and corresponding state agencies to ensure strict compliance with cGMP and other government regulations and corresponding foreign standards. Although we do not have day-to-day control over third-party manufacturers compliance with these regulations and standards, we are responsible for ensuring compliance with such regulations and standards.

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- We may not own, or may have to share, the intellectual property rights to any improvements made by our third-party manufacturers in the manufacturing process for our TCR therapeutic candidates.

- Our third-party manufacturers could breach or terminate their agreement with us.

Our contract manufacturers are also subject to the same risks we face in developing our own manufacturing capabilities, as described above. Each of these risks could delay our clinical trials, the approval, if any, of our TCR therapeutic candidates by the FDA or the commercialization of our TCR therapeutic candidates or result in higher costs or deprive us of potential product revenue. We have insurance to cover certain costs and expenses related to business interruption, which is capped at £3.0 million in the aggregate.

In addition, we will rely on third parties to perform release tests on our TCR therapeutic candidates prior to delivery to patients. If these tests are not appropriately performed and test data are not reliable, patients could be put at risk of serious harm.

We have a shared development history with Immunocore, and as a result are reliant on resources and other support from Immunocore, which if not present could result in delays in our ability to progress new TCR therapeutic candidates to market.

Our TCR technology was originally developed by Avidex, and was subsequently acquired by Medigene in 2006. We were formed as a new, separate company and licensed our TCR technology for T-cell therapy from Medigene in July 2008. Immunocore was subsequently formed as a new separate company and licensed its TCR technology for soluble TCRs from Medigene later in 2008 to develop soluble TCR proteins. Immunocore currently owns approximately 6.35% of the ordinary shares in Adaptimmune. The holders of approximately 36.6% of our ordinary shares also hold shares of Immunocore. These ordinary shareholders and their affiliates own approximately 56.4% of the equity interests in Immunocore, and Immunocore and its shareholders and their affiliates own approximately 43.0 % of the ordinary shares in Adaptimmune. Until March 31, 2014, our Chief Executive Officer, or CEO, was also the CEO of Immunocore and until July 16, 2015 he was on the board of Immunocore. Two of our directors, Ian Laing and Jonathan Knowles, our chairman, also serve on the board of Immunocore, of which Dr. Knowles is also chairman, and two of our greater than 5% ordinary shareholders, Nicholas Cross and George Robinson, are significant shareholders in, and are directors of, Immunocore. Our scientific co-founder, Bent Jakobsen, is also an employee of Immunocore.

Both Adaptimmune and Immunocore focus on technologies that are based on TCR therapies. Each company focuses on distinct applications of, and utilizes different, TCRs. Immunocore uses soluble TCRs whereas Adaptimmune uses cellular TCR therapeutic candidates. Both soluble TCRs and Adaptimmune s TCR therapeutic candidates rely on the engineering of TCRs to create affinity-enhanced TCRs. In Adaptimmune s case, once the engineered affinity-enhanced TCR has been generated, the gene encoding that engineered TCR is transduced into patient T cells. With soluble TCRs, there is no transduction. For soluble TCRs, the engineered affinity-enhanced TCRs are combined with an antibody fragment, anti-CD3, and it is this combined TCR/anti- CD3 candidate that is then used to treat patients directly. The combined candidates are called ImmTACs. As a result, the end therapeutic candidates being developed by each company are different in terms of end structure, affinity, require different manufacturing and administration routes and are likely to have different properties in patients. For example, ImmTACs are not anticipated to persist beyond a few hours in a patient following administration, whereas Adaptimmune s TCR therapeutics have been shown to persist in patients for years; ImmTACs are likely to require higher amounts of target peptide to be present and hence Adaptimmune s TCR therapeutics may address cancer cells with lower levels of antigen; ImmTACs rely on activating the patient s existing T cells through an anti-CD3-CD3 interaction, whereas Adaptimune s TCR therapeutic candidates activate T cells through direct binding to the target peptide and this results in a different mechanism of action being seen in *in vitro* tests.

Notwithstanding the differences between Immunocore s and Adaptimmune s end products, there is a risk that both companies could potentially develop products or therapies that target the same peptide and are directly competitive and/or address the same indications and patient populations. For example, both companies could develop therapeutic candidates to the same peptide target and hence have a product addressing the same patient populations in the same way as any other competing technology. In addition, both Immunocore and Adaptimmune have entered into collaboration agreements with GSK, which could decide over time to devote greater time and resources to Immunocore at the expense of Adaptimmune.

We have a collaboration agreement with Immunocore regarding target identification and T-cell cloning which provides joint access to all currently identified peptide targets and use of Immunocore employees in conducting such identification. We are in the process of implementing our own T-cell cloning capabilities and plan to implement target identification, but will continue to identify targets jointly with Immunocore through our target collaboration agreement. However, there is a risk that Immunocore could refuse to provide such services on an ongoing basis or alternatively, be unable to provide such services. This may result in delay or termination of our planned research and development activities, which could have a material impact on our ability to develop or bring additional TCR therapeutic candidates to market. In addition, under the terms of the target collaboration agreement, Immunocore may terminate such agreement for any reason with six months notice and it is very unlikely that we could find a suitable replacement and would therefore have to develop these capabilities ourselves, which might take a long time and may delay our planned research and development activities.

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Under the terms of the target collaboration agreement, we also share a database of identified targets with Immunocore which has resulted from our joint target identification efforts. The contents of this target database are highly confidential and if disclosed to a third party, either as a result of a breach of the confidentiality terms between us and Immunocore or through a change of control in Immunocore, our business could be adversely impacted. If Immunocore is acquired, restructured or otherwise subject to a change of control or otherwise becomes insolvent or lacks liquidity, we could become associated with a third party and the working relationship between the two companies could be compromised. In any of these circumstances, Immunocore may cease cooperating with us or refuse or be unable to provide planned resources which could have a material adverse effect on our business.

In addition, many of the patents relating to our underlying core technology in TCR engineering, are co-owned by us and Immunocore pursuant to an assignment and license agreement. Under this agreement, each of Immunocore and Adaptimmune utilize the jointly owned patents and know-how, with Adaptimmune focused on the treatment of patients with engineered TCR therapeutic candidates and Immunocore focused on the treatment of patients with soluble TCRs. Under the agreement, each of Immunocore and Adaptimmune grants the other an exclusive, royalty-free, irrevocable license, with the right to sub-license, to certain jointly owned patents and know-how. However, there is the potential that Immunocore could develop a soluble TCR product targeting the same cancer target that one of our TCR therapeutic candidates is targeting, and therefore compete directly with us.

We occupy a significant proportion of our corporate headquarters at Milton Park, Oxfordshire, United Kingdom, where we conduct most of our operations, including our in-house research and laboratory facilities, under subleases from Immunocore. These subleases contain rolling mutual break option provisions that could be effective from June 1, 2017 onwards, on service of six months prior notice. In September 2015, we entered into an agreement directly with the owner of Milton Park for the construction and lease of a new approximately 67,000 square foot laboratory and office building. We have a transitional services agreement with Immunocore under which Dr. Bent Jakobsen, a scientific co-founder of both Adaptimmune and Immunocore, will continue to devote time to each company. If our relationship with Immunocore deteriorated, whether as a result of a change at that company or due to external events affecting Immunocore, then notwithstanding our additional building scheduled for construction, our relationship with Immunocore as our current landlord and/or our access to Dr. Bent Jakobsen could be adversely affected which could harm our business.

We rely on third parties to conduct our 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 of or commercialize our TCR therapeutic candidates.

We depend upon independent investigators and collaborators, such as universities, medical institutions, CROs and strategic partners to conduct our preclinical programs and sponsored clinical trials under agreements with us. We expect to have to negotiate budgets and contracts with CROs and trial sites (either directly or through a third party consultant), which may result in delays to our development timelines and increased costs. We rely heavily on these third parties over the course of our clinical trials, and we do not have day-to-day control of their activities. Nevertheless, we are responsible for ensuring that each of our trials is conducted in accordance with applicable protocols and legal, regulatory and scientific standards, and our reliance on third parties does not relieve us of our regulatory responsibilities. We and these third parties are required to comply with cGCPs, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for TCR therapeutic candidates in clinical development. Regulatory authorities enforce these cGCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of these third parties fail to comply with applicable cGCP regulations and guidelines, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot provide assurances that, upon inspection, such regulatory authorities will determine that any of our clinical trials comply with the cGCP regulations. In addition, our clinical trials must be conducted with biologic product produced under cGMPs and will require a large number of subjects. Our failure or any failure by these third parties to comply with these regulations or to support BLA for approval of our NY-ESO TCR therapeutic candidate for the treatment of a sufficient number of patients may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of these third parties violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

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Any third parties conducting our clinical trials are not and will not be our employees and, except for remedies available to us under our agreements with such third parties which could be limited, we cannot control whether or not they devote sufficient time and resources to our ongoing clinical trials and preclinical programs. These third parties may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug or biologic development activities, which could affect their performance on our behalf. If these third parties 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 or regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to complete development of, obtain regulatory approval of, or successfully commercialize our TCR therapeutic candidates. As a result, our financial results and the commercial prospects for our TCR therapeutic candidates would be harmed, our costs could increase and our ability to generate revenue could be delayed.

Switching or adding third parties to conduct our clinical trials involves substantial cost and requires extensive management time and focus. In addition, there is a natural transition period when a new third party commences work. As a result, delays may occur, which can materially impact our ability to meet our timelines for bringing our TCR therapeutic candidates to market, if at all.

The Christie NHS Foundation Trust in the United Kingdom sponsors a European investigator-initiated gastro-esophageal cancer study using our NY-ESO TCR therapeutic candidate. Given that we are not the sponsor of this clinical program we cannot control the protocol used in such clinical programs, the procedures used in such clinical programs, the manufacture and supply of the therapy used in the program or the timescales under which such clinical programs are performed. The clinical programs form part of a European Framework grant collaboration program called ATTACK 2 (Adoptive engineered T-cell Targeting to Activate Cancer Killing) which is led by the University of Manchester. Management of the collaboration program is via a consortium of members, including us (the ATTACK Consortium) and we have limited control over decisions taken by the majority of the other ATTACK Consortium members. We cannot guarantee whether the clinical programs will be carried out in accordance with regulatory requirements and performance of these clinical programs could affect our clinical programs including our ability to obtain regulatory approval of, or successfully commercialize our TCR therapeutic candidates.

We rely on third parties to obtain reagents and raw materials.

The manufacture of our TCR therapeutic candidates requires access to a number of reagents and other raw materials from third parties. Such third parties may refuse to supply such reagents or other raw materials or alternatively refuse to supply on commercially reasonable terms. There may also be capacity issues at such third-party suppliers that impact our ability to increase production of our TCR therapeutic candidates.

Some of the materials used in the manufacture and processing of our TCR therapeutic candidates may only be supplied by one or a few vendors, which means that, should those vendors be unable to supply, for whatever reason, our ability to manufacture TCR therapeutic candidates and progress TCR therapeutic candidates through clinical trials could be severely impacted and result in additional delays. Such failure to supply could also impact other supply relationships with other third parties and potentially result in additional payments being made or required in relation to such delays.

Risks Related to Our Intellectual Property

Our TCR therapeutic candidates could be at risk of biosimilar development.

Expedited routes or abbreviated procedures for obtaining regulatory approval for products aiming to target the same cancer peptide as our TCR therapeutic candidates may be available to third parties, which we cannot control or prevent. For example, third parties could develop affinity-enhanced TCRs binding to the same targets and regulatory authorities may accept that they are interchangeable with our corresponding TCR therapeutic candidates and, as a result, grant regulatory approval for such competing products. Entry into the market of such competing products may impact the price of our TCR therapeutic candidates and the extent of commercialization possible in relation to such TCR therapeutic candidates.

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We may be forced to litigate to enforce or defend our intellectual property rights, and/or the intellectual property rights of our licensors.

We may be forced to litigate to enforce or defend our intellectual property rights against infringement and unauthorized use by competitors, and to protect our trade secrets. In so doing, we may place our intellectual property at risk of being invalidated, held unenforceable, narrowed in scope or otherwise limited. Further, an adverse result in any litigation or defense proceedings may increase the risk of non-issuance of pending applications. In addition, if any licensor fails to enforce or defend its intellectual property rights, this may adversely affect our ability to develop and commercialize our TCR therapeutic candidates and to prevent competitors from making, using, and selling competing products. Any such litigation could be very costly and could distract our management from focusing on operating our business. The existence and/or outcome of any such litigation could harm our business, results of operations and financial condition.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential and proprietary 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. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our ordinary shares.

We may not be able to protect our proprietary technology in the marketplace or the cost of doing so may be prohibitive or excessive.

Our success will depend, in part, on our ability to obtain patents, protect our trade secrets and operate without infringing on the proprietary rights of others. We rely upon a combination of patents, trade secret protection (i.e., know-how), and confidentiality agreements to protect the intellectual property of our TCR therapeutic candidates. The scope and validity of patents in the pharmaceutical field involve complex legal and scientific questions and can be uncertain. Where appropriate, we seek patent protection for certain aspects of our TCR therapeutic candidates and technology. Filing, prosecuting and defending patents throughout the world would be prohibitively expensive, so our policy is to patent technology in jurisdictions with significant commercial opportunities. However, patent protection may not be available for some of the TCR therapeutic candidates or technology we are developing. If we must spend significant time and money protecting or enforcing our patents, designing around patents held by others or licensing, potentially for large fees, patents or other proprietary rights held by others, our business results of operations and financial condition may be harmed. We may not develop additional proprietary products that are patentable.

Many companies have encountered significant problems in protecting and enforcing intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property rights, particularly those relating to pharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business.

In addition, patents have a limited lifespan. In most countries, including the United States, the standard expiration of a patent is 20 years from the effective filing date. Various extensions of patent term may be available in particular countries, however in all circumstances the life of a patent, and the protection it affords, has a limited term. If we encounter delays in obtaining regulatory approvals, the period of time during which we could market a product under patent protection could be reduced. We expect to seek extensions of patent terms where these are available in any countries where we are prosecuting patents. Such possible extensions include those permitted under the Drug Price Competition and Patent Term Restoration Act of 1984 in the United States, which permits a patent term extension of up to five years to cover an FDA-approved product. The actual length of the extension will depend on the amount of patent term lost while the product was in clinical trials. However, the applicable authorities, including the FDA in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions

than we request. If this occurs, our competitors may be able to take advantage of our investment in development and clinical trials by referencing our clinical and non-clinical data, and then may be able to launch their product earlier than might otherwise be the case.

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Any loss of, or failure to obtain, patent protection could have a material adverse impact on our business. We may be unable to prevent competitors from entering the market with products that are similar to or the same as our TCR therapeutic candidates.

Further given that our technology relates to the field of genetic engineering, political pressure or ethical decisions may result in a change to the scope of patent claims for which we may be eligible. Different patent offices throughout the world may adopt different procedures and guidelines in relation to what is and is not patentable and as a result different protection could be obtained in different areas of the world which may impact our ability to maximize commercialization of our technology.

We may also incur increased expenses and cost in relation to the filing and prosecution of patent applications where third parties choose to challenge the scope or oppose the grant of any patent application or, following grant, seek to limit or invalidate any patent. On April 13, 2015, we received notification of a third party observation filed against one of the patent applications (PCT/GB2013/053320) jointly owned with Immunocore Limited and covering one aspect of our underlying processes. The third party observation cites a reference which the third party considers to be novelty destroying in relation to claims 1-14 of our patent application. We are currently evaluating this notification. Any increased prosecution or defense required in relation to such patents and patent applications, whether relating to this third party observation or any other third party challenge or opposition, entails increased cost and resource commitment to the business and may result in patents and patent applications being abandoned, invalidated or narrowed in scope.

We may be unable to adequately prevent disclosure of trade secrets and other proprietary information.

We rely on trade secrets to protect our proprietary know-how and technological advances, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. We rely, in part, on confidentiality agreements with our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to protect our trade secrets and other proprietary information. These agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. In addition, others may independently discover our trade secrets and proprietary information. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights. Failure to obtain or maintain trade secret protection, or failure to adequately protect our intellectual property, could enable competitors to develop generic products or use our proprietary information to develop other products that compete with our TCR therapeutic candidates or have additional, material adverse effects upon our business, results of operations and financial condition.

In addition, we provide samples to third parties under material transfer agreements, including to research institutions or other organizations that we cannot control. There is a risk that such third parties could disclose details of those samples or carry out further research in relation to provided samples which results in intellectual property rights that block our future freedom to operate, and to which we may not be able to obtain a license on commercially acceptable terms or at all. In addition, provision of samples and our confidential information to such parties could facilitate or assist such parties in development of competing products.

If third parties claim that our activities or products infringe upon their intellectual property, our operations could be adversely affected.

There is a substantial amount of litigation, both within and outside the United States, involving patents and other intellectual property rights in the pharmaceutical industry. We may, from time to time, be notified of claims that we are infringing upon patents, trademarks, copyrights, or

other intellectual property rights owned by third parties, and we cannot provide assurances that other companies will not, in the future, pursue such infringement claims against us or any third-party proprietary technologies we have licensed. If we were found to infringe upon a patent or other intellectual property right, or if we failed to obtain or renew a license under a patent or other intellectual property right from a third party, or if a third party that we were licensing technologies from was found to infringe upon a patent or other intellectual property rights of another third party, we may be required to pay damages, including triple damages if the infringement is found to be willful, suspend the manufacture of certain TCR therapeutic candidates or reengineer or rebrand our TCR therapeutic candidates, if feasible, or we may be unable to enter certain new product markets. Any such claims could also be expensive and time- consuming to defend and divert management s attention and resources. Our competitive position could suffer as a result. In addition, if we have declined to enter into a valid non-disclosure or assignment agreement for any reason, we may not own an invention or intellectual property rights and may not be adequately protected. Although we have reviewed certain third-party patents and patent filings that we believe may be relevant to our TCR therapeutic candidates, we have not conducted a full freedom-to-operate search or analysis for such TCR therapeutic candidates, and we may not be aware of patents or pending or future patent applications that, if issued, would block us from commercializing our TCR therapeutic candidates. Thus, we cannot guarantee that we can successfully commercialize TCR therapeutic candidates in a way that will not infringe any third party s intellectual property.

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Licenses may be required from third parties in relation to any TCR therapeutic candidates offered by us.

We may identify third-party intellectual property rights that are required to enable the further development, commercialization, manufacture or development of our TCR therapeutic candidates. Licenses to such intellectual property rights may or may not be available on commercial terms that are acceptable to us. As a result we may incur additional license fees for such intellectual property rights, or the cost and expenses to identify an alternative route for commercialization, that does not require the relevant third-party intellectual property rights, or the cost and diversion of resources required to challenge any such third party intellectual property rights.

We are aware of a family of patent applications owned by The Board of Trustees of the University of Illinois which include two issued U.S. patents (U.S. 6,759,243 and 7,569,357) which were issued with very broad claims relating to high affinity TCRs. We believe that U.S. Patent 7,569,357, because of certain claim recitations, is not an impediment to our presently contemplated TCR therapeutic candidates. We requested re-examination of U.S. Patent 6,759,243 at the USPTO. In that re-examination, the USPTO adopted our position and rejected all claims under re-examination as anticipated or obvious, and in a related pending patent application of The Board of Trustees of the University of Illinois, in an August 18, 2014 Office Action, the USPTO also adopted our position and rejected the claims based on our arguments and evidence of our re-examination request. Through the re-examination process we have been successful in achieving a narrowing of all of the claims of U.S. Patent 6,759,243. While we believe U.S. Patent 6,759,243 will be nonetheless invalid in the form it will issue after re-examination, we do not believe the patent after re-examination will be an impediment to our presently contemplated TCR therapeutic candidates, because of the recitations added by the patentee during re-examination and the U.S. codified doctrine of intervening rights. Furthermore, these U.S. patents will likely expire prior to any commercial supply by us of any TCR therapeutic candidate. There is a risk that the owner of the family of patent applications may still try to enforce such patent applications against us which would divert resources and result in increased costs to defend against such enforcement.

We have identified third party European patent applications which relate to high affinity TCR proteins and methods. We have filed third-party observations in relation to one of these third party European patent applications. The claims as drafted are broad and as a result could cover soluble TCRs having a specific level of binding and carrying one or more mutations in a complementarity determining region, or CDR, irrespective of the method by which the TCRs are produced. Should these patent applications proceed to grant in Europe with claims of such broad scope, we will need to consider filing Opposition proceedings against the grant of the European patents at the European Patent Office and/or filing for revocation of the national patents derived from the European patents before relevant national patent offices and/or courts.

We have also identified a family of third party patents under which we may require a license in relation to a structural component of our lentiviral vector (cPPT) prior to any commercialization of TCR therapeutic candidates. We believe such licenses are available and we are in discussions to procure a license or freedom to operate under the relevant patent rights.

We may also require licenses under third-party patents covering certain peptide sequences or the use of those peptides. Such licenses will require payment of sums by us and we cannot guarantee that the terms of such licenses will be available on commercially acceptable terms or at all, which could limit the peptides which can be used by us and the efficacy of the final affinity- enhanced TCRs that we are able to offer.

Further or other third-party patents and patent applications may be identified from time to time that require prospective action by us to prevent the grant of broad claims. Such prospective action requires time and expense and also impacts on the resources generally available to us.

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Where we license certain technology from a third party, the prosecution, maintenance and defense of the patent rights licensed from such third party may be controlled by the third party which may impact the scope of patent protection which will be obtained or enforced.

Where we license patent rights or technology from a third-party, control of such third-party patent rights may vest in the licensor, particularly where the license is non-exclusive or field restricted. This may mean that we are not able to control or affect the scope of the claims of any relevant third-party patent or have control over any enforcement of such a patent. Where a licensor brings an enforcement action, this could negatively impact our business or result in additional restrictions being imposed on the license we have and the scope of such license, or result in invalidation or limitation of the scope of the licensed patent. In addition, should we wish to enforce the relevant patent rights against a third person, we may be reliant on consent from the relevant licensor or the cooperation of the licensor. The licensor may refuse to bring such action and leave us unable to restrict competitor entry into the market.

Issued patents protecting our TCR therapeutic candidates could be found invalid or unenforceable if challenged in court or at the USPTO.

If we or one of our licensing partners initiate legal proceedings against a third party to enforce a patent protecting one of our TCR therapeutic candidates, the defendant could counterclaim that the patent protecting our TCR therapeutic candidate, as applicable, is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace, and there are numerous grounds upon which a third party can assert invalidity or unenforceability of a patent. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post grant review, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). Such proceedings could result in revocation or amendment to our patents in such a way that they no longer cover our TCR therapeutic candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we, our patent counsel and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection for our TCR therapeutic candidates. Such a loss of patent protection could have a material adverse impact our business, financial condition and results of operations.

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

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both technological and legal complexity, and is therefore costly, time-consuming and inherently uncertain. In addition, the United States has recently enacted and is currently implementing wide-ranging patent reform legislation. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. For example, in the recent case, Assoc. for Molecular Pathology v. Myriad Genetics, Inc., the U.S. Supreme Court held that certain claims to DNA molecules are not patentable. While we do not believe that any of the patents owned or licensed by us will be found invalid based on this decision, we cannot predict how future decisions by the courts, the U.S. Congress or the USPTO may impact the value of our patents.

Our ability to protect our intellectual property rights in territories outside of the United States may vary and thus affect our ability to obtain revenue from our TCR therapeutic candidates.

Filing, prosecuting and defending patents on our TCR therapeutic candidates in all countries throughout the world would be prohibitively expensive, and the extent of intellectual property rights may be less extensive than those which can be obtained in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and 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 products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

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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 biopharmaceutical products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions 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.

Risks Related to Employee Matters and Managing Growth

We depend upon our key personnel and our ability to attract and retain employees.

We are heavily dependent on the ongoing employment and involvement of certain key employees in particular, James Noble, our Chief Executive Officer, Dr. Helen Tayton-Martin, our Chief Operating Officer, Dr. Gwendolyn Binder-Scholl, our Executive Vice-President of Translational Sciences, Rafael Amado, our Chief Medical Officer and Adrian Rawcliffe, our Chief Finance Officer. We do not hold key-man insurance for our senior managers. In addition, James Noble and Dr. Helen Tayton-Martin, are in a personal relationship. They are our co-founders, two of our most senior executive officers and are a vital part of our business. If the personal relationship ended or they could otherwise not amicably work with each other, one of them may decide to leave us which would materially harm our business.

In addition, we anticipate a requirement to expand the personnel available to us very rapidly in order to achieve our planned business activities and aims. Such expansion is dependent on our ability to recruit experienced and suitably trained employees or consultants, and to retain such employees on a long term basis. Our ability to take our existing pipeline of TCR therapeutics and to meet the demands of the GSK collaboration may be compromised or delayed where we are unable to recruit sufficient personnel on a timely basis.

To induce employees to remain at our company, in addition to salary and cash incentives, we have provided share options that vest over time, with higher awards of share options being made to senior employees. The value to employees of share options that vest over time may be significantly affected by movements in our share price that are beyond our control, and may at any time be insufficient to counteract more lucrative offers from other companies. Despite our efforts to retain valuable employees, members of our management, scientific and development teams may terminate their employment with us on short notice. Although we have employment agreements with all of our employees, in the United Kingdom, these employment agreements provide for mutual six months notice periods in the case of Mr. Noble and Dr. Tayton-Martin; mutual three months notice periods in the case of senior managers and mutual one month notice periods for all other employees. In the United States, these employment agreements provide for at-will employment except that our employment agreement with Dr. Binder-Scholl provides for a mutual one month notice period, and our employment agreements with Dr. Rafael Amado, our Chief Medical Officer, and Adrian Rawcliffe, our Chief Financial Officer, provide that Dr. Amado and Mr. Rawcliffe must provide 60 days written notice for termination without cause. This means that any of our employees in the United States, except for Dr. Binder-Scholl, Dr. Amado and Mr. Rawcliffe, could leave our employment at any time, with or without notice. Our success also depends on our ability to continue to attract, retain and motivate highly skilled junior, mid-level and senior managers as well as junior, mid-level and senior scientific and medical personnel.

We will need to grow the size and capabilities of our organization, and we may experience difficulties in managing this growth.

As of June 30, 2015, we had 116 full-time equivalent employees. As our development and commercialization plans and strategies develop, we must add a significant number of additional managerial, operational, sales, marketing, financial, and other personnel. Future growth will impose significant added responsibilities on members of management, including:

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- identifying, recruiting, integrating, maintaining, and motivating additional employees;

- managing our internal development efforts effectively, including the clinical and FDA review process for our TCR therapeutic candidates, while complying with our contractual obligations to contractors and other third parties; and

- improving our operational, financial and management controls, reporting systems, and procedures.

Our future financial performance and our ability to commercialize our TCR therapeutic candidates will depend, in part, on our ability to effectively manage any future growth, and our management may also have to divert a disproportionate amount of its attention away from day-to-day activities in order to devote a substantial amount of time to managing these growth activities.

We also rely on third parties to provide certain of our manufacturing and quality capabilities. See Risks Related to Our Reliance Upon Third Parties.

If we are not able to effectively expand our organization by hiring new employees and expanding our groups of consultants and contractors, we may not be able to successfully implement the tasks necessary to further develop and commercialize our TCR therapeutic candidates and, accordingly, may not achieve our research, development, and commercialization goals.

We expect to face intense competition, often from companies with greater resources and experience than we have.

Immunotherapy is an intensely competitive area with many of the large pharmaceutical companies having products and therapies already in clinical trials for cancer indications and autoimmune diseases. The larger resources of these companies may enable them to take therapies all the way through the regulatory process, while we will require additional investment or input from collaborators such as GSK to take our TCR therapeutic candidates through the regulatory process and commercialization. Smaller or early-stage companies may also prove to be significant competitors, particularly if such companies align with pharmaceutical partners and compete for patients. Results obtained by such competitors in clinical trials could also impact our ability to obtain regulatory approval or delay such approval in the event of a safety issue or other negative clinical result associated with similar T-cell or TCR therapeutic candidates.

In particular, we face competition from chimeric antigen receptor T cell, or CAR-T, technologies from companies such as Novartis AG/University of Pennsylvania, Kite Pharma, Inc./Amgen Inc./National Cancer Institute, bluebird bio, Inc./Celgene Corporation/Baylor College of Medicine, Intrexon Corporation/Ziopharm Oncology, Inc./MD Anderson Cancer Center, Juno Therapeutics, Inc./Celgene Corporation/Fred Hutchinson Cancer Research Center/Memorial Sloan Kettering Cancer Center, Cellectis SA/Pfizer Inc. and Bellicum Pharmaceuticals Inc. In the TCR space, we face competition from Juno Therapeutics, Inc., Kite Pharma, Inc., Medigene AG and Takara Bio, Inc. Kite Pharma has a murine derived TCR product in development targeting NY-ESO-1. Should Kite Pharma or any of our other competitors be successful in advancing a TCR product targeting NY-ESO-1 through development, our ability to develop and advance our NY-ESO TCR therapeutic candidate could be

adversely affected. We may also face competition from other non-TCR and non-cell based treatments such as antibody and check point inhibitor therapies offered by companies such as Amgen Inc., AstraZeneca plc, Bristol-Myers Squibb Company, Incyte Corporation, Merck & Co., Inc., and Roche Holding Ltd. Even if we obtain regulatory approval for our TCR therapeutic candidates, we may not be the first to market, which could affect both demand for and price of our TCR therapeutic candidates.

Although Immunocore is focused on soluble TCRs rather than engineered TCR therapeutic candidates, we could also face competition from Immunocore if it develops or acquires products directed at the same targets or indications as our TCR therapeutic product candidates.

Moreover, many of our employees have come from a shared background within Immunocore and there is an awareness within Immunocore of certain of our confidential information on the technology platform controlled through confidentiality agreements. This knowledge could be used by Immunocore to facilitate its own developments or to target competitive products against our products placing it in a preferable position as compared to third party competitors.

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Failure of our information technology systems could significantly disrupt the operation of our business.

Our ability to execute our business plan and to comply with regulators requirements with respect to data control and data integrity, depends, in part, on the continued and uninterrupted performance of our information technology systems and similar systems used by third-party providers that we rely on. These systems are vulnerable to damage from a variety of sources, including telecommunications or network failures, malicious human acts and natural disasters. Moreover, despite network security and back-up measures, some of our servers are potentially vulnerable to physical or electronic break-ins, computer viruses and similar disruptive problems. Despite the precautionary measures we have taken to prevent unanticipated problems that could affect our information systems, sustained or repeated system failures or problems arising during the upgrade of any of our information systems that interrupt our ability to generate and maintain data, and in particular to operate our proprietary technology platform, could adversely affect our ability to operate our business. In addition, where disruption to such systems occurs at third-party providers, we may have limited ability to find alternative providers in any required timeframes or at all, and such disruption could significantly affect our ability to proceed with clinical or analytical or development programs.

Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses.

Our operations and those of our third party suppliers and collaborators could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes or other extreme weather conditions, medical epidemics, labor disputes or other business interruptions. While the company has business interruption insurance policies in place, any interruption could seriously harm our ability to timely proceed with any clinical programs or to supply TCR therapeutic candidates on a commercial basis or for use in clinical programs.

We are exposed to risks related to currency exchange rates.

We conduct a significant portion of our operations outside the United Kingdom. Because our financial statements are presented in pounds sterling, changes in currency exchange rates have had and could have a significant effect on our operating results. In addition, our arrangements with GSK are denominated in pounds sterling. Exchange rate fluctuations between local currencies and the pound sterling create risk in several ways, including the following: weakening of the pound sterling may increase the pound sterling cost of overseas research and development expenses and other costs outside the United Kingdom; strengthening of the pound sterling may decrease the value of any future revenues denominated in other currencies; the exchange rates on non-sterling transactions and cash deposits can distort our financial results; and commercial pricing and profit margins are affected by currency fluctuations.

We may be classified as a passive foreign investment company in any taxable year and U.S. holders of our ordinary shares could be subject to adverse U.S. federal income tax consequences.

The rules governing passive foreign investment companies, or PFICs, can have adverse effects for U.S. federal income tax purposes. The tests for determining PFIC status for a taxable year depend upon the relative values of certain categories of assets and the relative amounts of certain kinds of income. The determination of whether we are a PFIC depends on the particular facts and circumstances (such as the valuation of our assets, including goodwill and other intangible assets) and may also be affected by the application of the PFIC rules, which are subject to differing interpretations. Based on our estimated gross income, the average value of our assets, including goodwill and the nature of our active business, we do not believe that we are classified as a PFIC for U.S. federal income tax purposes for our taxable year ended June 30, 2015.

If we are a PFIC, U.S. holders of our ordinary shares would be subject to adverse U.S. federal income tax consequences, such as 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 under U.S. federal income tax laws and regulations. A U.S. holder of our ordinary shares may be able to mitigate some of the adverse U.S. federal income tax consequences described above with respect to owning the ordinary shares if we are classified as a PFIC, provided that such U.S. investor is eligible to make, and validly makes, a mark-to-market election. In certain circumstances a U.S. Holder can make a qualified electing fund election to mitigate some of the adverse tax consequences described with respect to an ownership interest in a PFIC by including in income its share of the PFIC s income on a current basis. However, we do not currently intend to prepare or provide the information that would enable a U.S. Holder to make a qualified electing fund election.

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Investors should consult their own tax advisors regarding all aspects of the application of the PFIC rules to our ordinary shares. For more information related to classification as a PFIC, see Taxation U.S. Federal Income Taxation Passive Foreign Investment Company Considerations.

Risks Related to Ownership of our American Depositary Shares (ADSs)

The price of our ADSs may be volatile.

Many factors may have a material adverse effect on the market price of the ADSs, including but not limited to:

- the commencement, enrollment or results of our planned clinical trials;
- the loss of any of our key scientific or management personnel;
- announcements of the failure to obtain regulatory approvals or receipt of a complete response letter from the FDA;
- announcements of undesirable restricted labeling indications or patient populations, or changes or delays in regulatory review processes;
- announcements of therapeutic innovations or new products by us or our competitors;
- adverse actions taken by regulatory agencies with respect to our clinical trials, manufacturing supply chain or sales and marketing activities;
- changes or developments in laws or regulations applicable to our TCR therapeutic candidates;
- any adverse changes to our relationship with licensors, manufacturers or suppliers;

- the failure of our testing and clinical trials;
- unanticipated safety concerns;
- the failure to retain our existing, or obtain new, collaboration partners;
- announcements concerning our competitors or the pharmaceutical industry in general;
- the achievement of expected product sales and profitability;
- the failure to obtain reimbursements for our TCR therapeutic candidates or price reductions;
- manufacture, supply or distribution shortages;
- actual or anticipated fluctuations in our operating results;
- our cash position;
- changes in financial estimates or recommendations by securities analysts;
- potential acquisitions;
- the trading volume of ADSs on Nasdaq;
- sales of our ADSs by us, our executive officers and directors or our shareholders in the future;

- general economic and market conditions and overall fluctuations in the U.S. equity markets; and

- changes in accounting principles.

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In addition, the stock market in general, and Nasdaq and biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our ADSs, regardless of our actual operating performance. Further, a decline in the financial markets and related factors beyond our control may cause the price of our ADSs to decline rapidly and unexpectedly.

Substantial future sales of our ADSs in the public market, or the perception that these sales could occur, could cause the price of the ADSs to decline and dilute shareholders.

Substantial future sales of our ADSs in the public market, or the perception that these sales could occur, could cause the market price of the ADSs to decline. Each ADS represents six ordinary shares and 11,250,000 ADSs, representing 67,500,000 ordinary shares, have been freely transferable without restriction or additional registration under the U.S. Securities Act of 1933, as amended (the Securities Act), since our IPO. The remaining 357,211,900 ordinary shares are subject to a lock-up period, which we anticipate will expire on November 1, 2015. Any or all of these shares may be released prior to expiration of the lock-up period at the discretion of the lead underwriter for our IPO. Subsequent to the expiration of the lock-up or earlier release of the shares by the lead underwriter, and following conversion into ADSs, these shares will be available for sale subject to volume limitations and other restrictions as applicable under Rule 144 under the Securities Act. To the extent any of these shares are sold into the market, particularly in substantial quantities, the market price of our ADSs could decline.

We also entered into a registration rights agreement on February 23, 2015, pursuant to which we have agreed, under certain circumstances, to file a registration statement to register the resale of the shares held by certain of our existing shareholders, as well as to cooperate in certain public offerings of such shares. In addition, we have registered all our ordinary shares that we may issue under our equity compensation plans and, as a result, they can be freely sold in the public market upon issuance and following conversion into ADSs, but subject to volume limitations applicable to affiliates under Rule 144. Additionally, the majority of ordinary shares that may be issued under our equity compensation plans also remain subject to vesting in tranches over a four year period. As of June 30, 2015, an aggregate of 5,199,615 options over our ordinary shares had vested and become exercisable. If a large number of our ADSs are sold in the public market after they become eligible for sale, the sales could reduce the trading price of our ADSs and impede our ability to raise future capital.

Future issuances of ordinary shares pursuant to our equity incentive plans could result in additional dilution of the percentage ownership of our shareholders. We filed a Registration Statement on Form S-8 on May 6, 2015 that covers an aggregate of 66,999,747 ordinary shares reserved for issuance pursuant to: (i) the Adaptimmune Therapeutics plc 2015 Share Option Scheme and the Adaptimmune Therapeutics plc Company Share Option Plan; and (ii) certain options granted by the Company in consideration for the release of equivalent options granted by Adaptimmune Limited to certain employees, directors and consultants under the Adaptimmune Limited Company Share Option Plan, the Adaptimmune Limited Share Option Scheme and the Adaptimmune Limited 2014 Share Option Scheme.

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 Securities and Exchange Commission than U.S. companies. This may limit the information available to holders of the ADSs.

We are a foreign private issuer, as defined in the Securities and Exchange Commission s, or 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 Exchange Act of 1934, as amended (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.

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For so long as we are 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 June 30 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.

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

We rely on a provision in Nasdaq s corporate governance rules that allows us to follow English corporate law and the Companies Act 2006 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: have a majority of the board of directors consist of independent directors; require non-management directors to meet on a regular basis without management present; have a quorum for shareholder meetings of not less than 331/3% of the outstanding shares of the Company s voting stock; promptly disclose any waivers of the code for directors or executive officers that should address certain specified items; and seek shareholder approval for the implementation of certain equity compensation plans and issuances of ordinary shares.

In accordance with our Nasdaq listing, our Audit Committee is required to comply with the provisions of Section 301 of the Sarbanes-Oxley Act and Rule 10A-3 of the Exchange Act, both of which are also applicable to Nasdaq-listed U.S. companies. However, because we are a foreign private issuer, 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.

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.

We are a foreign private issuer and therefore 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 December 31, 2015, 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 July 1, 2016. In order to maintain our current status as a foreign private issuer, either (a) a majority of our ordinary shares 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 may not be U.S. citizens or residents, (ii) more than 50% of our assets cannot be located in the United States and (iii) our business must be administered principally outside the United States. If we lost this status, 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. For example, the annual report on Form 10-K requires domestic issuers to disclose executive compensation information on an individual basis with specific disclosure regarding the domestic compensation philosophy, objectives, annual total compensation (base salary, bonus, equity compensation) and potential payments in connection with change in control, retirement, death or disability, while the annual report on Form 20-F permits foreign private issuers to disclose compensation information on an aggregate basis. We would also have to report our results under U.S. Generally Accepted Accounting Principles, rather than under International Financial Reporting Standards, as a domestic registrant. We would also have to mandatorily comply with U.S. federal proxy requirements, and our officers, directors and principal shareholders would become subject to the short-swing profit disclosure and recovery provisions of Section 16 of the Exchange Act.

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 costs we would incur as a foreign private issuer. As a result, we expect that a loss of foreign private issuer status would increase our legal and financial compliance costs and would make some activities highly time consuming and costly.

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We are an emerging growth company and we cannot be certain that the reduced disclosure requirements applicable to emerging growth companies will not make our ADSs less attractive to investors.

We are an emerging growth company, as defined in the Jumpstart Our Business Start-ups Act of 2012, or the JOBS Act, and have elected to take advantage of the following provisions of the JOBS Act: the exemption from the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act; a requirement of only two years of audited financial statements in addition to any required interim financial statements and correspondingly reduced disclosure in management s discussion and analysis of financial condition and results of operations; not providing all of the compensation disclosure that may be required of non-emerging growth public companies under the U.S. Dodd-Frank Wall Street Reform and Consumer Protection Act; not disclosing certain executive compensation-related items such as the correlation between executive compensation and performance and comparisons of the Chief Executive Officer s compensation to employee compensation; not complying with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor s report providing additional information about the audit and the financial statements (auditor discussion and analysis and an extended transition period to comply with new or revised accounting standards applicable to public companies). In addition, to the extent that we no longer qualify as a foreign private issuer, we have elected to take advantage of (1) reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements; and (2) exemptions from the requirements of holding a non-binding advisory vote on executive compensation including golden parachute compensation. As a result of these elections, our future financial statements may not be comparable to companies that comply with these obligations earlier and our investors may not have access to certain information they may deem important.

Our independent registered public accounting firm will not be required to provide an attestation report on the effectiveness of our internal control over financial reporting as long as we qualify as an emerging growth company, which may increase the risk that weaknesses or deficiencies in our internal control over financial reporting go undetected and may make it more difficult for investors and securities analysts to evaluate our company. We may take advantage of these reporting exemptions until we are no longer an emerging growth company. We will remain an emerging growth company until the earliest of (i) the last day of the fiscal year in which we have total annual gross revenue of $1.0 billion or more; (ii) the last day of our fiscal year following the fifth anniversary of May 6, 2015, the date our ADSs began trading; (iii) the date on which we have issued more than $1.0 billion in nonconvertible debt during the previous three years; and (iv) the date on which we are deemed to be a large accelerated filer under the rules of the SEC. 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, there may be a less active trading market for our ADSs, and the price of our ADSs may be more volatile and may decline.

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, requires that beginning with our second annual report following our IPO, management assess and report annually on the effectiveness of our internal controls over financial reporting and identify any material weaknesses in our internal controls over financial reporting. Although Section 404(b) of the Sarbanes-Oxley Act requires our independent registered public accounting firm to issue an annual report that addresses the effectiveness of our internal controls 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) of the Sarbanes-Oxley Act until such time as we are no longer an emerging growth company.

We expect our first Section 404(a) assessment will take place for our annual report for our fiscal year ending June 30, 2016. 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, we 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) of the

Sarbanes-Oxley Act. In order to maintain and improve the effectiveness of our disclosure controls and procedures and internal controls over financial reporting, we will need to expend significant resources and provide significant management oversight. Implementing any appropriate changes to our internal controls 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.

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If either we are unable to conclude that we have effective internal controls 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 controls over financial reporting as required by Section 404(b) of the Sarbanes-Oxley Act, 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 of the Sarbanes-Oxley Act, we may not be able to remain listed on Nasdaq.

We incur significant increased costs as a result of operating as a company whose ADSs are publicly traded in the United States, and our management is required to devote substantial time to new compliance initiatives.

As a company whose ADSs are publicly traded in the United States since May 6, 2015, we have incurred, and will continue to incur, significant legal, accounting, insurance and other expenses that we did not previously incur as a private company. In addition, the Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act and related rules implemented by the SEC and Nasdaq have imposed various requirements on public companies including requiring establishment and maintenance of effective disclosure and financial controls. Our management and other personnel need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased, and will continue to increase, our legal and financial compliance costs and will make some activities more time-consuming and costly. Our insurance costs have increased, particularly for directors and officers liability insurance, and we may be required to incur further substantial increased costs to maintain the same or similar coverage or be forced to accept reduced coverage in future. These laws and regulations could also make it more difficult and expensive for us to attract and retain qualified persons to serve on our board of directors, our board committees or as our executive officers. Furthermore, if we are unable to satisfy our obligations as a public company, we could be subject to delisting of the ADSs from Nasdaq, fines, sanctions and other regulatory action and potentially civil litigation.

U.S. investors may have difficulty enforcing civil liabilities against us, our directors, members of senior management and the experts named in this annual report.

Some of our directors, members of senior management and the experts named in this Annual Report are non-residents of the United States, and all or a substantial portion of 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. Mayer Brown International LLP, our English solicitors, has advised us that there is doubt as to whether English courts would enforce certain civil liabilities under U.S. securities laws in original actions or judgments of U.S. courts based upon these civil liability provisions. In addition, awards of punitive damages in actions brought in the United States or elsewhere may be unenforceable in the United Kingdom. An award for monetary damages under the U.S. securities laws would be considered punitive if it does not seek to compensate the claimant for loss or damage suffered and is intended to punish the defendant. The enforceability of any judgment in the United Kingdom will depend on the particular facts of the case as well as the laws and treaties in effect at the time. 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.

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

We are incorporated under English law. The rights of holders of ordinary shares and, therefore, certain of the rights of holders of ADSs, are governed by English law, including the provisions of the Companies Act 2006, and by our Articles of Association. These rights differ in certain respects from the rights of shareholders in typical U.S. corporations. See Item 10 B Description of Share Capital Differences in Corporate Law in this Annual Report for a description of the principal differences between the provisions of the Companies Act 2006 applicable to us and, for

example, the Delaware General Corporation Law relating to shareholders rights and protections.

Provisions in the U.K. City Code on Takeovers and Mergers may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our shareholders.

The U.K. City Code on Takeovers and Mergers, or the Takeover Code, applies, among other things, to an offer for a public company whose registered office is in the United Kingdom (or the Channel Islands or the Isle of Man) and whose securities are not admitted to trading on a regulated market in the United Kingdom (or the Channel Islands or the Isle of Man) if the company is considered by the Panel on Takeovers and Mergers, or the Takeover Panel, to have its place of central management and control in the United Kingdom (or the Channel Islands or the Isle of Man). This is known as the residency test. The test for central management and control under the Takeover Code is different from that used by the U.K. tax authorities. Under the Takeover Code, the Takeover Panel will determine whether we have our place of central management and control in the United Kingdom by looking at various factors, including the structure of our Board, the functions of the directors and where they are resident.

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If at the time of a takeover offer the Takeover Panel determines that we have our place of central management and control in the United Kingdom, we would be subject to a number of rules and restrictions, including but not limited to the following: (1) our ability to enter into deal protection arrangements with a bidder would be extremely limited;(2) we might not, without the approval of our shareholders, be able to perform certain actions that could have the effect of frustrating an offer, such as issuing shares or carrying out acquisitions or disposals; and (3) we would be obliged to provide equality of information to all bona fide competing bidders.

Item 4. Information on the Company.

A. History and Development of the Company

Adaptimmune Therapeutics plc was founded on December 3, 2014 as part of a corporate restructuring and is a public limited company incorporated under the laws of England and Wales. On May 6, 2015, we completed our IPO of American Depositary Shares, or ADSs, on the Nasdaq Global Select Market. Our ADSs are traded under the symbol ADAP.

Our U.K. subsidiary, Adaptimmune Limited, was founded in July 2008 and is focused on our research and development activities. Our U.S. subsidiary, Adaptimmune LLC, was founded in February 2011 and is focused on our clinical trials operations.

On April 1, 2015, we completed a corporate reorganization. Pursuant to this reorganization, on February 23, 2015, all shareholders of Adaptimmune Limited exchanged each of the Series A preferred shares and ordinary shares held by them for newly issued Series A preferred shares and ordinary shares of Adaptimmune Therapeutics Limited on a one-for-100 basis, resulting in Adaptimmune Limited becoming a wholly-owned subsidiary of Adaptimmune Therapeutics Limited. On March 20, 2015, all holders of options over ordinary shares of Adaptimmune Limited exchanged each of their options for equivalent options over ordinary shares of Adaptimmune Therapeutics Limited. On April 1, 2015, pursuant to the final step in our corporate reorganization, Adaptimmune Therapeutics Limited re-registered as a public limited company with the name Adaptimmune Therapeutics plc.

Immediately prior to the admission to trading of our ADSs on the Nasdaq Global Select Market, all Series A preferred shares of Adaptimmune Therapeutics plc converted to ordinary shares on a one-for-one basis.

Our registered and principal executive offices are located at 101 Park Drive, Milton Park, Abingdon, Oxfordshire OX14 4RY, United Kingdom, our general telephone number is (+44) 1235 430000 and our internet address is http://www.adaptimmune.com. Our website and the information contained on or accessible through our website are not part of this document. Our agent for service of process in the United States is Adaptimmune LLC, is located at 2 Commerce Square, Suite 1700, 2001 Market Street, Philadelphia, PA, 19103.

In the three year period ended June 30, 2015, we had invested a total of £4.0 million in equipment and facilities. After the year ended June 30, 2015, we entered into agreements for the construction, fit-out and 25 year lease of a new approximately 67,000 square foot laboratory and office facility in the United Kingdom and the construction, fit-out and 15 year lease of a new approximately 47,400 square foot manufacturing,

laboratory and office facility in the United States.

B. Business

Overview

We are a clinical-stage biopharmaceutical company focused on novel cancer immunotherapy products based on our T-cell receptor platform. We have developed a comprehensive proprietary platform that enables us to identify cancer targets in the form of peptides, which are short sequences of amino acids, find and genetically engineer T-cell receptors, or TCRs, and produce TCR therapeutic candidates for administration to patients. We engineer TCRs to increase their affinity to cancer-specific peptides, including our lead target peptides, NY-ESO-1 and MAGE-A10, in order to target and then destroy cancer cells in patients. Unlike current antibodies and therapies that are based on the use of chimeric antigen receptor T cells, or CAR-Ts, our TCR therapeutic candidates are able to target intracellular as well as extracellular cancer antigens. This capability significantly increases the breadth of targets, particularly as intracellular targets are known to be more closely associated with cancer, but are inaccessible with other autologous T-cell immunotherapy approaches. We believe this approach will lead to TCR therapeutic candidates that have the potential to significantly impact cancer treatment and clinical outcomes of patients with cancer.

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Our lead program is an affinity-enhanced TCR therapeutic targeting the NY-ESO-1, or NY-ESO, cancer antigen. This program is under option to GSK. We are conducting Phase 1/2 clinical trials in the U.S. for our NY-ESO TCR therapeutic candidate in patients with solid tumors and hematological malignancies including synovial sarcoma, multiple myeloma, melanoma and ovarian cancer. As of June 30, 2015, we had administered our NY-ESO TCR therapeutic candidate to 47 patients across several cancer indications. In both synovial sarcoma and multiple myeloma, we have seen responses and evidence of tumor reduction in patients with highly refractory cancers. In our synovial sarcoma trial, as of June 30, 2015, 12 patients had received our NY-ESO TCR therapeutic candidate. As a result of the encouraging responses seen in this initial synovial sarcoma trial, the trial has now been expanded to include an additional 20 patients. Results from the multiple myeloma trial following auto-SCT, showed a 59% complete or near complete response rate at 100 days post-administration in 22 patients with active disease at the time of transplant. The NY-ESO engineered T cells have persisted in the myeloma trial for up to six months in all but one patient and, in a subset of patients, for two years following administration. In addition, based on our clinical data to date, we believe our NY-ESO TCR therapeutic candidate has a promising benefit/risk profile. Our NY-ESO TCR therapeutic candidate is also being used in an investigator-initiated clinical trial in the United Kingdom in patients with esophageal cancer.

We expect to report further data on these trials, as well as additional trials, in 2015 and 2016. If we continue to receive further encouraging clinical data, we plan to accelerate the clinical program for our NY-ESO TCR therapeutic candidate, in partnership with GSK. We believe our NY-ESO TCR therapeutic candidate may be eligible for expedited regulatory approval pathways, including fast track, breakthrough therapy and accelerated approval.

Our IND for our second program, a TCR therapeutic candidate directed at MAGE-A10,was accepted by the FDA in June 2015. This program is not partnered with GSK. The IND is now open and is directed at patients with Stage IIIb or Stage IV non-small cell lung cancer (NSCLC). The initial clinical program will be an open label Phase 1/2 dose escalating study of our MAGE-A10 TCR therapeutic candidate in patients with advanced NSCLC and will assess safety and tolerability of our therapeutic candidate in those patients.

We have a number of other programs outside of the GSK collaboration. Specifically, we plan to submit an Investigational New Drug Application, or IND, for our TCR therapeutic candidate directed at Alpha Fetoprotein, or AFP, during 2016. In addition to this program, we expect to leverage our TCR technology platform to continue to build our pipeline of proprietary TCR therapeutic candidates. We have identified over 30 intracellular target peptides that are preferentially expressed in cancer cells and have ongoing unpartnered research programs on twelve of these. We believe these twelve unpartnered research programs are relevant to a wide range of cancer indications. We also have ongoing early stage research programs relevant to autoimmune indications.

Our expertise and leadership in the field of TCRs is underscored by the large pipeline of TCRs we have identified and validated and by the promising early data with our NY-ESO TCR therapeutic candidate in both solid tumors and hematological malignancies. The following table summarizes our most advanced TCR therapeutic candidates:

(1) GSK retains an exclusive option to license NY-ESO TCR for all indications.

(2) Investigators carrying out study have voluntarily suspended patient recruitment pending investigation of a patient death occurring 46 days after T-cell infusion.

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We retain full ownership of our current preclinical pipeline of engineered TCR therapeutic candidates, including our MAGE-A10 and AFP TCR therapeutic candidates together with twelve additional unpartnered research programs.

Cancer is a leading cause of death worldwide and is characterized by the uncontrolled growth of abnormal cells whose ability to evade the immune system s surveillance is a key factor in their proliferation and persistence. Despite advances made in the treatments available to cancer patients, there continues to be a high unmet need for additional products and treatments, especially for patients with recurrent tumors or cancer types that are resistant to current therapeutic alternatives. Immunotherapy is a form of cancer treatment that uses a patient s own immune system to combat cancer and is one of the most actively pursued areas of research by biotechnology and pharmaceutical companies today. Interest in immunotherapy is largely driven by recent compelling efficacy data in cancers with historically bleak outcomes and by the potential to achieve a cure or functional cure for some patients. We believe that immunotherapy has the potential to become the primary cancer treatment for recurrent tumors or cancer types that are resistant to current therapeutic alternatives.

While the field of immunotherapy in cancer has now achieved proof of concept and yielded significant durable responses in multiple tumor types, there remain major tumor types (e.g., colon, pancreatic and prostate) as well as patient groups within responsive tumors (e.g., subsets of patients with melanoma and lung, renal and ovarian cancers) that do not respond to current immunotherapy approaches. One theory to explain this non-responsiveness is that certain tumors require direct immune stimulation. The CAR-T technologies seek to deliver activated T cells towards malignancies to initiate an immune response. The primary challenges in the field have been to achieve an acceptable efficacy and safety profile, or therapeutic index and successfully to target solid tumors. As such, the major successes in CAR-T technologies have primarily been in hematological malignancies. Our research efforts are focused entirely on targeting tumors in ways that may result in an improved therapeutic index and have potential applications in solid tumors as well as hematological malignancies. We believe our TCR technology, in contrast to that of CAR-T, allows for more specificity in targeting tumors versus healthy tissue through the ability to target intracellular peptides. In addition, we have invested heavily in an extensive preclinical safety testing program that is designed to minimize any off-target cross-reactivity of our TCR therapeutic candidates.

The immune system plays an important role in targeting and destroying cancer cells. Specifically, T cells, which are a type of white blood cell, and their receptors create a natural system that is designed to scan the body for diseased cells. In general, cells process proteins internally and then convert these proteins into peptide fragments which are then presented on the cell surface by a protein complex called the Human Leukocyte Antigen, or HLA. TCRs naturally scan these peptide fragments to search for abnormalities. Binding of naturally occurring TCRs to cancer targets, however, tends to be very poor because cancer proteins appear very similar to naturally occurring proteins on healthy cells and TCRs that recognize what the body sees as self-proteins are eliminated during early human development.

We engineer naturally occurring TCRs and enhance their ability to target and bind to cancer peptides thereby enabling a highly targeted immunotherapy. Our proprietary technology platform includes the identification of target peptides, successful engineering of affinity-enhanced TCRs, preclinical safety testing and optimized manufacturing processes suitable for producing engineered TCR therapeutic candidates for use in clinical trials and commercialization. Engineering TCRs requires balancing the need for higher affinity to the target peptide with the risk of cross-reactivity, which increases at higher affinities. We believe this is one of our core competitive advantages given our ability to overcome the challenging nature of this process and develop affinity-enhanced TCRs.

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Once we identify a specific cancer target, we create an engineered affinity-enhanced TCR, which then undergoes extensive preclinical safety testing before administration to patients. The process for treating a patient with an engineered TCR therapeutic candidate involves extracting the patient s T cells and then combining the extracted cells with our delivery system containing the gene for our affinity-enhanced TCR, through a process known as transduction. Our delivery system uses a type of virus known as lentivirus to transduce the patient s T cells and is referred to as a lentiviral vector. The transduced T cells are then expanded and infused into the patient. When these T cells encounter an HLA-peptide complex, they multiply and initiate the destruction of the targeted cancer cells.

Our NY-ESO TCR therapeutic candidate represents the culmination of years of engineering and preclinical research and, to date, we have produced encouraging clinical data in synovial sarcoma and multiple myeloma. We have also utilized our proprietary TCR technology platform to develop a pipeline of TCR therapeutic candidates that we believe may be effective in a variety of cancer types that are unresponsive to currently available and experimental therapies.

Under our collaboration and license agreement with GSK, GSK funds the development of, and has an option to obtain an exclusive license to, our NY-ESO TCR therapeutic candidate. In addition, GSK has the right to nominate four additional target peptides. The first of these additional targets will be selected from a pool of three targets, with the pool having already been jointly chosen by GSK and us. Following completion of initial research on these three targets, GSK is entitled to nominate one TCR therapeutic candidate. In addition, three other targets may be selected by GSK in the future. These targets are outside of our twelve unpartnered research programs and any other programs relating to targets where Adaptimmune initiates development of a TCR therapeutic candidate. We retain full ownership of our current pipeline of engineered TCR therapeutic candidates other than our NY-ESO TCR therapeutic candidate, including the MAGE-A10 and AFP TCR therapeutic candidates together with TCR therapeutic candidates in twelve additional unpartnered research programs.

We have a strong portfolio of patents covering the engineering of TCRs and composition of matter of our lead therapeutic candidates, our proprietary TCR technology platform and certain aspects of our manufacturing processes.

Our Strengths

- **Our lead program has provided preliminary evidence of clinical responses in hematological malignancies and solid tumors that have historically been hard to treat.** We are conducting ongoing clinical trials for our NY-ESO TCR therapeutic candidate. As of June 30, 2015, we had seen one complete response and four confirmed partial responses out of 11 evaluable patients in our synovial sarcoma trial and a 59% complete and near complete response rate in 22 evaluable patients in our multiple myeloma trial in conjunction with auto-SCT, assessed at 100 days. In addition, based on our clinical data to date, we believe our NY-ESO TCR therapeutic candidate has a promising tolerability profile.

- **We have developed a comprehensive proprietary technology platform centered on the development of TCR therapeutic candidates and associated process and manufacturing capabilities.** Our proprietary technology platform covers identification of target peptides, successful identification and engineering of affinity-enhanced TCRs, preclinical safety testing and optimized manufacturing processes suitable for producing engineered TCR therapeutic candidates for use in clinical trials and commercialization. We believe our technology platform, which has been

developed over a decade, will enable development of additional TCR therapeutic candidates targeting cancers that have previously been difficult to treat.

- **We have identified a large and growing pool of cancer targets for which we can develop additional TCR therapeutic candidates.** We have identified over 30 intracellular target peptides that are preferentially expressed in cancer cells and have ongoing unpartnered research programs on twelve of these. Because our technology relies upon the body s natural system of processing intracellular proteins and most cancer peptides are located intracellularly, the number of peptides that we can target with our engineered TCR therapeutic candidates is potentially large. Our approach contrasts with CAR-T technologies which use antibody binding recognition systems to artificially activate T cells and can only bind to whole surface proteins expressed on the targeted cell. While our TCR therapeutic candidates are initially suitable for patients with HLA A2, we believe our platform will be applicable to multiple HLA types, enabling broad coverage of the HLA types that make up the majority of the patient population.

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- **We have a strong and growing intellectual property portfolio to protect our products and proprietary platform.** We have a strong intellectual property portfolio covering the target identification, affinity enhancement and comprehensive preclinical testing processes as well as composition of matter claims over our engineered TCR therapeutic candidates.

- **Our strategic alliance with GSK provides additional support in product development and regulatory experience.** We believe our strategic partner, GSK, provides experience in manufacturing, biologic development and regulatory planning and quality systems. Further, we expect to use knowledge gained from our NY-ESO TCR therapeutic candidate program to improve the development pathways for our unpartnered TCR therapeutic candidate programs.

- **We have a highly knowledgeable and experienced management team with extensive industry experience and expertise in the United States and in Europe.** Our senior management, which has substantial experience in the biopharmaceutical industry, includes our CEO, James Noble, who has 24 years of experience serving on the boards of public and private companies in the biotechnology sector from Europe and the United States, including seven years as our founding CEO and a further six years as the founding CEO of Avidex Ltd, our predecessor company. Our Chief Operating Officer, Dr. Helen Tayton-Martin, has 23 years of experience in the pharmaceutical, biotechnology and consulting industries in disciplines including preclinical and clinical development, outsourcing, strategic planning, due diligence and business development. Our Chief Medical Officer, Dr. Rafael Amado, has 12 years of experience within the biotech and pharmaceutical industries, including serving in senior oncology R&D positions with GSK, where he led the development of a pipeline of products in novel areas of cancer biology. Our Chief Financial Officer, Mr. Adrian Rawcliffe, has 17 years of experience within the pharmaceutical industry, including senior roles with GSK with responsibility for business development and finance activities for GSK s Pharmaceuticals R&D business. Our Executive Vice-President of Translational Sciences, Dr. Gwendolyn Binder-Scholl, has 14 years of industry and academic experience in cellular and gene therapy translational research and drug development.

Our Business Strategy

Our strategic objective is to build a global oncology business with an extensive portfolio of engineered TCR therapeutic candidates that have the potential to significantly impact the clinical outcomes of patients with cancer. In order to achieve our objective, we are focused on the following strategies:

Rapidly advance our NY-ESO TCR therapeutic candidate into registrational trials. We are collaborating with GSK to advance our NY-ESO TCR therapeutic candidate and expand and accelerate our clinical trials into additional sites, both in the United States and in Europe. We believe data from these trials, if positive, may enable us to go directly into one or more registrational or pivotal clinical trials. We are currently conducting Phase 1/2 clinical trials in the United States in multiple cancer types including synovial sarcoma, multiple myeloma, melanoma and ovarian cancer and expect to

commence an additional clinical trial for non-small cell lung cancer in 2015.

Advance our MAGE-A10, AFP and other therapeutic candidates through clinical development. We retain full development and commercialization rights to our MAGE-A10 and AFP therapeutic candidates. The IND for our MAGE-A10 therapeutic candidate was accepted by the FDA in June 2015 and we currently plan to file an IND for our AFP therapeutic candidate in 2016. We believe that our MAGE-A10 TCR therapeutic candidate has the potential to be effective in several solid tumors, including lung cancer. Currently, we do not intend to partner our MAGE-A10 or AFP TCR therapeutic candidates or our other preclinical TCR therapeutic candidates.

Advance further TCR therapeutic candidates from our unpartnered portfolio to the product development stage. We currently have twelve active unpartnered research programs on potential TCR therapeutic candidates. We intend to advance these research programs into preclinical and clinical development as soon as practicable.

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Leverage our TCR technology platform by continuing to identify cancer targets that are not accessible by current antibody and CAR-T approaches. We intend to continue to generate our TCR therapeutic candidates from our fully integrated technology platform, which enables the systematic identification and validation of suitable target peptides, T-cell cloning, engineering of TCRs and comprehensive preclinical testing processes.

Continue to improve potency and durability of response to our TCR therapeutic candidates. We intend to continue further developing our TCR therapeutic candidates by improving potency and durability and also exploring the addition of other components in our lentiviral vector, which would be expressed in the TCR therapeutic candidate alongside the engineered TCR.

Optimize and expand our process development and manufacturing capabilities to maintain our leadership position in the TCR space. We plan to optimize the manufacture, supply, associated analytical expertise and quality systems for our TCR therapeutic candidates to ensure that our manufacturing capability is sufficient for later stage clinical trials and commercial supply.

Leverage our existing strategic alliance with GSK. We expect to capitalize on GSK s drug development and regulatory expertise and commercial capabilities to bring our partnered therapeutic products to market. We expect to apply knowledge gained from our NY-ESO TCR therapeutic candidate collaboration program with GSK to the development and commercialization of other TCR therapeutic candidates in our pipeline.

Expand our intellectual property portfolio. We intend to continue building on our technology platform, comprised of intellectual property, proprietary methods and know-how in the field of TCRs. These assets form the foundation for our ability to not only strengthen our product pipeline, but also to defend and expand our position as a leader in the field of TCRs.

Background on TCRs

There are two modes of action by which the body s natural immune system targets diseased cells. The first uses an antibody recognition system, which targets whole proteins on the cell surface. The other is through TCRs that target the HLA peptide complex. The HLA peptide complex derives from intracellular target proteins that are broken down into short peptide fragments, which are captured by the HLA for presentation on the cell surface. TCRs target and bind to a specific HLA peptide complex, as shown in the illustration below, resulting in the destruction of those targeted cells. The target peptides that are presented by the HLA peptide complex include the whole array of proteins expressed by a cell, not just transmembrane or cell-surface proteins. The majority of cancer targets are located inside the cell.

For our initial NY-ESO TCR therapeutic candidate, we are targeting HLA A-2, which is found in approximately 50% of the U.S. Caucasian population and is one of the most common HLA types globally. Among patients with a specific HLA type, the same peptide is presented consistently, which means that any engineered TCR therapeutic candidate targeting that peptide will be able to target the same peptide presented in nearly all patients of that HLA type. The MAGE-A10 and AFP TCR therapeutic candidates also target HLA A-2. We are also working on programs for TCR therapeutic candidates that target the other most common HLA types.

Limitations of Natural Affinity TCRs and the Importance of Engineering

Binding of naturally occurring TCRs to any presented cancer peptides can be very poor for three reasons:

- Very few TCRs are capable of recognizing cancer-specific target peptides because cancer proteins (and the target peptides presented on HLA from cancer cells) appear very similar to naturally occurring proteins and any related high-affinity TCRs are eliminated early in human development.

- Cancer cells reduce the HLA presentation such that the TCR can no longer naturally recognize the target as a cancer cell.

- The body has no capacity to enhance the affinity of a TCR to the cancer HLA peptide complex, unlike antibodies where affinity maturation occurs in response to exposure to the disease protein.

This means that the natural immune system is unable to recognize and respond to most cancer cells and, even if it does respond, the response is typically very poor.

Our Engineered TCR Therapeutic Candidates

Our engineered TCR therapeutic candidates usually start with naturally occurring TCRs, which we then enhance in order to increase their ability to recognize and bind to cancer target peptides presented by the HLA peptide complex. We believe this has the potential to result in a targeted and effective treatment.

The TCRs consist of two associated protein chains: the alpha ( ) and beta ( ) chains. Each of the chains has two regions: a variable region and a constant region. The constant region sits next to the T-cell membrane and the variable region of the two chains binds to the target peptides. The variable region of each TCR chain has three hyper-variable complementarity determining regions, or CDRs. Our technology modifies these CDRs in order to enhance affinity to the cancer cell s HLA peptide complex.

By genetically engineering the TCR sequence, we produce an enhanced TCR with increased affinity for the cancer target peptides. This process improves the ability of the engineered T cell to recognize cancer targets that are present at very low levels and subsequently activate the immune system. It is not known a priori what affinity will be required for each TCR to be effective. We therefore produce libraries of affinity-enhanced TCRs from which we select a panel, which we test for potency and potential for cross-reactivity, or binding to non-cancerous cells. The effect of enhancing TCR affinity can be shown in the chart below:

We then select the TCR that we believe will allow us to develop the most effective TCR therapeutic candidate, which we test for ability to destroy cancer cells (potency) and ability to leave non-cancerous cells intact (minimal cross-reactivity).

The two circles above show results from tests designed to see whether a T cell is activated in the presence of a cancer cell. Activation is shown in this test by the presence of dark spots. The circle on the left shows that a natural affinity T-cell receptor does not recognize the cancer cells and is therefore not activated. The circle on the right shows that a higher affinity T-cell receptor does recognize the same cancer cells and is therefore activated to destroy them.

Differences between TCRs and CAR-Ts

Current alternative T-cell therapies in development utilize CAR-T technologies to modify T cells for therapeutic effect. T cells do not naturally express anything that would normally recognize a whole protein. CAR-Ts attach an antibody fragment to a T cell to recognize a whole surface protein expressed on the target cell, a recognition system that does not occur naturally. Therefore, this antibody fragment must be artificially linked to a number of signaling domain proteins within the T cell designed to activate the T cell once the antibody recognition fragment binds to a protein on the target cell. Although not HLA-restricted in the same way as our TCR therapies, use of CAR-Ts is limited by the relatively small number of identified cancer targets expressed on the cell surface and which can be bound by the CAR-T technology.

The following illustration shows the different targets being addressed by typical CAR-T cells and our engineered TCR therapeutic candidates.

The main differences between our TCR therapeutic candidates and CAR-T therapies are as follows:

Nature of Recognition System. Our engineered TCRs enhance the affinity of the natural TCR system using the cell s own internal signaling machinery, which means that there is no need to change the T cell in other ways. In contrast, the CAR-T technology adds an antibody recognition system to a T cell, creating a construct that is not seen in nature. CAR-T technology, therefore, has to alter the intracellular machinery in order to activate the T cell.

Greater Number of Targets. TCRs recognize peptide fragments from proteins present within the cell and expressed on the cell s surface, whereas CAR-Ts can only recognize whole proteins expressed on the cell s surface. TCRs are capable of targeting a greater number of proteins and may be able to more selectively target cancer cells and target a broader array of tumor types.

Expression on Healthy Tissue. To date, the identified targets of CAR-T technologies are not only more limited in number, but also expressed on healthy tissue. Our TCR therapies are selected against targets which are either not generally expressed on healthy tissue or expressed only in certain patient sub-populations or at minimal levels.

HLA Restriction. TCRs recognize proteins that are presented to the immune system as a peptide bound to an HLA type, and are therefore limited to a certain HLA type. HLA types vary across the human population, but we are targeting HLA A2, which is found in approximately 50% of the U.S. Caucasian population and is one of the most common HLA types globally. Unlike TCRs, CAR-Ts are capable of recognizing the target protein on the cell surface regardless of HLA type.

By choosing the target peptides that our engineered TCR therapeutic candidates recognize, our therapeutics can potentially be directed to cancers that are currently untreatable or have poor clinical outcomes. Our engineered TCR therapeutic candidates recognize specific cancer targets that may be present on several different tumor types, including solid tumors. The expression of these cancer targets may also be associated with higher-grade and/or late-stage tumors, which are generally associated with a poor prognosis.

Our Technology Platform

Our current engineered TCR therapeutic candidates are dependent on our integrated and proprietary technology platform that has been developed over more than 10 years.

Target Peptide Identification

We have identified and validated over 30 intracellular target cancer peptides. Our proprietary identification system provides target peptides suitable for commencing a TCR therapeutic candidate program. We believe our twelve target peptides that have been prioritized for engineered TCR therapeutic candidate development all have very low levels of cross-reactivity to non-cancerous cells and therefore are well suited for development.

Validation and identification of potential targets requires (a) analysis of presentation of the relevant target peptides in cancer cells; (b) analysis of presentation of the relevant target peptide in healthy tissue for prediction of cross-reactivity; and (c) validation of presentation on the cancer cell surface.

Identification and Generation of an Engineered TCR Therapeutic Candidate

Once the target peptide has been identified and validated, we can generate an engineered TCR therapeutic candidate through isolation of the natural TCRs followed by genetic engineering. Our internal process is reliant on the following factors:

- Our ability to identify and quickly develop engineered TCR therapeutic candidates through a proprietary process enabling rapid identification and cloning of TCRs and hence progression to engineered TCRs capable of binding to any selected target peptide.

- Our ability to make stable, soluble TCRs to enable measurement and analysis of engineered TCR proteins and resulting identification of engineered TCRs required for target peptide binding. This requires the use of our proprietary di-sulfide bond methodology.

- Our ability to utilize a proprietary phage display system for TCRs. Phage display is a technique widely used in antibody research to enhance affinity of monoclonal antibodies for therapy. In our experience, antibody phage display systems do not work with TCRs. We have therefore developed and use a proprietary phage display approach that enables isolation of engineered TCRs and, as a result, we are able to select engineered TCRs from a large, diversified library.

Preclinical Testing

We have developed a proprietary preclinical screening program that seeks to minimize any potential off-target binding or cross-reactivity and thereby aims to improve the safety profile of our products. All engineered TCR therapeutic candidates will be subjected to this rigorous preclinical screening program. We developed and optimized this program as a result of off-target cross-reactivity in one of our previous TCR therapeutic candidates, MAGE-A3, in which cross-reactivity is believed to have caused two deaths in clinical programs. The preclinical screening program seeks to identify the amino acids to which the engineered TCR therapeutic candidate will bind within any target peptide, thereby identifying those amino acids that are important for TCR recognition of any target peptide. That information can then be deployed to identify other off-target sequences within the human body that could also be bound.

Our preclinical screening program identifies potential cross-reactivity including binding to peptides presented on other HLA types (allo-reactivity), platelet activation and reactivity in different cell systems (e.g., cardiomyocytes, hepatocytes, endothelial cells, astrocytes and neurons). Our preclinical screening program is split into three main stages: molecular analysis, human cell testing and potency/efficacy testing.

- *Molecular analysis* uses a variety of techniques to systematically identify peptides within the human body that are similar to the target peptide and which therefore might be bound by the affinity-enhanced engineered TCR. The testing is intended to identify any potential cross-reactivity. Within the affinity-enhanced TCR the amino acids which are important for binding to a peptide are identified by substitution of the relevant amino acids. Based on identification of those binding amino acids, variations of the target peptide which are also capable of being bound by the engineered TCR are then identified. Theoretical cross-reactivity against peptides within the human body which have any of the amino acid sequences capable of being bound by the affinity-enhanced engineered TCR can then be identified and investigated to see if such peptides are actually presented on cells and whether they can be bound by the affinity-enhanced engineered TCR.

- *Human cell testing* is used to assess whether the affinity-enhanced engineered TCR binds to samples of normal cells and whole blood samples.

- *Potency/efficacy testing* is used to assess the potency and efficacy of the affinity-enhanced engineered TCR.

Delivery of TCR Therapeutic Candidates to Patients

Patients eligible for clinical trials with our engineered TCR therapeutic candidates have a portion of their white blood cells collected using a process called leukapheresis, a procedure in which a patient s blood is extracted and the white blood cells are separated from the remaining fractions. The extracted white blood cells are transferred to a U.S. central manufacturing facility operated by a contract development and manufacturing organization (currently Progenitor Cell Therapy LLC) for manufacturing of the TCR therapeutic candidate that we administer to the patient. CD4 and CD8 T cells are isolated from the white blood cells and mixed with our lentiviral vector to transduce the T cells with the genes encoding the affinity-enhanced TCRs and also with the artificial peptide presenting cell microbeads (antibody-bound magnetic Dynabeads® CD3/CD28) to expand the T cells. The transduced T cells are then expanded for nine to 12 days, and

concentrated and frozen to permit release testing. Cell product can be stored long term until the patient is ready to receive the infusion, although typically patients receive the cell product within 21 to 28 days after their leukapheresis.

We use a lentiviral vector to transfer the modified genes for the affinity-enhanced TCR into patient T cells. The lentiviral vector is referred to as a self-inactivating vector derived from HIV-1 and was chosen because it has an enhanced biosafety profile and produces stable modified cells. The vector includes the transgene required for production of engineered TCRs and also three packaging plasmids. We continue to make a number of enhancements to the vector and cell processing as we further develop our TCR therapeutic candidates.

All of our current engineered TCR therapeutic candidates in clinical trials utilize an initial lympho-depletion chemotherapy conditioning step to activate proliferation and enhance the effectiveness of our TCR therapeutic candidate.

The diagram below illustrates the process by which our TCR therapeutic candidates are prepared and administered to patients.

Next Generation Technology Platform Development

Manufacturing

In parallel with our ongoing clinical programs and underlying target peptide identification work, we are aiming to optimize the processes for our lentiviral vector and engineered TCR therapeutic candidate manufacturing processes to produce a version 1.5 process for each. Our goal is to achieve a more consistent and efficient manufacturing process and therefore reduce the cost of supply.

We intend to make a number of changes to our current manufacturing process. Our current version 1.0 manufacturing process is manually intensive, and we are now streamlining some of these manual steps by simplifying the process to select the initial T cells. We are also introducing cryopreservation steps which make the logistics of administering our TCR therapeutic candidates more flexible for patients and will also enable us to treat patients outside the United States. Finally, we are changing the growth medium that we use in the later parts of the process to a standard growth medium which prevents the need to make media specific for the process.

In addition to development of the version 1.5 processes, we are working towards automation of manufacture to produce a version 2.0 process and we intend to bring these activities in-house. We are also working with third-party contractors to develop companion diagnostics for screening of patient tumors for the presence of target peptides for use with our TCR therapeutic candidates.

Generation 2 Therapeutics

We believe that there is also further room to enhance the potency and durability of our TCR therapeutic candidates, for instance by adding further active proteins into the lentiviral delivery system. These enhancements are designed to result in generation 2 engineered TCR therapeutic candidates for future clinical programs.

Our TCR Therapeutic Candidates

NY-ESO TCR Therapeutic Candidate

The following table summarizes the indications for our NY-ESO TCR therapeutic candidate:

(1) GSK retains an exclusive option to license NY-ESO TCR for all indications.

(2) Investigators carrying out study have voluntarily suspended patient recruitment pending investigation of a patient death occurring 46 days after T-cell infusion.

Our first engineered TCR therapeutic candidate, our NY-ESO TCR therapeutic candidate, targets the NY-ESO-1 target peptide. In-house testing to assess the presence of this target peptide across cancer types suggests that this therapy has utility for treating synovial sarcoma, multiple myeloma, melanoma, ovarian and esophageal cancers. Phase 1/2 trials are ongoing in these indications.

We currently sponsor all of our U.S. clinical trials. We submitted our IND for our NY-ESO TCR therapeutic candidate in December 2010, and clinical trials are running at nine clinical trial sites across the United States, including the National Cancer Institute, University of Pennsylvania, University of Maryland, The Children s Hospital of Philadelphia and Memorial Sloan Kettering Cancer Center. There is also one investigator-initiated trial in the United Kingdom using our NY-ESO TCR therapeutic candidate in patients with esophageal cancer.

Our NY-ESO TCR therapeutic candidate has generally been well tolerated in our U.S. clinical trials with approximately 20% of patients suffering adverse events of grade 3 or above. Adverse events that have been reported in these trials in more than 15% of patients and considered at least possibly related to our NY-ESO TCR therapeutic candidate include diarrhea, rash, fever, fatigue, disturbed liver function tests, low neutrophil or lymphocyte count, nausea and anemia. Several events in our U.S. clinical trials have been classified as serious adverse events. Related serious adverse events seen in our sponsored clinical programs and occurring in more than one patient include neutropenia, pyrexia, Cytokine-Release Syndrome, Graft Versus Host Disease (GVHD) and dehydration. GVHD impacting the skin and gastrointestinal tract, has only been reported in our myeloma transplant study involving auto-SCT. To date, in our sponsored trials, we have also seen a suspected unexpected serious adverse reaction of grade 4 supraventricular tachycardia, or SVT, in one patient and grade 4 respiratory failure and grade 4

febrile neutropenia in a second patient.

Synovial Sarcoma Trial

Synovial sarcoma, a cancer of the connective tissue, accounts for approximately 6% to 10% of all soft tissue sarcomas. Approximately one third of synovial sarcomas occur in childhood and the peak incidence is in the third decade of life, with 70% of sarcomas occurring in patients younger than 40 years old. The majority of patients who develop metastatic soft tissue sarcomas are currently incurable, with 75% to 80% of patients not surviving past two to three years. First line therapy typically involves radiotherapy and chemotherapy, as well as surgical resection where possible. There are limited additional treatment options for unresectable, recurrent and metastatic synovial sarcoma, which is nearly always fatal, and systemic therapy is mainly used to provide palliation and slow disease progression. In 2012, the FDA granted approval for marketing of pazopanib hydrochloride (marketed as Votrient) for treatment of soft tissue sarcoma in patients who had received prior chemotherapy. Based on Votrient s prescribing information, progression-free survival time for patients with synovial sarcoma receiving pazopanib was 4.1 months (0.9 months on placebo), and in 246 patients with all types of soft tissue sarcomas, there were 11(4%) partial responses but no complete responses.

We are currently conducting a Phase 1/2 open-label clinical trial of our NY-ESO TCR therapeutic candidate in patients with synovial sarcoma. The target peptide to which our NY-ESO TCR therapeutic candidate is directed is believed to be present in 60-70% of synovial sarcoma patients. Patients in this trial all had unresectable, metastatic or recurrent synovial sarcomas with low life expectancy. We are investigating the primary efficacy response using RECIST (Response Evaluating Criteria in Solid Tumors) 1.1 criteria:

- ***Complete Response (CR)***: Disappearance of all target and non-target lesions.

- ***Partial Response (PR)***: At least a 30% decrease in the sum of the diameters of target lesions, taking as reference the baseline sum diameters, without the appearance of new, and/or unequivocal progression of existing, non-target lesions.

- ***Stable Disease (SD)***: Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for Progressive Disease (PD).

As of June 30, 2015, a total of 12 patients had been infused with our NY-ESO TCR therapeutic candidate. Of the first 11 patients, five have responded with the best overall response described in the table below. The one CR remained between month three and up to month nine before small lesions reappeared and the patient relapsed. Four patients have had a confirmed partial response continuing for over three months.

Patient	NY-ESO Staining(1) (archival tissue)	Best Overall Response	Period over which Best Overall Response seen
200	2-3+ >50%	**SD**	1 month
201	3+ 100%	**CR**	9 months
202	3+ 30%	**PR**	9 months
204	2-3+ 50%	**PR**	6 months
205	3+ ~100%	**PR**	4 months
261	3+ >99%	**SD**	1 month
206	2+ >50%	**SD**	1 month
207	3+ >80%	**SD**	1 month
208	3+ >95%	**PR**	6 months (2)
263	3+ >50%	**PD**	1 month(3)
230	2-3+ 100%	**SD**	2 months
209	Pending	**Pending**	

(1) Staining describes the degree of NY-ESO present in each patient s tumor (3+ is the highest).

(2) PR ongoing

(3) Previously recorded as a PR at 1 month by investigator.

The clinical course of the patient with a CR is illustrated below. In the first row, prior to treatment with our NY-ESO TCR therapeutic candidate (referred to below as Baseline), the patient scans show several measurable and multiple other lesions throughout the lungs. In the second row (referred to below as Day +2) and reflecting the position two days after administration of our TCR therapeutic candidate, the lesions appear worse owing to inflammation caused by T-cell activity. In the final row 101 days after administration of our TCR therapeutic candidate (referred to below as Day 101), the lesions have disappeared from the patient scans.

Source: Melinda Merchant, M.D., Ph.D. CTOS, Berlin, October 2014

The clinical course of one of the patients with a partial response is illustrated below. In the first picture prior to treatment with our NY-ESO TCR therapeutic candidate, there is a large, un-resectable lesion behind the knee. In the second picture, at one month after administration of our TCR therapeutic candidate, there is a noticeable reduction in the size of the lesion. By the third picture, at two months after administration of our TCR therapeutic candidate, there was an approximately 70% reduction in lesion size. The lesion could then be resected.

Source: Melinda Merchant, M.D., Ph.D. CTOS, Berlin, October 2014

As of February 28, 2015, of the first 10 patients, four patients were diagnosed with grade 1 to 3 Cytokine-Release Syndrome, which resolved with supportive therapy and none required steroid treatment. To date we have reported three suspected unexpected serious adverse reactions. The first of these related to a grade 4 SVT. The patient had a lesion in the chest close to the heart and had had an episode of SVT, prior to administration of our NY-ESO TCR therapeutic candidate. Following administration, the patient had two further episodes of SVT, which resolved with treatment. These SVT episodes were thought possibly related to our TCR therapeutic candidate causing inflammation of the chest lesion and consequent irritation of the right atrium provoking the SVT. A further patient experienced grade 4 respiratory failure and grade 4 febrile neutropenia which was considered possibly related to the T cell therapy. The chart below lists all serious adverse events of grade 3 or above that were thought possibly related to our TCR therapeutic candidate and were observed in patients during the trial and through June 30, 2015 by the principal investigator in the trial.

Patient ID	Diagnosis by PI	Outcome	Relationship
261	Cytokine-Release Syndrome	Recovered	Definite
208	Supraventricular tachycardia	Recovered	Possible
208	Enterocolitis	Recovered	Possible
263	Skin rash	Recovered	Possible

Based on the positive responses to date and acceptable toxicity, we have extended the trial to include an additional 20 patients in U.S. sites, in two additional cohorts. In the prior cohort, patients whose tumor expressed the NY-ESO cancer antigen at high levels received a single course of cyclophosphamide and fludarabine for lymphodepletion prior to administration of our NY-ESO TCR therapeutic. In the next cohort of 10 patients, patients with lower expression levels of the NY-ESO cancer antigen will be treated using the same treatment regimen. Cohort 3 will enroll patients whose tumor expresses high levels of the NY-ESO cancer antigen but the treatment regimen will not include the use of fludarabine. These cohorts are designed to standardize the optimal cell dose, determine the optimal level of the NY-ESO target peptide on screening and the regimen of chemotherapy given to patients before administration of our NY-ESO TCR therapeutic candidate. The first patient in these additional cohorts was infused with our NY-ESO TCR therapy in August 2015.

Multiple Myeloma Trials (Transplant and Non-transplant)

Multiple myeloma is a cancer that forms in a type of white blood cell (plasma cells) and is characterized by the proliferation of those plasma cells within bone marrow. Its prevalence in the United States is reported to be approximately 77,600 cases with approximately 24,000 new cases in 2014. Average five-year survival rates are estimated to be less than 45% with survival rates depending on factors such as age, stage of diagnosis and suitability for auto-SCT, which is used as part of the treatment for eligible patients with multiple myeloma. Despite recent therapeutic advances, multiple myeloma remains a treatable but incurable cancer. Patients are typically treated with repeat rounds of combination therapy with the time intervals to relapse becoming shorter with each successive line of therapy. The majority of patients eventually have a relapse which cannot be further treated. At this late stage, median survival is only six to nine months and treatment is primarily palliative to reduce symptoms and manage quality of life.

We have conducted a Phase 1/2, open-label, two-site clinical trial in 25 multiple myeloma patients who were eligible for an auto-SCT. This Phase 1/2 clinical trial was open to patients with high risk or relapsed multiple myeloma, who have few remaining treatment options and low life expectancy. Prior to enrollment in the clinical trial, patients had received on average three prior therapies and the trial included six patients that had a prior auto-SCT. Sixty percent of tumors contained cytogenetic abnormalities that represent negative prognostic indicators.

We assessed disease response in accordance with the International Uniform Response Criteria for myeloma assessment and the additional criteria of nCR which was consistent with the methods employed by the Bone Marrow Transplantation Clinical Trials Network where:

- ***Complete Response (CR)*** means negative immunofixation detection of serum and urine monoclonal, or M-protein, disappearance of any soft tissue plasmacytomas, and less than 5% plasma cells in bone marrow. M-protein is a characteristic feature of multiple myeloma as it is produced by malignant plasma cells, or myeloma cells.

- ***Near Complete Response (nCR)*** means disease that is detected by positive immunofixation, less than 5% plasma cells in the marrow, and no increase in size or number of lytic bone lesions.

Interim results from our Phase 1/2 clinical trial in multiple myeloma patients were reported in Nature Medicine, published on July 20, 2015. The summary report indicated encouraging responses in a high risk myeloma population. Our NY-ESO TCR therapeutic candidate was administered to patients four days after a high dose of melphalan, which is a standard chemotherapeutic agent used prior to auto-SCT, and two days following auto-SCT. The protocol requires that patients are evaluated at six weeks and at three and six months post infusion. The majority of adverse events were related to the high dose of melphalan. Possibly related Serious Adverse Events, or SAEs, reported at that time were neutropenia, thrombocytopenia and GI and metabolic disorders, including diarrhea, colitis, hyponatremia and hypomagnesemia.

To date, 25 patients have been infused and have undergone response assessment at day 100. Response rates continue to be encouraging in patients with active disease at the time of transplant, with a 59% CR/nCR (13 of 22 evaluable patients to have undergone response assessment at day 100) as compared to 24-38% CR/nCR rates at 100 days in other studies treating myeloma with stem cell transplants alone and with stem cell transplants with bortezomib, respectively, as shown in the figure below:

Clinical Responses to NY-ESO T cells at Day 100 in auto-SCT vs. Historical Data

Source: Comparison Meta-Analysis: Sonneveld et al, JCO September 2013

The table below illustrates total response shown in the 25 patients to have undergone response assessment at day 100. Three patients were not assessable as they had ongoing clinical responses at the time of transplant due to bridging therapy received after enrollment and before transplant. These patients were excluded from percentages so as not to bias results by including patients without active disease.

Best Response by day 100	**Number of patients**	**% Total**
CR	3	14%
nCR	10	45%
VGPR	2	9%
PR	5	23%
SD	1	5%
PD	1	5%
Total evaluable	22	100%
Not assessable*	3	N/A

* Patients with VGPR or better going into transplant

The below images show the impact of the NY-ESO T cells in a patient with a complete response at day 56. The image on the top left shows a histology slide of diseased marrow with abnormal plasma cells. The image on the top right shows a normalized bone marrow from a patient with a CR at day 56. The image on the bottom left is from a patient who had a secondary metastasis (plasmacytoma noted by the arrow), which originated from the plasma tumor cells in the marrow and cleared after treatment, as shown by the arrow in the image on the bottom right.

Source: Aaron Rapoport, MD, ASH, December 2012

The results obtained from the multiple myeloma trial have provided us with promising preliminary clinical data on our NY-ESO TCR therapeutic candidate, including the association of our TCR therapeutic candidate with tumor-peptide directed T-cell responses in high risk patients. No on-target, off-tumor or off-target toxicities were observed and robust T-cell expansion was seen. As of June 30 2015, the NY-ESO engineered T cells have persisted in multiple myeloma patients in our trial for six months in all but one patient and in nine of 10 patients who have reached at least two years post T-cell administration.

Six patients in the trial experienced SAEs that were possibly related to administration of our TCR therapeutic candidate and all SAEs were resolved. The adverse events of grade 3 and above considered to be possibly related to administration of our TCR therapeutic candidate by the principal investigator, apart from patient 261 that was upgraded by us, in the trial are listed below as of June 30, 2015:

Patient ID	Diagnosis by PI	Outcome	Relationship
202	Neutropenia	Recovered	Possible
202	Hypoxia	Recovered	Possible
204	Hyponatremia	Recovered	Possible
209	Graft Versus Host Disease GI	Recovered	Probable
209	Neutrophil count decreased	Recovered	Possible
253	Dehydration	Recovered	Possible
261	Pyrexia	Recovered	Possible
265	Graft Versus Host Disease GI	Recovered	Definite
265	Pyrexia	Recovered	Probable
265	Diarrhea	Recovered	Probable

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A second Phase 1/2, open-label, multiple-site clinical trial in multiple myeloma is also underway for patients who are ineligible for auto-SCT. The trial is still in its early stages with 10 patients targeted for recruitment, and two patients infused as of June 30, 2015.

Melanoma Trial

It is estimated that there were approximately 76,100 new cases of melanoma of the skin and an estimated 9,700 people died of this disease in the United States in 2014. Five-year survival for Stage 3 melanoma (lymphatic involvement) ranges from about 40% to 75% and for Stage 4 (metastatic) is approximately 15% to 20% in the United States. Patients with Stage 4 melanoma suffer an especially poor prognosis with a median survival of six to 10 months.

We are conducting a Phase 1/2 open-label clinical trial in melanoma. The trial is designed to include six melanoma patients, all of whom failed prior treatment. Our TCR therapeutic candidate will be administered after lympho-depleting chemotherapy. We will initially observe patients and then assess their response at four weeks, eight weeks and 12 weeks by CT imaging of the chest, abdomen and pelvis. Patients with progressive disease at 12 weeks will be offered alternative treatment options. Patients with SD, PR and CR will remain on trial until progression.

We are recruiting patients with Stage 3 or Stage 4 melanoma. To date, three patients have been infused with our NY-ESO TCR therapeutic candidate. As of June 30, 2015, one patient had experienced an SAE of engraftment fever that was probably related to our TCR therapeutic candidate. Lack of responses in the first two patients prompted a review of the method of antigen screening. Enrollment in our melanoma trial was delayed until implementation of a new immuno-histochemistry assay, which helps ensure that patients being treated have enough peptide positive cells to be expected to respond to our NY-ESO TCR therapeutic candidate. Recruitment has now resumed using this new assay, which we believe will enable us to identify patients with increased prospects for being eligible to receive our TCR therapeutic candidate.

Ovarian Cancer Trial

Epithelial ovarian cancer is the leading cause of death from gynecologic cancer in the United States and the country s fifth most common cause of cancer mortality in women. There were approximately 22,000 new cases of ovarian cancer and an estimated 14,200 people died of this disease in the United States in 2014. Overall, the five-year survival rate is 44%. If the cancer is detected early, at the localized stage when the cancer is only in the part of the body where it started, the five-year survival rate is 92%. However, if the cancer is found in the regional and distant stages, when the cancer has spread, the five-year survival rate is 27%. The majority of cases (61%) are detected at the distant stage. Only 15% are detected at the localized stage. No treatment is available for patients with refractory or resistant metastatic ovarian cancer.

We are conducting an open-label, Phase 1/2 ovarian cancer trial. The primary trial objective is to determine the safety and tolerability of our NY-ESO TCR therapeutic candidate with chemotherapy preconditioning in patients who have refractory or resistant Stage 3/4 ovarian cancer. This trial involves the treatment of 10 patients, and five patients have been treated so far. Patients who have refractory or platinum resistant disease (i.e., disease has recurred in less than six months) or who have had two previous lines of chemotherapy are targeted for this clinical trial. Overall, the prognosis for such patients is poor. Following the administration of treatment, we evaluate responses in patients daily for the first week, weekly until four weeks, and then at eight weeks, 12 weeks and at six and nine months.

The first patient treated in our ovarian cancer trial experienced a grade 3 Cytokine-Release Syndrome at day seven post-infusion, concomitant with a significant proliferation of the engineered T cells that constituted about 100% of the peripheral blood at day 14. The patient s tumor markers were also falling during this time. To manage the Cytokine-Release Syndrome, the patient was treated with high dose steroids that abrogated the engineered T-cell function. The protocol was subsequently modified to allow for use of the anti-IL6R antibody, tocilizumab, for treatment of Cytokine-Release Syndrome in future patients, which has been shown to control Cytokine-Release Syndrome without abrogating the anti-tumor response. The patient later reported an SAE of dehydration. The next four patients did not experience a response, which we believe is due to a dose de-escalation of the pre-conditioning chemotherapy that was implemented in these patients, as well as one patient having very low levels of the target peptide. As of June 30, 2015, febrile neutropenia has also been reported as an SAE in one patient as being possibly related to administration of our NY-ESO TCR therapeutic candidate in this trial. The trial has been revised to use the same regimen of chemotherapy as in the synovial sarcoma trial, and to standardize target marker antigen eligibility levels and the cell dose.

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Investigator-initiated European Esophageal Cancer and Melanoma Trials

We are part of a collaboration program called ATTACK 2 (Adoptive engineered T-cell Targeting to Activate Cancer Killing). The investigated-intiated clinical program is funded by a European Union Framework Seven (FP7) grant and is sponsored by The Christie Trials Co-ordination Unit. The progam is intended to cover two Phase 1/2 clinical trials at seven clinical sites in the United Kingdom, Netherlands, Italy and Sweden using our NY-ESO TCR therapeutic candidate. The objectives are:

- in a first trial to evaluate our NY-ESO TCR therapeutic candidate in esophageal cancer. This trial is intended to be a Phase 1/2 trial with two stages. The first stage is designed to determine effectiveness in 15 patients and, if successful, will be expanded to a second stage for a total of up to 28 patients.

- in a second trial to evaluate different cell populations transduced with our NY-ESO TCR therapeutic candidate in patients with metastatic melanoma.

Both of the above clinical programs use our NY-ESO TCR therapy which is currently prepared and administered under a different protocol to that used in our clinical programs. To date, two patients have been treated in the United Kingdom, one of whom passed away 46 days post T-cell infusion. As of the date of this Annual Report, the underlying cause of death is still under investigation by the ATTACK Consortium. Enrollment to this study has been placed on hold by the study sponsor pending the results of these investigations.

MAGE-A10 TCR Therapeutic Candidate

The following table summarizes our MAGE-A10 TCR therapeutic candidate program:

MAGE-A10 is a target peptide expressed in a number of solid tumor cell types, including lung cancer. Lung cancer is the third most common form of cancer in the United States. It is estimated that approximately 224,000 new cases were diagnosed in 2014, accounting for about 13% of all cancer diagnoses. However, lung cancer is the leading cause of cancer deaths in both men and women and it is estimated that there were approximately 159,000 deaths from lung cancer in the United States in 2014. The one-year and five-year survival rates for lung cancer during

2003 to 2009 were 43% and 17%, respectively. One reason for the relatively poor prognosis is that only 15% of lung cancers are diagnosed at an early stage. For non-small cell lung cancer (NSCLC), which accounts for 84% of lung cancer in the United States, surgery is the treatment of choice for early stage disease. Advanced stage disease requires the use of chemotherapy or radiotherapy, however, median survival even in fit patients remains short at 8 to 10 months.

We believe our MAGE-A10 TCR therapeutic candidate has the potential ability to bind its target peptides in multiple cancer types expressing the MAGE-A10 antigen. No off-target cross-reactivity concerns have been identified to date although allo-reactivity responses to one rare HLA gene were observed. Patients with this gene will be excluded from the trial. An IND for our MAGEA-10 TCR therapeutic candidate was accepted by the FDA in June 2015, and we anticipate starting clinical trials by the end of 2015 depending on the timescales associated with site initiation and patient recruitment. The initial clinical program will be an open label Phase 1/2 dose escalating study in patients with advanced stage NSCLC expressing the MAGE-A10 peptide antigen. The primary objectives of the study are to assess safety and tolerability of our MAGE-A10 TCR therapeutic candidate in patients. Secondary objectives include the assessment of efficacy and durability of persistence.

Our Preclinical Pipeline Programs

Our AFP therapeutic candidate

AFP is a target peptide associated with hepatocellular carcinoma. It is estimated that there were 33,000 new cases of liver cancer (including intrahepatic bile duct cancers) in the United States during 2014, 80% of these cases being hepatocellular carcinoma. Liver cancer incidence rates are about three times higher in men than in women.

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From 1990 to 2009, the mortality from liver cancer has increased 63% in men and 41% in women and it is estimated that in 2014 in the United States 23,000 people died from liver cancer. Approximately 40% of hepatocellular carcinoma is diagnosed at an early stage and may be amenable to surgery (resection or liver transplantation) and/or locoregional procedures (radiofrequency ablation or embolization). With early diagnosis, the five-year survival rate is 29%, but decreases to 10% for regional and 3% for distant stages of the disease. Overall, the five-year survival rate for liver cancer remains low at approximately 16% and has not improved significantly over the past four decades.

An affinity-enhanced TCR has been identified and preclinical testing is ongoing in relation to our AFP TCR therapeutic candidate. Preclinical safety testing is nearly complete and we are in the process of preparing an IND submission, which is planned for 2016.

Early Stage Programs

In addition to the AFP program, we have identified over 30 additional intracellular target peptides that are preferentially expressed in cancer cells and have active unpartnered research programs on twelve of these. The target peptides subject to the further research programs are not observed in normal human tissue and as a result make ideal targets for our TCR therapeutic candidates. The research programs are at different stages of development, but in all cases we have commenced initial validation on the targets and have started working on identification of a TCR which binds to the target peptides.

The GSK Strategic Collaboration

We entered into a strategic collaboration with GSK in May 2014 regarding the development, manufacture and commercialization of TCR therapeutic candidates.

Under the collaboration and license agreement, the NY-ESO TCR therapeutic candidate program and associated manufacturing optimization work will be conducted by us in collaboration with GSK. GSK has an option to obtain an exclusive worldwide license to the NY-ESO therapeutic candidate program, exercisable during specified time periods after we have delivered a Phase 1/2 data package for the program to GSK. If the option is exercised, GSK will assume full responsibility for the NY-ESO therapeutic candidate program. The agreement sets out the work required by us under a development plan that runs through 2019 and aims to provide clinical proof of concept data enabling pivotal clinical trial implementation for the existing NY-ESO therapeutic candidate by 2017 and for a generation 2 therapy.

In addition, GSK also has the right to nominate four additional targets. The first of these additional targets will be selected from a pool of three targets, which have already been jointly selected by GSK and us. Following completion of initial research on these three targets, GSK is entitled to nominate one TCR therapeutic candidate. In addition, three other targets may be selected by GSK, excluding the twelve additional unpartnered research programs described above and any other programs where we initiate development of a TCR therapeutic candidate for the relevant target.

Upon nomination by GSK of any of the four additional targets, we will grant to GSK an exclusive option on each such target, which can be exercised up to four months after approval of an IND in relation to a TCR therapeutic candidate directed against the nominated target.

Nomination also triggers the start of a collaboration program to develop the relevant TCR therapeutic candidate directed to the nominated target peptide.

Following exercise of an option, we will grant to GSK an exclusive worldwide license under intellectual property rights specific to the TCR therapeutic candidates developed under the relevant collaboration programs. GSK will be fully responsible for all further development and commercialization of the relevant TCR therapeutic candidates, at its expense. The licenses do not include any right for GSK to develop alternative affinity-enhanced TCRs using our intellectual property rights or to develop other TCR therapeutic candidates directed to different target peptides. Under the agreement, we are also prohibited from independently developing or commercializing TCR therapeutics directed at the targets subject to outstanding options granted to GSK.

Under the collaboration and license agreement, we received an upfront payment of £25 million and are entitled to various milestone payments based on the achievement of specified development and commercialization milestones by either us or GSK. As previously announced, these milestone payments have a potential value of approximately $350 million over the next seven years.

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The $350 million assumes that GSK exercises options in relation to three targets and that in relation to at least two of these targets (including our NY-ESO TCR therapeutic candidate) application for market authorization in the United States and Europe has been filed. In December 2014, we received a payment of £2.5 million upon the parties decision to continue Cohort 1 of the Phase 1/2a ovarian cancer trial utilizing the NY-ESO therapeutic candidate, and in January 2015 we received a payment of £2 million upon the parties selection of four maximum lead priority generation 2 therapy programs for inclusion in the development plan. Development and commercialization milestones are payable on a collaboration program by collaboration program basis, the level being dependent on various development decisions taken during each collaboration program. For the collaboration program relating to the NY-ESO therapeutic candidate, in addition to the milestones already received, we may be eligible to receive up to $340 million in potential development and commercialization milestones.

In addition to the development milestones, we are entitled to royalties from GSK on all GSK sales of TCR therapeutic products licensed under the agreement, varying between a mid-single-digit percentage and a low-double-digit percentage of net sales, subject to certain agreed reductions, dependent on the cumulative annual net sales for each calendar year. Royalties are payable while there is a jointly owned or solely owned valid patent claim covering the TCR therapeutic in the country in which the relevant TCR therapeutic is being sold and, in each case, for a minimum of 10 years from first commercial sale of the relevant TCR therapeutic. Sales milestones also apply once any TCR therapeutic covered by the GSK collaboration and license agreement is on the market.

The GSK collaboration and license agreement is effective until all payment obligations expire, including any ongoing royalty payments due in relation to GSK s sale of any covered TCR therapeutic candidates. The agreement can also be terminated on a collaboration program-by-collaboration program basis by GSK for lack of feasibility or inability to meet certain agreed requirements. Both parties have rights to terminate the agreement for material breach upon 60 days written notice or immediately upon insolvency of the other party. GSK has additional rights to terminate either the agreement or any specific license or collaboration program on provision of 60 days notice to us. Additional payments may be due to us as a result of such termination, and where we continue any development of any TCR therapeutic candidate resulting from a terminated collaboration program, depending on the stage of development, royalties may be payable to GSK at a mid-single-digit percentage rate of net sales. We also have rights to terminate any license where GSK ceases development or withdraws any licensed TCR therapeutic in specified circumstances.

GSK and Novartis have publicly announced that Novartis has opt-in rights over GSK s current and future oncology research and development pipeline. As part of that announced transaction, GSK has agreed to sell the rights to GSK s marketed oncology portfolio, related research and development activities and the AKT Inhibitors currently in development. GSK has also agreed to grant Novartis preferred partner rights for co-development and commercialization of GSK s current and future oncology pipeline products for a period of 12.5 years from completion of the various transactions between GSK and Novartis,. The relevant agreement grants Novartis a right of first negotiation over the co-development or commercialization of any GSK Relevant Development Product in a major market. A Relevant Development Product as defined in the public announcement is a product in development for the treatment, palliation, diagnosis or prevention of all cancers, including immunology, epigenetics and treatment of solid or hematologic tumors (excluding in all cases, vaccines). According to the public announcement made by GSK, the right of first negotiation lasts for 12.5 years from completion of the various transactions between GSK and Novartis and applies where GSK decides to seek a third party partner for co-development or commercialization of, or to whom to divest rights to, a Relevant Development Product in a global or major market or where GSK proposes to seek a marketing authorization for a Relevant Development Product in a major market.

Details of the relationship are also set out in Risk Factors Risks Related to Our Reliance Upon Third Parties We rely heavily on GSK for our NY-ESO TCR therapeutic candidate clinical program, which may also affect other TCR therapeutic candidates .

Other Core Alliances and Contract Organization Collaborations

We have a number of collaborations that are important to our continued ability to offer and supply our engineered TCR therapeutic candidates.

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Core Collaborations

ThermoFisher Scientific

We have entered into a series of license and sub-license agreements with ThermoFisher Scientific (formerly Life Technologies) that provide a field-based exclusive license under certain intellectual property rights owned or controlled by ThermoFisher in relation to the methods of use of the ThermoFisher Dynabeads® CD3/CD28 technology to isolate, activate and expand T cells and enable transfection of the T cells with any TCR genes. We are also in the process of negotiating a supply agreement for the supply of the ThermoFisher Dynabeads® CD3/CD28.

Immunocore Limited

We currently have an assignment and license agreement in place with Immunocore that relates to certain co-owned patents, patent applications and rights in know-how that originally was developed by Avidex and subsequently acquired by Medigene. Adaptimmune and Immunocore each utilize the jointly owned patents and know-how within separate fields or applications, with our focus being on the treatment of patients with engineered TCR therapeutic candidates and Immunocore s focus being on the treatment of patients with soluble TCRs. There are no termination rights for either Immunocore or us in the assignment and license agreement.

We also have a target collaboration agreement with Immunocore regarding target identification and T-cell cloning which provides joint access to all currently identified peptide targets and use of Immunocore employees in conducting such identification and T-cell cloning. This collaboration agreement can be terminated by either party in the event of insolvency or generally on six months notice.

See Related Party Transactions Agreements with Immunocore Limited and Risk Factors Risks Related to Our Reliance Upon Third Parties We have a shared development history with Immunocore Limited, or Immunocore, and as a result are reliant on resources and other support from Immunocore, which if not present could result in delays in our ability to progress new TCR therapeutic candidates to market.

Intellectual Property

We actively seek to protect the intellectual property and proprietary technology that we believe is important to our business, including seeking, maintaining, enforcing and defending patent rights for our therapeutics and processes, whether developed internally or licensed from third parties. Our success will depend on our ability to obtain and maintain patent and other protection including data/market exclusivity for our TCR therapeutic candidates and platform technology, preserve the confidentiality of our know-how and operate without infringing the valid and enforceable patents and proprietary rights of third parties. See Risk Factors Risks Related to Our Intellectual Property.

Our policy is to seek to protect our proprietary position generally by filing an initial priority filing at the U.K. Intellectual Property Office, or UKIPO, and the U.S. Patent Trademark Office, USPTO. This is followed by the filing of a patent application under the Patent Co-operation Treaty claiming priority from the initial application(s) and then application for patent grant in, for example, the United States, Europe (including major European territories), Japan, Australia, New Zealand, India and Canada. In each case, we determine the strategy and territories required after discussion with our patent professionals to ensure that we obtain relevant coverage in territories that are commercially important to us and our TCR therapeutic candidates. We will additionally rely on data exclusivity, market exclusivity and patent term extensions when available, including as relevant exclusivity through orphan or pediatric drug designation. We also rely on trade secrets and know-how relating to our underlying platform technology and TCR therapeutic candidates. Prior to making any decision on filing any patent application, we consider with our patent professionals whether patent protection is the most sensible strategy for protecting the invention concerned or whether the invention should be maintained as confidential.

As of June 30, 2015, we owned or jointly owned approximately 172 granted patents (of which 13 are U.S.-issued patents) and 29 pending patent applications (of which 10 are U.S. patent applications). These patents and patent applications include claims directed to our TCR therapeutic candidates, our platform technology used to identify and generate engineered TCR therapeutic candidates and our manufacturing and process technology.

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NY-ESO

We own granted patents covering the composition of matter of our NY-ESO TCR therapeutic candidate. The patent claims are directed to the engineered TCR therapeutic candidate and in particular the amino acid substitutions required for such engineered TCR therapeutic candidate. The patent has been granted in major territories including Australia, Europe (Switzerland, Germany, Denmark, France, United Kingdom, Ireland and the Netherlands), New Zealand, Japan and the United States. These granted patents are expected to expire in May 2025.

MAGE-A10

We own patent applications covering the composition of matter of our MAGE-A10 TCR therapeutic candidate. The patent application claims are directed to the engineered TCR therapeutic candidate and in particular the amino acid substitutions required for such engineered TCR therapeutic candidate. The patent applications have been filed with the UKIPO and with the USPTO.

AFP

We own a patent application covering the composition of matter of our AFP therapeutic candidate. As with our NY-ESO and MAGE-A10 TCR therapeutic candidates, the patent application claims are directed to the engineered TCR therapeutic candidate and in particular the amino acid substitutions required for such engineered TCR therapeutic candidate. An initial priority patent application was filed in the UKPTO and a patent application under the applicable Patent Co-operation Treaty has since been filed claiming priority from that U.K. patent application.

Platform Technology Patents and Patent Applications

We jointly own a number of platform technology patents and patent applications. These are jointly owned with Immunocore Limited and are directed to certain aspects of the process that we use to engineer our TCR therapeutic candidates. For example, patents directed to the di-sulphide bond stabilization technique required to solubilize TCRs for isolation, characterization and validation have been issued in major territories including Australia, Canada, China, major European territories (including the United Kingdom, France, Germany, Spain and Italy), India, Hong Kong, Japan, the United States and South Africa and are expected to expire beginning in 2022. Patents have also been granted in relation to our phage display approach for TCRs and are expected to expire beginning in 2023. The priority patent application was filed in 2002 and patents are now granted in the United States, Australia, Canada, China, major European territories (including the United Kingdom, France, Germany, Spain and Italy), Japan, South Africa, India, Norway and New Zealand. Other examples include an issued patent directed to a method for increasing the affinity of given TCRs to a target peptide (expected to expire in 2025) and patent applications directed to decreasing off-target reactivity and selection for the affinity-enhanced TCRs.

Manufacturing Process Patents and Patent Applications

We also have know-how and patent applications that we own which relate to the manufacture of our TCR therapeutic candidates. For example, we have filed a U.S. patent application and a patent application under the applicable Patent Cooperation Treaty, which claim priority from initial priority patent applications filed at the USPTO and UKIPO, which is directed to a particular modification to the lentiviral vector technology. We believe this modification enhances the safety profile of the lentiviral vector technology.

Exclusive License for Bead Products

In December 2012, we entered into two agreements, a license and a sub-license, with Life Technologies Corporation (part of ThermoFisher). The license agreement grants us a field-based exclusive license under certain intellectual property rights owned or controlled by ThermoFisher in relation to the methods of use of the ThermoFisher Dynabeads® CD3/CD28 technology to isolate, activate and expand T cells and enable transfection of the T cells with any TCR genes to manufacture our licensed products and use and sell those TCR products to treat cancer, infectious disease and/or autoimmune disease. The licensed field relates to the *ex-vivo* activation and expansion of human T cells containing engineered TCRs for use as a therapy for treating cancer, infectious disease and/or autoimmune disease and where the therapy comprises the steps of (a) removing a sample containing T cells from a patient; (b) isolating T cells from that sample using the ThermoFisher bead product or similar magnetic beads; (c) transfecting those isolated T cells with a gene or genes encoding engineered TCRs of known antigen specificity; (d) activating and expanding the population of those engineered T cells using the ThermoFisher bead product or similar magnetic beads; and (e) introducing the expanded, engineered T cells back into the same patient. The license is not sub-licensable but we are able to sub-contract manufacture of the licensed products to our contract manufacturing organizations. Our sub-licensees have access to the required license directly from ThermoFisher under the above-described intellectual property rights on terms equivalent to those we have obtained from ThermoFisher in relation to our partnered licensed products.

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We have granted an option under the license agreement to ThermoFisher to take an exclusive license under any improvements made by or for, or controlled by, us to the ThermoFisher patented technology to the extent any such improvements are dominated by the patent rights licensed to us. Any license will be outside of the exclusive field we have been granted, namely engineered T-cell therapy.

Under the license agreement, we have to demonstrate reasonable commercial efforts to carry out development and commercialization of the licensed products and we are required to make certain expenditures for research and development relating to the commercialization of the licensed products. This obligation is deemed satisfied upon first commercial sale of a licensed product. We have certain payment obligations under the license agreement including an upfront license fee of $335,000, which has already been paid, minimum annual royalty (in the low tens of thousands of U.S. dollars prior to licensed product approval and thereafter at a level of 50% of running royalties in the previous year), milestone payments (payable for each licensed product on achievement of certain development and commercialization milestones per licensed product) and a low single-digit running royalty payable on the net selling price of each licensed product. The license agreement will last until the expiration of the latest to expire of the licensed patent rights. The license agreement can be terminated before the end of its term by mutual agreement, by ThermoFisher on the occurrence of certain events (failure to use reasonable commercial efforts, willful making of a false statement of a material fact, breach of antitrust laws or other laws, material breach of the agreement, payment default or if we have challenged the validity or enforceability of any of the licensed patents). The license may also be terminated in the event of insolvency by either party.

We also have a field-based exclusive sub-license under certain other patents which cover the method of use of the Dynabeads® CD3/CD28 and are controlled by ThermoFisher under a head-license from the University of Michigan, the U.S. Navy and the Dana-Farber Cancer Institute. The sub-license has the same relevant exclusivity scope and field-based restrictions and many of the terms are equivalent to those set out in the main license agreement with ThermoFisher, including the same requirement to demonstrate reasonable commercial efforts to carry out development and commercialization of the licensed products as in the main license agreement with ThermoFisher. We have certain payment obligations under the sub-license agreement including an upfront license fee of $665,000, which has already been paid, minimum annual royalty (in the tens of thousands of U.S. dollars prior to product approval and thereafter at a level of 50% of running royalties in the previous year), milestone payments (payable for each sub-licensed product on achievement of certain development and commercialization milestones per sub-licensed product) and a low single-digit running royalty payable on the net selling price of each sub-licensed product. The sub-license agreement will last until the expiration of the latest to expire of the sub-licensed patent rights. The sub-license agreement can be terminated before the end of its term by mutual agreement, by ThermoFisher or the head licensors on the occurrence of certain events (failure to use reasonable commercial efforts, willful making of a false statement of a material fact, failure to adequately meet any requirement for public use required under Federal regulations, breach of antitrust laws or other laws, material breach of the agreement, payment default or if we have challenged the validity or enforceability of any of the sub-licensed patents). The sub-license may also be terminated in the event of insolvency by either party. The sub-license has an additional requirement that any manufacture of engineered TCR products for sale in the United States must occur in the United States and reserves rights for the U.S. government to use the technology in accordance with 35 USC §200 *et seq.* and for the University of Michigan, and Dana-Farber Cancer Institute to use the technology for non-commercial research purposes. The aggregate milestone payments payable per product under the license and sub-license agreements do not exceed $5 million.

See Risk Factors Risks Related to Our Reliance Upon Third Parties We rely heavily on Thermo Fisher Scientific Inc., or ThermoFisher, and the technology we license from them.

Other Third-Party Intellectual Property Rights

We use a transient transfection system for manufacture of our lentivirus vector and for the transfer of engineered TCR therapeutic candidates into patient T cells in order to express the affinity-enhanced TCRs.

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Third-party patents do exist that purport to cover some or all of our current vectors or our process for manufacture. However, the majority of these patents will expire prior to any commercial supply by us of any TCR therapeutic candidates and we do not currently require a license. Whether licenses are required under any remaining third-party patents or other third-party patents depends on what steps we take going forward in relation to our lentiviral transduction process and any changes made to that process. We may, however, need to negotiate a license under any remaining third party patents or develop alternative strategies for dealing with any remaining third party patents if licenses are not available on commercially acceptable terms or at all.

We are aware of a family of patent applications owned by The Board of Trustees of the University of Illinois which include two issued U.S. patents (U.S. 6,759,243 and 7,569,357) which were issued with very broad claims relating to high affinity TCRs. We believe that U.S. Patent 7,569,357, because of certain claim recitations, is not an impediment to the presently contemplated TCR therapeutic candidates. We requested re-examination of U.S. Patent 6,759,243 at the USPTO. In that re-examination, the USPTO adopted our position and rejected all claims under re-examination as anticipated or obvious, and in a related pending patent application of The Board of Trustees of the University of Illinois, in an August 18, 2014 Office Action, the USPTO also adopted our position and rejected the claims based on our arguments and evidence of our re-examination request. Through the re-examination process we have been successful in achieving a narrowing of all of the claims of U.S. Patent 6,759,243. While we believe U.S. Patent 6,759,243 will be nonetheless invalid in the form it will issue after re-examination, we do not believe the patent after re-examination will be an impediment to the presently contemplated TCR therapeutic candidates, including inter alia because of the recitations added by the patentee during re-examination and the U.S. codified doctrine of intervening rights. Furthermore, these U.S. patents will likely expire prior to any commercial supply by us of any TCR therapeutic candidate.

From time to time we will use samples or cell lines obtained from third parties in order to identify either suitable targets or TCRs that bind to certain targets. The agreements under which samples are provided vary between third parties and certain third parties require entry into license agreements. These agreements may also contain payment obligations relating to the use of the various samples or the information obtained from use of those samples.

Laws and Regulations Regarding Patent Terms

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application. In the United States, a patent term may be shortened if a patent is terminally disclaimed over another patent or as a result of delays in patent prosecution by the patentee. A patent s term may be lengthened by a patent term adjustment, which compensates a patentee for administrative delays by the USPTO in granting a patent. The patent term of a European patent is 20 years from its effective filing date, which, unlike in the United States, is not subject to patent term adjustments in the same way as U.S. patents.

The term of a patent that covers an FDA-approved drug or biologic may also be eligible for patent term extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug or biologic is under regulatory review. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be extended. Similar provisions are available in Europe and other jurisdictions to extend the term of a patent that covers an approved drug, for example Supplementary Protection Certificates. In the future, if and when our products receive FDA approval, we expect to apply for patent term extensions on patents covering those products. We anticipate that some of our issued patents may be eligible for patent term extensions but such extensions may not be available and therefore our commercial monopoly may be restricted. See Risk Factors Risks Related to Our Intellectual Property We may not be able to protect our proprietary technology in the marketplace or the cost of doing so may be prohibitive or excessive.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our scientific knowledge, technology and development experience provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions, governmental agencies and public and private research institutions. Any TCR therapeutic candidates that we successfully develop and commercialize will compete with existing products and new products that may become available in the future.

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Immunotherapy is an active area of research and a number of immune-related products have been identified in recent years that are alleged to modulate the immune system. Many of these products utilize dendritic cells, a form of immune cell that presents cancer target peptides to T cells and that can in turn result in T-cell activation.

More recently, bi-specific antibodies and checkpoint inhibitors have been identified as having utility in the treatment of cancer. Bi-specific antibodies commonly target both the cancer peptide and the TCR, thus bringing both cancer cells and T cells into close proximity to maximize the chance of TCR binding and hence an immune response to the cancer cells. Checkpoint inhibitors on the other hand work by targeting receptors that inhibit T-cell effectiveness and proliferation and essentially activate the T cells.

Other engineered T-cell therapeutics have also been identified using antibody recognition systems engineered into T cells, so-called CAR-T cells. These and other competitors in the TCR space include: Juno Therapeutics Inc., Kite Pharma Inc. / National Institutes of Health, or NIH, Medigene AG and Takara Bio Inc. In the CAR-T space, competitors include: Bellicum Pharmaceuticals, Inc., bluebird bio, Inc. / Celgene Corporation./ Baylor College of Medicine, Cellectis SA / Pfizer Inc., Juno Therapeutics Inc. / Celgene Corporation ./ Fred Hutchinson Cancer Research Center / Memorial Sloan Kettering Cancer Center, Kite Pharma, Inc. / Amgen, Inc. / NIH/, Intrexon Corporation / Ziopharm Oncology, Inc. / MD Anderson Cancer Center and Novartis AG / University of Pennsylvania.

We do not believe that any of these competitors offer the same form of affinity-enhancement as our engineered TCR therapeutic candidates and, due to the low presentation of target peptide-HLA antigen on relevant cancer cells, those with TCR-based approaches are unlikely to be as effective. For example, Kite Pharma Inc. is in the process of, among other things, developing genetically engineered T-cells that bind directly to cancer cells. We believe this technology relies on the modification of T cells to express certain cancer-specific receptors, namely TCRs and CAR-Ts. Kite Pharma has a murine derived TCR product in development targeting NY-ESO-1. Novartis also has substantial interest in the development of CAR-Ts. Juno Therapeutics Inc. has developed an engineered TCR therapeutic candidate where the end TCR is purported to have enhanced affinity through stem-cell selection. The therapeutic is produced in a very different way from the affinity-enhanced TCRs we produce, and we believe there is limited ability to control the enhancement obtained. Takara Bio Inc. has developed a naturally occurring TCR that binds to the MAGE A-4 target peptide and the therapeutic is in clinical trials. The TCR is not affinity-enhanced. Medigene has also reported development of an engineered TCR therapeutic candidate produced by selection from HLA-mismatched donors rather than affinity-enhancement. We believe that this is still in preclinical stages and is potentially directed at melanoma.

Immune Design Corp. has a vaccine in clinical trials which is not TCR-based. The vaccine targets the NY-ESO peptide in humans and again relies on binding to target peptides presented at low levels on target cells to stimulate natural low affinity T-cell responses. The treatment is not patient-specific.

Government Regulation and Product Approvals

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of pharmaceutical products. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

The failure to comply with applicable U.S. requirements at any time during the product development process, approval process or after approval may subject an applicant and/or sponsor to a variety of administrative or judicial sanctions, including refusal by the FDA to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by the FDA and the Department of Justice, or DOJ, or other governmental entities.

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FDA Approval Process

In the United States, pharmaceutical products are subject to extensive regulation by the United States Food and Drug Administration, or the FDA. The Federal Food, Drug, and Cosmetic Act, or the FDC Act, and other federal and state statutes and regulations, govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling, and import and export of pharmaceutical products. Biological products used for the prevention, treatment, or cure of a disease or condition of a human being are subject to regulation under the FDC Act, except the section of the FDC Act which governs the approval of new drug applications, or NDAs. Biological products are approved for marketing under provisions of the Public Health Service Act, or PHSA, via a Biologics License Application, or BLA. However, the application process and requirements for approval of BLAs are very similar to those for NDAs, and biologics are associated with similar approval risks and costs as drugs. Failure to comply with applicable U.S. requirements may subject a company to a variety of administrative or judicial sanctions, such as FDA refusal to approve pending NDAs or BLAs, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties, and criminal prosecution.

Biological product development for a new product or certain changes to an approved product in the United States typically involves preclinical laboratory and animal tests, the submission to the FDA of an investigational new drug application, or IND, which must become effective before clinical testing may commence, and adequate and well-controlled clinical trials to establish the safety and effectiveness of the drug for each indication for which FDA approval is sought. Satisfaction of FDA pre-market approval requirements typically takes many years and the actual time required may vary substantially based upon the type, complexity, and novelty of the product or disease.

Preclinical tests include laboratory evaluation of product chemistry, formulation, and toxicity, as well as animal trials to assess the characteristics and potential safety and efficacy of the product. The conduct of the preclinical tests must comply with federal regulations and requirements, including good laboratory practices. The results of preclinical testing are submitted to the FDA as part of an IND along with other information, including information about product chemistry, manufacturing and controls, and a proposed clinical trial protocol. Long term preclinical tests, such as animal tests of reproductive toxicity and carcinogenicity, may continue after the IND is submitted.

A 30-day waiting period after the submission of each IND is required prior to the commencement of clinical testing in humans. If the FDA has neither commented on nor questioned the IND within this 30-day period, the clinical trial proposed in the IND may begin.

Clinical trials involve the administration of the investigational biologic to healthy volunteers or patients under the supervision of a qualified investigator. Clinical trials must be conducted: (i) in compliance with federal regulations; (ii) in compliance with good clinical practice, or GCP, an international standard meant to protect the rights and health of patients and to define the roles of clinical trial sponsors, administrators, and monitors; as well as (iii) under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. Each protocol involving testing on U.S. patients and subsequent protocol amendments must be submitted to the FDA as part of the IND.

The FDA may order the temporary, or permanent, discontinuation of a clinical trial at any time, or impose other sanctions, if it believes that the clinical trial either is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. The trial protocol and informed consent information for patients in clinical trials must also be submitted to an institutional review board, or IRB, for approval. An IRB may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB s requirements, or may impose other conditions.

Clinical trials to support BLAs for marketing approval are typically conducted in three sequential phases, but the phases may overlap. In Phase 1, the initial introduction of the biologic into healthy human subjects or patients, the product is tested to assess metabolism, pharmacokinetics, pharmacological actions, side effects associated with increasing doses, and, if possible, early evidence on effectiveness. Phase 2 usually involves trials in a limited patient population to determine the effectiveness of the drug or biologic for a particular indication, dosage tolerance, and optimum dosage, and to identify common adverse effects and safety risks. If a compound demonstrates evidence of effectiveness and an acceptable safety profile in Phase 2 evaluations, Phase 3 trials are undertaken to obtain the additional information about clinical efficacy and safety in a larger number of patients, typically at geographically dispersed clinical trial sites, to permit the FDA to evaluate the overall benefit-risk relationship of the drug or biologic and to provide adequate information for the labeling of the product.

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In most cases, the FDA requires two adequate and well-controlled Phase 3 clinical trials to demonstrate the efficacy of the biologic. A single Phase 3 trial with other confirmatory evidence may be sufficient in rare instances where the trial is a large multicenter trial demonstrating internal consistency and a statistically very persuasive finding of a clinically meaningful effect on mortality, irreversible morbidity or prevention of a disease with a potentially serious outcome and confirmation of the result in a second trial would be practically or ethically impossible.

After completion of the required clinical testing, a BLA is prepared and submitted to the FDA. FDA approval of the BLA is required before marketing of the product may begin in the United States. The BLA must include the results of all preclinical, clinical, and other testing and a compilation of data relating to the product s pharmacology, chemistry, manufacture, and controls. The cost of preparing and submitting a BLA is substantial. The submission of most BLAs is additionally subject to a substantial application user fee, currently exceeding $2,335,000, and the manufacturer and/or sponsor under an approved new drug application are also subject to annual product and establishment user fees, currently exceeding $110,000 per product and $569,000 per establishment. These fees are typically increased annually.

The FDA has 60 days from its receipt of a BLA to determine whether the application will be accepted for filing based on the agency s threshold determination that it is sufficiently complete to permit substantive review. Once the submission is accepted for filing, the FDA begins an in-depth review. The FDA has agreed to certain performance goals in the review of BLAs. Most such applications for standard review biologic products are reviewed within 10 months of the date the FDA files the BLA; most applications for priority review biologics are reviewed within six months of the date the FDA files the BLA. Priority review can be applied to a biologic that the FDA determines has the potential to treat a serious or life-threatening condition and, if approved, would be a significant improvement in safety or effectiveness compared to available therapies. The review process for both standard and priority review may be extended by the FDA for three additional months to consider certain late-submitted information, or information intended to clarify information already provided in the submission.

The FDA may also refer applications for novel biologic products, or biologic products that present difficult questions of safety or efficacy, to an advisory committee typically a panel that includes clinicians and other experts for review, evaluation, and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. Before approving a BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. Additionally, the FDA will inspect the facility or the facilities at which the biologic product is manufactured. The FDA will not approve the product unless compliance with current good manufacturing practice, or cGMP, is satisfactory and the BLA contains data that provide substantial evidence that the biologic is safe, pure, potent and effective in the indication studied.

After the FDA evaluates the BLA and the manufacturing facilities, it issues either an approval letter or a complete response letter. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing, or information, in order for the FDA to reconsider the application. If, or when, those deficiencies have been addressed to the FDA s satisfaction in a resubmission of the BLA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included.

An approval letter authorizes commercial marketing of the biologic with specific prescribing information for specific indications. As a condition of BLA approval, the FDA may require a risk evaluation and mitigation strategy, or REMS, to help ensure that the benefits of the biologic outweigh the potential risks. REMS can include medication guides, communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The requirement for a REMS can materially affect the potential market and profitability of the product. Moreover, product approval may require substantial post-approval testing and surveillance to monitor the product s safety or efficacy. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

Changes to some of the conditions established in an approved application, including changes in indications, labeling, or manufacturing processes or facilities, require submission and FDA approval of a new BLA or BLA supplement before the change can be implemented. A BLA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and actions in reviewing BLA supplements as it does in reviewing BLAs.

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FDA Guidance Governing Gene Therapy Products

The FDA has issued various guidance documents regarding gene therapies, which outline additional factors that the FDA will consider at each of the above stages of development and relate to, among other things, the proper preclinical assessment of gene therapies; the chemistry, manufacturing, and controls information that should be included in an IND application; the proper design of tests to measure product potency in support of an IND application or BLA; and measures to observe delayed adverse effects in subjects who have been exposed to investigational gene therapies when the risk of such effects is high.

If a gene therapy trial is conducted at, or sponsored by, institutions receiving NIH funding for recombinant DNA research, a protocol and related documentation must be submitted to, and the study registered with, the NIH Office of Biotechnology Activities, or OBA, pursuant to the NIH Guidelines for Research Involving Recombinant DNA Molecules, prior to the submission of an IND to the FDA. In addition, many companies and other institutions not subject to the NIH Guidelines voluntarily follow them. The NIH convenes the Recombinant DNA Advisory Committee, or RAC, a federal advisory committee, to discuss protocols that raise novel or particularly important scientific, safety or ethical considerations at one of its quarterly public meetings. The OBA notifies the FDA of the RAC s decision regarding the necessity for full public review of a gene therapy protocol. RAC proceedings and reports are posted to the OBA website and may be accessed by the public.

Fast Track Designation and Accelerated Approval

The FDA is required to facilitate the development, and expedite the review, of biologics that are intended for the treatment of a serious or life-threatening disease or condition for which there is no effective treatment and which demonstrate the potential to address unmet medical needs for the condition. Under the fast track program, the sponsor of a new biologic candidate may request that the FDA designate the candidate for a specific indication as a fast track biologic concurrent with, or after, the filing of the IND for the candidate. The FDA must determine if the biologic candidate qualifies for fast track designation within 60 days of receipt of the sponsor s request.

Under the fast track program and FDA s accelerated approval regulations, the FDA may approve a biologic for a serious or life-threatening illness that provides meaningful therapeutic benefit to patients over existing treatments based upon a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments.

In clinical trials, a surrogate endpoint is a measurement of laboratory or clinical signs of a disease or condition that substitutes for a direct measurement of how a patient feels, functions, or survives. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. A biologic candidate approved on this basis is subject to rigorous post- marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval trials, or confirm a clinical benefit during post-marketing trials, will allow the FDA to withdraw the biologic from the market on an expedited basis. All promotional materials for biologic candidates approved under accelerated regulations are subject to prior review by the FDA.

In addition to other benefits such as the ability to use surrogate endpoints and engage in more frequent interactions with the FDA, the FDA may initiate review of sections of a fast track product s BLA before the application is complete. This rolling review is available if the applicant

provides, and the FDA approves, a schedule for the submission of the remaining information and the applicant pays applicable user fees. However, the FDA s time period goal for reviewing an application does not begin until the last section of the BLA is submitted. Additionally, the fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Breakthrough Therapy Designation

The FDA is also required to expedite the development and review of the application for approval of biological products that are intended to treat a serious or life-threatening disease or condition where preliminary clinical evidence indicates that the biologic may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints.

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Under the breakthrough therapy program, the sponsor of a new biologic candidate may request that the FDA designate the candidate for a specific indication as a breakthrough therapy concurrent with, or after, the filing of the IND for the biologic candidate. The FDA must determine if the biological product qualifies for breakthrough therapy designation within 60 days of receipt of the sponsor s request.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan drug designation to biological products intended to treat a rare disease or condition, generally a disease or condition that affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and making a product available in the United States for such disease or condition will be recovered from sales of the product. Orphan drug designation must be requested before submitting a BLA. After the FDA grants orphan drug designation, the generic identity of the biological product and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. The first BLA applicant to receive FDA approval for a particular active moiety to treat a particular disease with FDA orphan drug designation is entitled to a seven-year exclusive marketing period in the United States for that product for that indication. During the seven-year exclusivity period, the FDA may not approve any other applications to market a biological product containing the same active moiety for the same disease, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity. A product is clinically superior if it is safer, more effective or makes a major contribution to patient care. Orphan drug exclusivity does not prevent the FDA from approving a different drug or biological product for the same disease or condition, or the same biological product for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the BLA user fee.

Disclosure of Clinical Trial Information

Sponsors of clinical trials of FDA-regulated products, including biological products, are required to register and disclose certain clinical trial information. Information related to the product, patient population, phase of investigation, trial sites and investigators, and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to discuss the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed until the new product or new indication being studied has been approved. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs.

Pediatric Information

Under the Pediatric Research Equity Act, or PREA, NDAs or BLAs or supplements to NDAs or BLAs must contain data to assess the safety and effectiveness of the biological product for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the biological product is safe and effective. The FDA may grant full or partial waivers, or deferrals, for submission of data. Unless otherwise required by regulation, PREA does not apply to any biological product for an indication for which orphan designation has been granted.

Additional Controls for Biologics

To help reduce the increased risk of the introduction of adventitious agents, the PHSA emphasizes the importance of manufacturing controls for products whose attributes cannot be precisely defined. The PHSA also provides authority to the FDA to immediately suspend licenses in situations where there exists a danger to public health, to prepare or procure products in the event of shortages and critical public health needs, and to authorize the creation and enforcement of regulations to prevent the introduction or spread of communicable diseases in the United States and between states.

After a BLA is approved, the product may also be subject to official lot release as a condition of approval. As part of the manufacturing process, the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official release by the FDA, the manufacturer submits samples of each lot of product to the FDA together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer s tests performed on the lot. The FDA may also perform certain confirmatory tests on lots of some products, such as viral vaccines, before releasing the lots for distribution by the manufacturer. In addition, the FDA conducts laboratory research related to the regulatory standards on the safety, purity, potency, and effectiveness of biological products. As with drugs, after approval of biologics, manufacturers must address any safety issues that arise, are subject to recalls or a halt in manufacturing, and are subject to periodic inspection after approval.

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Biosimilars

The Biologics Price Competition and Innovation Act of 2009, or BPCIA, creates an abbreviated approval pathway for biological products shown to be highly similar to or interchangeable with an FDA-licensed reference biological product. Biosimilarity sufficient to reference a prior FDA-approved product requires that there be no differences in conditions of use, route of administration, dosage form, and strength, and no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency. Biosimilarity must be shown through analytical trials, animal trials, and a clinical trial or trials, unless the Secretary waives a required element. A biosimilar product may be deemed interchangeable with a prior approved product if it meets the higher hurdle of demonstrating that it can be expected to produce the same clinical results as the reference product and, for products administered multiple times, the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. On March 6, 2015, the FDA approved the first biosimilar product under the BPCIA. Complexities associated with the larger, and often more complex, structures of biological products, as well as the process by which such products are manufactured, pose significant hurdles to implementation, which is still being evaluated by the FDA.

A reference biologic is granted 12 years of exclusivity from the time of first licensure of the reference product, and no application for a biosimilar can be submitted for four years from the date of licensure of the reference product. The first biologic product submitted under the abbreviated approval pathway that is determined to be interchangeable with the reference product has exclusivity against a finding of interchangeability for other biologics for the same condition of use for the lesser of (i) one year after first commercial marketing of the first interchangeable biosimilar, (ii) eighteen months after the first interchangeable biosimilar is approved if there is no patent challenge, (iii) eighteen months after resolution of a lawsuit over the patents of the reference biologic in favor of the first interchangeable biosimilar applicant, or (iv) 42 months after the first interchangeable biosimilar s application has been approved if a patent lawsuit is ongoing within the 42-month period.

Post-Approval Requirements

Once a BLA is approved, a product will be subject to certain post-approval requirements. For instance, the FDA closely regulates the post-approval marketing and promotion of biologics, including standards and regulations for direct-to-consumer advertising, off-label promotion, industry- sponsored scientific and educational activities and promotional activities involving the internet. Biologics may be marketed only for the approved indications and in accordance with the provisions of the approved labeling.

Adverse event reporting and submission of periodic reports is required following FDA approval of a BLA. The FDA also may require post-marketing testing, known as Phase 4 testing, REMS, and surveillance to monitor the effects of an approved product, or the FDA may place conditions on an approval that could restrict the distribution or use of the product. In addition, quality control, biological product manufacture, packaging, and labeling procedures must continue to conform to cGMPs after approval. Biologic manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies. Registration with the FDA subjects entities to periodic unannounced inspections by the FDA, during which the agency inspects manufacturing facilities to assess compliance with cGMPs. Accordingly, manufacturers must continue to expend time, money, and effort in the areas of production and quality-control to maintain compliance with cGMPs. Regulatory authorities may withdraw product approvals or request product recalls if a company fails to comply with regulatory standards, if it encounters problems following initial marketing, or if previously unrecognized problems are subsequently discovered.

FDA Regulation of Companion Diagnostics

If safe and effective use of a therapeutic product depends on an *in vitro* diagnostic, then the FDA generally will require approval or clearance of the diagnostic, known as a companion diagnostic, at the same time that the FDA approves the therapeutic product. The FDA has generally required *in vitro* companion diagnostics intended to select the patients who will respond to cancer treatment to obtain a pre-market approval, or PMA, for that diagnostic simultaneously with approval of the therapeutic. The review of these *in vitro* companion diagnostics in conjunction with the review of a cancer therapeutic involves coordination of review by the FDA s Center for Biologics Evaluation and Research and by the FDA s Center for Devices and Radiological Health.

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The PMA process, including the gathering of clinical and preclinical data and the submission to and review by the FDA, can take several years or longer. It involves a rigorous premarket review during which the applicant must prepare and provide the FDA with reasonable assurance of the device s safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing and labeling. PMA applications are subject to an application fee, which exceeds $250,000 for most PMAs. In addition, PMAs for certain devices must generally include the results from extensive preclinical and adequate and well-controlled clinical trials to establish the safety and effectiveness of the device for each indication for which FDA approval is sought. In particular, for a diagnostic, the applicant must demonstrate that the diagnostic produces reproducible results when the same sample is tested multiple times by multiple users at multiple laboratories. As part of the PMA review, the FDA will typically inspect the manufacturer s facilities for compliance with the Quality System Regulation, or QSR, which imposes elaborate testing, control, documentation and other quality assurance requirements.

PMA approval is not guaranteed, and the FDA may ultimately respond to a PMA submission with a not approvable determination based on deficiencies in the application and require additional clinical trial or other data that may be expensive and time-consuming to generate and that can substantially delay approval. If the FDA s evaluation of the PMA application is favorable, the FDA typically issues an approvable letter requiring the applicant s agreement to specific conditions, such as changes in labeling, or specific additional information, such as submission of final labeling, in order to secure final approval of the PMA. If the FDA concludes that the applicable criteria have been met, the FDA will issue a PMA for the approved indications, which can be more limited than those originally sought by the applicant. The PMA can include post-approval conditions that the FDA believes necessary to ensure the safety and effectiveness of the device, including, among other things, restrictions on labeling, promotion, sale and distribution.

After a device is placed on the market, it remains subject to significant regulatory requirements. Medical devices may be marketed only for the uses and indications for which they are cleared or approved. Device manufacturers must also establish registration and device listings with the FDA. A medical device manufacturer s manufacturing processes and those of its suppliers are required to comply with the applicable portions of the QSR, which cover the methods and documentation of the design, testing, production, processes, controls, quality assurance, labeling, packaging and shipping of medical devices. Domestic facility records and manufacturing processes are subject to periodic unscheduled inspections by the FDA. The FDA also may inspect foreign facilities that export products to the United States.

Anti-Kickback, False Claims Laws

In addition to FDA restrictions on marketing of pharmaceutical products, several other types of state and federal laws have been applied to restrict certain marketing practices in the pharmaceutical industry in recent years. These laws include anti-kickback statutes, false claims statutes, and other statutes pertaining to health care fraud and abuse. The federal healthcare program anti-kickback statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce, or in return for, purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid, or other federally financed healthcare programs. The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively, the Healthcare Reform Act, amended the intent element of the federal statute so that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it. 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. Violations of the anti-kickback statute are punishable by imprisonment, criminal fines, civil monetary penalties, and exclusion from participation in federal healthcare programs. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution or other regulatory sanctions, the exemptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchases, or recommendations may be subject to scrutiny if they do not qualify for an exemption or safe harbor.

Federal false claims laws prohibit any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to have a false claim paid. This includes claims made to programs

where the federal government reimburses, such as Medicaid, as well as programs where the federal government is a direct purchaser, such as when it purchases off the Federal Supply Schedule. Recently, several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly inflating drug prices they report to pricing services, which in turn were used by the government to set Medicare and Medicaid reimbursement rates, and for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product.

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In addition, certain marketing practices, including off-label promotion, may also violate false claims laws. Additionally, the Healthcare Reform Act amended the federal false claims law such that a violation of the federal healthcare program anti-kickback statute can serve as a basis for liability under the federal false claims law. The majority of states also have statutes or regulations similar to the federal anti-kickback law and false claims laws, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

Other federal statutes pertaining to healthcare fraud and abuse include the civil monetary penalties statute, which prohibits the offer or payment of remuneration to a Medicaid or Medicare beneficiary that the offerer/payor knows or should know is likely to influence the beneficiary to order a receive a reimbursable item or service from a particular supplier, and the healthcare fraud statute, which prohibits knowingly and willfully executing or attempting to execute a scheme to defraud any healthcare benefit program or obtain by means of false or fraudulent pretenses, representations, or promises any money or property owned by or under the control of any healthcare benefit program in connection with the delivery of or payment for healthcare benefits, items, or services.

Other Federal and State Regulatory Requirements

The Centers for Medicare & Medicaid Services, or CMS, has issued a final rule that implements a statutory requirement under the Healthcare Reform Act that requires applicable manufacturers of drugs, devices, biologicals, or medical supplies that are covered under Medicare, Medicaid, or the Children s Health Insurance Program, or CHIP, to begin collecting and reporting annually information on payments or transfers of value to physicians and teaching hospitals, as well as investment interests held by physicians and their immediate family members. Manufacturers had to begin collecting information in 2013, with the first reports due in 2014. On September 30, 2014, CMS posted the first round of data in searchable form on a public website. Failure to submit required information may result in civil monetary penalties.

In addition, several states now require prescription drug companies to report expenses relating to the marketing and promotion of drug products and to report gifts and payments to individual physicians in these states. Other states prohibit various other marketing-related activities. Still other states require the posting of information relating to clinical trials and their outcomes. In addition, California, Connecticut, Nevada, and Massachusetts require pharmaceutical companies to implement compliance programs and/or marketing codes. Several additional states are considering similar proposals. Compliance with these laws is difficult and time consuming, and companies that do not comply with these state laws face civil penalties.

Europe and Rest of the World Regulation

In addition to regulations in the United States, we will be subject to a variety of regulations in other jurisdictions both due to our location and the fact that we are engaging in clinical programs outside of the United States and will want to obtain worldwide regulatory approval for our TCR therapeutic candidates. Prior to supplying any TCR therapeutic candidate in any country or starting any clinical trials in any country outside of the United States we must obtain the requisite approvals from regulatory authorities in such countries. The existence of a United States regulatory approval does not guarantee that regulatory approvals will be obtained in other countries in which we wish to conduct clinical trials or market our TCR therapeutic candidates. In the EU, for example, a clinical trial application must be submitted to each country s national health authority and an independent ethics committee, much like the FDA and IRB, respectively prior to any clinical trial being conducted in the relevant country. A marketing authorization is then submitted prior to any commercial supply, again to each relevant country s national health authority.

The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, the clinical trials are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. However these requirements may well differ from country to country.

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Review and Approval of Drug Products outside of the United States

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of products. Whether or not it obtains FDA approval for a product, the company would need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. The approval process ultimately varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

Procedures Governing Approval of Products in the EU

Pursuant to the European Clinical Trials Directive, a system for the approval of clinical trials in the European Union has been implemented through national legislation of the member states. Under this system, an applicant must obtain approval from the competent national authority of a European Union member state in which the clinical trial is to be conducted. Furthermore, the applicant may only start a clinical trial after a competent ethics committee has issued a favorable opinion. Clinical trial application must be accompanied by an investigational medicinal product dossier with supporting information prescribed by the European Clinical Trials Directive and corresponding national laws of the member states and further detailed in applicable guidance documents.

To obtain marketing approval of a product under European Union regulatory systems, an applicant must submit a marketing authorization application, or MAA, either under a centralized or decentralized procedure. The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid for all European Union member states. The centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy products and products with a new active substance indicated for the treatment of certain diseases. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional.

Under the centralized procedure, the Committee for Medicinal Products for Human Use, or the CHMP, established at the EMA is responsible for conducting the initial assessment of a product. The CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. In this circumstance, the EMA ensures that the opinion of the CHMP is given within 150 days.

The decentralized procedure is available to applicants who wish to market a product in various European Union member states where such product has not received marketing approval in any European Union member states before. The decentralized procedure provides for approval by one or more other, or concerned, member states of an assessment of an application performed by one member state designated by the applicant, known as the reference member state. Under this procedure, an applicant submits an application based on identical dossiers and related materials, including a draft summary of product characteristics, and draft labeling and package leaflet, to the reference member state and

concerned member states. The reference member state prepares a draft assessment report and drafts of the related materials within 210 days after receipt of a valid application. Within 90 days of receiving the reference member state s assessment report and related materials, each concerned member state must decide whether to approve the assessment report and related materials.

If a member state cannot approve the assessment report and related materials on the grounds of potential serious risk to public health, the disputed points are subject to a dispute resolution mechanism and may eventually be referred to the European Commission, whose decision is binding on all member states.

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In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of drug products. Whether or not it obtains FDA approval for a product, the company would need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. The approval process ultimately varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

Marketing authorization is valid for five years in principle and the marketing authorization may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA or by the competent authority of the authorizing member state. To this end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. Once renewed, the marketing authorization is valid for an unlimited period, unless the Commission or the competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal. Any authorization which is not followed by the actual placing of the drug on the EU market (in case of centralized procedure) or on the market of the authorizing member state within three years after authorization ceases to be valid (the so-called sunset clause).

Legal Proceedings and Related Matters

From time to time, we may be party to litigation that arises in the ordinary course of our business. We do not have any pending litigation that, separately or in the aggregate, would, in the opinion of management, have a material adverse effect on our results of operations, financial condition or cash flows.

Employees

As of June 30, 2015, we had 116 full-time equivalent employees. Of these employees, 89 were in research and development (including in manufacturing and operations, and quality control and quality assurance) and 27 were in management and administrative functions (including business development, finance, intellectual property, information technology and general administration). We have never had a work stoppage and none of our employees are covered by collective bargaining agreements or represented by a labor union. We believe our employee relations are good.

C. Organizational Structure

The following is a list of our significant subsidiaries:

Name of undertaking	Country of registration	Activity	Percent holding
Adaptimmune Limited	England and Wales	Biotechnology Research and Development	100
Adaptimmune LLC	United States	Biotechnology Research and Development	100

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D. Property, Plants and Equipment

The following is a list of our existing leases. We have also set forth below additional information regarding new agreements that we recently entered into for the construction, fit-out and lease of new laboratory, manufacturing and office facilities in the United Kingdom and the United States.

Type	Location	Size (in square feet)	Expiry
Research & Development	Oxfordshire, United Kingdom	30,223	September 2020
Executive office	Oxfordshire, United Kingdom	9,738	June 2025
Executive office and Research & Development	Philadelphia, United States	29,773	August 2017

Our corporate headquarters and most of our operations, including our in-house research and laboratory facilities, are located at Milton Park, Oxfordshire, United Kingdom. The expiration date of all of our subleases of our research and laboratory facilities is September 21, 2020 and they each contain rolling mutual break option provisions effective from June 1, 2017 on service of six months prior written notice.

We believe that our office and research facilities in the United Kingdom are sufficient to meet our current needs. However, in anticipation of future demand, we have entered into an agreement effective from September 16, 2015 with MEPC Milton Park Limited, the owner of Milton Park, for the construction and lease of a new laboratory and office building of approximately 67,000 square feet in Oxfordshire.

Our clinical trial operations in the United States are managed through our subsidiary company, Adaptimmune LLC, located in Philadelphia. We believe that our office and research facilities in the United States are sufficient to meet our current needs. However, in anticipation of future demand, we have entered into an agreement effective from July 28, 2015 for the construction and lease of a new manufacturing, laboratory and office facility of approximately 47,400 square feet in Philadelphia.

Further details of our Plant and Equipment are given in Note 11 to our consolidated financial statements included elsewhere in this Annual Report.

Item 4A. Unresolved Staff Comments.

None

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 Item 3. Key information A. Selected Financial Data, and our consolidated financial statements included elsewhere in this Annual Report, which have been prepared in accordance with International Financial Reporting Standards, or IFRS, as issued by the International Accounting Standards Board, or IASB, and as adopted by the European Union and audited in accordance with the standards of the Public Company Accounting Oversight Board (United States).

The statements in this discussion regarding industry outlook, our expectations regarding our future performance, liquidity and capital resources and other non-historical statements are forward-looking statements. These forward-looking statements are subject to numerous risks and uncertainties, including, but not limited to, the risks and uncertainties described in Risk Factors and Forward-Looking Statements in this Annual Report. Our actual results may differ materially from those contained in or implied by any forward-looking statements.

Solely for the convenience of the reader, unless otherwise indicated, all pounds sterling amounts as at and for the year ended June 30, 2015 have been translated into U.S. dollars at the rate at June 30, 2015, the last business day of our year ended June 30, 2015, of £1.00 to $1.5727. These translations should not be considered representations that any such amounts have been, could have been or could be converted into U.S. dollars at that or any other exchange rate as at that or any other date.

We have historically conducted our business through Adaptimmune Limited and its subsidiary, and therefore our historical financial statements present the consolidated results of operations of Adaptimmune Limited. Following the Corporate Reorganization, our financial statements present the consolidated results of Adaptimmune Therapeutics plc.

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A. Operating Results.

Important Financial and Operating Terms and Concepts

Revenue

To date, we have not generated any revenue from the sales of our TCR therapeutic candidates. Our revenues have been solely derived from our collaboration and license agreement with GSK. The terms of this arrangement contain multiple milestones associated with: (i) co-development of our NY-ESO TCR therapeutic candidate, (ii) associated manufacturing optimization work and (iii) co-development of other TCR target programs. Fair value is attributable to these elements based on the value attributed to each by the partner. GSK is also obligated to pay us certain milestone fees, which are generally non-refundable and are payable upon satisfactory completion of specified research and development activities.

Other Income

We generate grant income primarily through research and development grant programs offered by the U.K. and EU governments. We recognize grant income when there is reasonable likelihood that we will receive the grant and we have complied with the terms of the grant.

We also have received income from Immunocore under a transitional services agreement.

Research and Development Expenses

Research and development expenses consist principally of:

- salaries for research and development staff and related expenses, including management benefits;
- costs for production of preclinical compounds and drug substances by contract manufacturers;

- fees and other costs paid to contract research organizations in connection with additional preclinical testing and the performance of clinical trials;

- costs of related facilities, materials and equipment;

- costs associated with obtaining and maintaining patents and other intellectual property;

- amortization and depreciation of tangible and intangible fixed assets used to develop our TCR therapeutic candidates; and

- share-based compensation expenses.

We expense research and development costs as incurred. We recognize costs for certain development activities based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors and our clinical sites.

During the fiscal year ended June 30, 2016, we plan to increase the number of clinical trials we are running, both in new indications (including our MAGE-A10 and AFP TCR therapeutic candidate) and as part of the GSK collaboration for our NY-ESO TCR therapeutic candidate. In order to commence these trials, we must incur in advance the costs of preclinical testing, vector production and other substances. The process optimization activities planned under the GSK collaboration will also require a large increase in the research and development expenses, which we expect will be funded by receipt of milestone payments from GSK. We expect to increase the number of staff employed in our research and development departments in order to invest in our future pipeline of TCR therapeutic candidates, develop our platform and manage clinical trials. This will significantly increase the related salaries and share-based compensation expenses, as well as require higher expenditures on facilities, materials and equipment.

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We expense research and development costs as incurred. We recognize costs for certain development activities based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors and our clinical sites.

Our research and development expenses may vary substantially from period to period based on the timing of our research and development activities, which depends upon the timing of initiation of clinical trials and the rate of enrollment of patients in clinical trials. We expect research and development expenses to increase as we advance the development of our preclinical TCR therapeutic candidates. The successful development of our TCR therapeutic candidates is highly uncertain. At this time, we cannot reasonably estimate the nature, timing and estimated costs of the efforts that will be necessary to complete the development of, or the period, if any, in which material net cash inflows may commence from, any of our TCR therapeutic candidates.

We may never succeed in achieving regulatory approval for any of our TCR therapeutic candidates. The duration, costs, and timing of clinical trials and development of our TCR therapeutic candidates will depend on a variety of factors, including:

- the scope, rate of progress, and expense of our ongoing as well as any additional clinical trials and other research and development activities;
- uncertainties in clinical trial enrollment rate;
- future clinical trial results;
- significant and changing government regulation; and
- the timing and receipt of any regulatory approvals.

A change in the outcome of any of these variables may significantly change the costs and timing associated with the development of that TCR therapeutic candidate. For example, if the FDA, or another regulatory authority, requires us to conduct clinical trials beyond those that we currently anticipate will be required for regulatory approval, or if we experience significant delays in enrollment in any of our clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development.

General and Administrative Expenses

Our general and administrative expenses consist principally of:

- salaries for employees other than research and development staff, including benefits;
- business development expenses, including travel expenses;
- professional fees for auditors and other consulting expenses not related to research and development activities;
- professional fees for lawyers not related to the protection and maintenance of our intellectual property;
- cost of facilities, communication, and office expenses;
- information technology expenses;
- amortization and depreciation of tangible and intangible fixed assets not related to research and development activities; and
- share-based compensation expenses.

We expect that our general and administrative expenses will continue to increase, primarily due to the costs of operating as a public company, such as additional legal, accounting, and corporate governance expenses, including expenses related to compliance with the Sarbanes-Oxley Act, directors and officers insurance premiums, and investor relations. In addition, we were initially formed without our own administrative infrastructure and therefore relied on Immunocore, a company with whom we have a shared history, to provide certain administrative services to us under a facilities and services agreement. Over the past year we have put in place our own administrative infrastructure and therefore no longer rely on Immunocore to provide administrative services to us.

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We also have a number of other agreements with Immunocore but we have always maintained separate financial statements. See Related Party Transactions Agreements with Immunocore Limited.

Finance Income and Costs

Finance income includes interest earned on our instant-access cash reserves as well as foreign exchange gains on cash held in U.S. dollars. Finance costs consist primarily of interest charged on any bank overdrafts and foreign exchange losses on cash held in U.S. dollars.

Taxation

We are subject to corporate taxation in the United Kingdom. Our subsidiary Adaptimmune LLC is subject to corporate taxation in the United States. Our tax recognized represents the sum of the tax currently payable or recoverable. No deferred tax assets are recognized on our losses carried forward because there is currently no indication that we shall make sufficient profits to utilize these tax losses.

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 our principal research subsidiary company, Adaptimmune Limited, is able to surrender the trading losses that arise from its research and development activities for a payable tax credit of up to 33.4% 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. Subcontracted research expenditures are eligible for a cash rebate of up to 21.7%. A large proportion of costs in relation to our pipeline research, clinical trials management and manufacturing development activities, all of which are being carried out by Adaptimmune Limited, are eligible for inclusion within these tax credit cash rebate claims.

We may not be able to claim such research and development tax credits on research and development expenditures in relation to the GSK collaboration and licensing agreement because they may be considered as subsidized expenditures. We may not be able to continue to claim research and development tax credits (R&D tax credits) in the future as we increase our personnel and expand our business because we may no longer qualify as an SME (small or medium-sized enterprise). In order to qualify as an SME for R&D tax credits, we must continue to be a company with fewer than 500 employees and also have either an annual turnover not exceeding 100 million or a balance sheet not exceeding 86 million.

Unsurrendered tax losses can be carried forward to be offset against future taxable profits. After accounting for tax credits receivable, there are accumulated tax losses for carry forward in the United Kingdom amounting to £23 million at June 30, 2015. No deferred tax asset is recognized in respect of accumulated tax losses on the basis that suitable future trading profits are not sufficiently certain.

We may also benefit in the future from the United Kingdom s patent box regime, which would allow certain profits attributable to revenues from patented products to be taxed at a rate that over time will be reduced to 10%. As we have many different patents covering our products, future upfront fees, milestone fees, product revenues, and royalties could be taxed at this favorably low 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. As such, we consider that the United Kingdom is a favorable location for us to continue to conduct our business for the long term.

Value Added Tax (VAT) is charged on all qualifying goods and services by VAT-registered businesses. An amount of 20% of the value of the goods or services is added to all sales invoices and is payable to the U.K. tax authorities. Similarly, VAT paid on purchase invoices is reclaimable from the U.K. tax authorities.

Critical Judgments in Applying our Accounting Policies

In the application of our accounting policies, we are required to make judgments, estimates, and assumptions about the value of assets and liabilities for which there is no definitive third party reference. The estimates and associated assumptions are based on historical experience and other factors that are considered to be relevant. Actual results may differ from these estimates.

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Our estimates and assumptions are reviewed on an ongoing basis. Revisions to accounting estimates are recognized in the period in which the estimate is revised if the revision affects only that period or in the period of the revisions and future periods if the revision affects both current and future periods.

The following are our critical judgments, except those involving estimation uncertainty, that we have made in the process of applying our accounting policies and that have the most significant effect on the amounts recognized in our consolidated financial statements included elsewhere in this Annual Report.

Revenue Recognition

We recognize revenue in accordance with IAS 18. Revenue is recognized to the extent that it obtains the right to consideration in exchange for its performance and is measured at the fair value of the consideration received excluding Value-Added Tax (VAT).

Our revenue to date has been derived solely from the supply of services under the GSK collaboration and licensing agreement and represents the value of contract deliverables. Payments under the agreement include advanced payments upon commencement of various work-streams or milestone payments.

If a payment is for multiple deliverables, judgment is required to attribute the fair value to the various elements. We do not consider there to be observable third party price information for the fair value of our deliverables; the most reliable evidence available to us for fair value attribution is the value of our deliverables separately negotiated with GSK, which is an acceptable basis under IAS 18. The only instance where a payment has been for multiple deliverables is the upfront consideration we received from GSK, which was allocated between the license agreement, a contribution to development activities and a contribution to new targets. Revenue for all of these is recognized as services are provided.

If a contract deliverable has only been partially completed at the balance sheet date, revenue is calculated by reference to the value of services performed as a proportion of the total services to be performed for each deliverable, or on a straight-line basis if the pattern of performance cannot be estimated. The amount of revenue recognized is limited to non- refundable amounts already received or reasonably certain to be received.

If payments are received from a customer in advance of services provided, the amounts are recorded as deferred income and are included within liabilities.

We consider payments reasonably certain to be received at the point that satisfactory criteria are agreed with GSK. We regularly review the proportion of total services to be performed for each deliverable or the period of time over which the revenue is deferred based on facts known at the time. The process involves review of monthly expenditures and inquiry with our personnel to monitor the performance of the GSK collaboration and license agreement. If circumstances arise that may change the original estimates of progress toward completion of a deliverable, then estimates are revised. These revisions may result in increases or decreases in estimated revenues and are reflected in income in the period in which the circumstances that give rise to the revision become known to management.

Performance of contract deliverables may vary significantly over time from initial estimates, and, therefore, the amount of revenue recognized is subject to variations. Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differs from the actual status and timing of services performed, we may report amounts that are too high or too low in any particular period. To date, there has been no material difference from our estimates to the amount of revenue that can be reliably recognized.

Research and Development Expenditures, including Clinical Trial Expenses

Research and development expenditures include direct and indirect costs of these activities, including staff costs and materials, as well as external contracts. All such expenditures are expensed as incurred unless the capitalization criteria of IAS 38 have been satisfied, in which case the costs are capitalized as intangible assets. To date, we do not believe any expenditure meets the capitalization criteria because of the uncertainty of successfully completing pivotal clinical trials and obtaining regulatory approval.

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As part of the process of preparing our financial statements, we are required to estimate our accrued 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 the actual cost. The majority of our service providers invoice us monthly in arrears for services performed. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. We may confirm the accuracy of our estimates with the applicable service providers and make adjustments if necessary. Examples of estimated accrued research and development expenses include fees paid to: CROs in connection with clinical trials; operators of investigative sites in connection with clinical trials; vendors in connection with preclinical development activities; and vendors related to product manufacturing, development and distribution of clinical supplies.

We base our expenses related to clinical trials on our estimates of the services received and efforts expended pursuant to contracts with multiple CROs that conduct and manage 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 clinical expense. Payments under some of these contracts depend on factors such as the successful enrollment of subjects 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 our estimate, we adjust the accrual or prepaid amount accordingly.

Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, we may report amounts that are too high or too low in any particular period. To date, there has been no material difference between our estimates and the amount actually incurred.

Key Sources of Estimation Uncertainty

The key assumptions concerning the future, and other key sources of estimation uncertainty at the balance sheet date, that have a significant risk of causing a material adjustment to the carrying amounts of assets and liabilities within the next year are discussed below.

Share-based Compensation

We award options to certain of our employees, directors and consultants to purchase shares in our parent company. All of these arrangements are settled in equity at a predetermined price and generally vest over a period of three to four years. All share options have a life of 10 years before expiration. We measure share-based compensation at the grant date based on the fair value of the award and we recognize it as an expense over the required service period, which is generally equal to the vesting period. We determine the fair value of our share options using the Black-Scholes option-pricing model, with a corresponding increase in reserves.

Our share-based compensation expense was as follows:

	Year Ended June 30,		
	2015	2014	2013
	£ (in thousands)		
General and administrative	1,819	130	48
Research and development	864	75	64
Total share-based compensation expense	£ 2,683	£ 205	112

In future periods we expect our share-based compensation expense to increase due in part to our existing unrecognized share-based compensation expenses and as we grant additional share-based awards to continue to attract and retain our employees.

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Valuation of Share Options

The Black-Scholes option pricing model requires the input of subjective assumptions, including assumptions about share price volatility, the expected life of share-based compensation awards, the risk free rate and the underlying share valuation.

Share price volatility

Based on our analysis of similar companies, we have concluded that a volatility of 60% is appropriate for our valuation of our share options. We intend to continue to consistently apply this methodology using the same comparable companies until a sufficient amount of historical information regarding the volatility of our own share price as a public company becomes available.

Expected life

We use a five-year expected life in valuing our share options beginning with the option grant date. The expected life we use in the calculation of share-based compensation is the time from the grant date to the expected exercise date. The life of the options depends on the option expiration date, volatility of the underlying shares and vesting features.

Risk free rate

IFRS 2 requires the use of the risk-free interest rate of the country in which the entity s shares are principally traded with a remaining term equal to the expected life of the option. We have applied the appropriate risk-free rate, using the Bank of England s estimates of gilt yield curve as of the respective share option grant dates.

Valuation of underlying shares

The Black-Scholes model requires an assumption of the underlying share price at the date that options are granted, which may be different from the option exercise price. Prior to our IPO, the valuation of our ordinary shares required a number of judgments and assumptions.

In valuing options granted prior to our IPO, we have considered the relevant guidance set forth in the American Institute of Certified Public Accountants Practice Aid: Valuation of Privately-Held Company Equity Securities Issued as Compensation . After considering the market approach, the income approach and the asset-based approach, we utilized the market approach to determine the estimated fair value of our ordinary shares based on our view that this approach was most appropriate for a clinical stage biopharmaceutical company at that point in our

business. To assess the valuation using the market approach we considered the likelihood of completing an IPO, recent transactions we entered into with investors around that time and the reports of an independent third party valuation firm.

On March 31, 2014, we issued 31,028,500 ordinary shares at a price of £0.14 per ordinary share to existing and new investors. These purchasers were aware of the possibility of a partnership with a large pharmaceutical company as well as other potential funding sources. At the time, there were no plans for an IPO and the majority of our shareholders did not subscribe to this offering. We subsequently issued share options on March 31, April 14, April 15, April 17 and April 30, 2014 with an exercise price of £0.112 per share. The underlying share price for each of these option grants for the purposes of the Black Scholes valuation was £0.14 per ordinary share, the same price of the shares purchased by investors on March 31, 2014. As part of the valuation analysis, our Board determined that there were no significant internal or external value generating events between March 31 and April 30, 2014 that would have materially altered the underlying share price.

On June 2, 2014, we announced our collaboration and license agreement with GSK and on September 23, 2014, we issued 175,841,800 Series A preferred shares at a price of £0.3557 per preferred share to new investors. These shares were convertible to ordinary shares at a rate of one-for-one upon a qualified IPO if it occurs within twelve months of issuance of the Series A preferred shares. On December 19 and December 31, 2014, we issued share options based on an underlying share price of £0.3557 per share. Following the issuance of these options, we received and considered a valuation prepared by an independent third-party valuation firm using the Market Approach for enterprise valuation, which incorporated the Probability Weighted Expected Return Method, or PWERM, and determined that £0.39 per share was the appropriate price to be used in the Black-Scholes Option Pricing Model, or OPM.

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In March 2015 we issued options with an exercise price of £0.50 per share based on a contemporaneous independent valuation analysis of our ordinary shares as at March 2, 2015 of £0.50 per share. At that point in time, we had not yet received guidance from the IPO underwriting team on a proposed preliminary price range for the IPO and the related valuation. On April 2, 2015, we held preliminary discussions of our IPO price with our underwriters and therefore we reassessed our original contemporaneous March 2, 2015 valuation of £0.50 for our ordinary shares considering this new information. For purposes of this reassessment, we revised our valuation of the share price by revisiting the PWERM methodology with the hindsight of the expected company valuation in the event of a successful IPO. With no significant internal or external value-generating events occurring between December 19, 2014 and April 2, 2015, we adopted a straight line approach to the increase in value over this period in determining an underlying share price of £0.86 per ordinary share for the March options.

Since May 2015, there is a publically observable ADS and related share price. Those options issued on May 11, 2015 were based on the IPO price of $17 per ADS, which is equivalent to £1.82 per ordinary share.

The following table summarizes by grant date the number of ordinary shares subject to options granted from March 2014 through May 2015, the per share exercise price of the award, the fair value of our ordinary shares on each grant date, and the per share estimated fair values of the awards:

Date of Issuance	Type of Award	Number of Shares	Exercise Price of Award per Share	Fair Value of each Ordinary Share at the Grant Date(1)	Per Share Estimated Fair Value of Awards(2)
March 2014	Option	5,627,700	£ 0.112	£ 0.14	£ 0.08
December 2014	Option	10,710,000	£ 0.3557	£ 0.39	£ 0.21
March 2015	Option	9,183,962	£ 0.50	£ 0.86	£ 0.55
May 2015	Option	1,885,615	£ 1.82	£ 1.82	£ 0.94

(1) The fair value of each ordinary share at the grant date represents the estimated value of each ordinary share after taking into account our most recently available valuations of our ordinary shares as well as additional information available to our Board. From May 11, 2015 the fair value reflects the publically observable price.

(2) The per share estimated fair value of awards reflects the weighted average fair value of options as estimated at the date of the applicable grant using the Black-Scholes option-pricing model.

Deferred Tax and Current Tax Credits

Tax on the profit or loss for the year comprises current and deferred tax. Tax is recognized in the income statement, except to the extent that it relates to items recognized directly in equity, in which case it is recognized in equity.

Current tax is the expected tax payable on the taxable income or loss for the year, using tax rates enacted or substantively enacted at the balance sheet date, and any adjustment to tax payable in respect of previous years.

Tax credits are accrued for the year based on calculations that conform to the U.K. research and development tax credit regime applicable to small and medium sized companies.

We may not be able to claim such research and development tax credits on research and development expenditures in relation to the GSK collaboration and licensing agreement because they may be considered as subsidized expenditures. We may not be able to continue to claim research and development tax credits (R&D tax credits) in the future as we increase our personnel and expand our business because we may no longer qualify as an SME (small or medium-sized enterprise). In order to qualify as an SME for R&D tax credits, we must continue to be a company with fewer than 500 employees and also have either annual revenues of less than 100 million or less than 86 million of assets on our balance sheet.

Deferred tax is provided on temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for taxation purposes. The amount of deferred tax provided is based on the expected manner of realization or settlement of the carrying amount of assets and liabilities, using tax rates enacted or substantively enacted at the balance sheet date.

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A deferred tax asset is recognized only to the extent that it is probable that future taxable profits will be available against which the asset can be utilized. No deferred tax assets are recognized on our losses carried forward because there is currently no indication that we shall make sufficient profits to utilize these tax losses.

Results of Operations

Comparison of Years Ended June 30, 2015 and 2014

The following table summarizes the results of our operations for the years ended June 30, 2015 and 2014, together with the changes to those items.

	Year Ended June 30,			Change Increase/ decrease	
	2015 $	2015 £	2014 £	£	%
	(in thousands, except for percentages)				
Revenue	**10,723**	**6,818**	**355**	**6,463**	NM
Research and development expenses	(23,196)	(14,749)	(7,356)	(7,393)	101%
General and administrative expenses	(11,325)	(7,201)	(1,602)	(5,599)	350%
Other income	727	462	165	297	180%
Operating loss	**(23,071)**	**(14,670)**	**(8,438)**	**(6,232)**	**74%**
Finance income	506	322	2	320	NM
Finance expense	(1,132)	(720)	(4)	(716)	NM
Loss before tax	**(23,697)**	**(15,068)**	**(8,440)**	**(6,628)**	**79%**
Taxation credit	2,105	1,339	982	357	36%
Loss for the year	**(21,592)**	**(13,729)**	**(7,458)**	**(6,271)**	**84%**

NM = not meaningful

Revenue

Revenue increased from £0.4 million for the year ended June 30, 2014 to £6.8 million for the year ended June 30, 2015 due to a full year of recognition of revenue under the collaboration and licensing agreement with GSK, which was entered into on May 30, 2014. Although it is difficult to project the progress through the deliverables of the collaboration and timing of future milestone income, we expect our revenue in the year to June 30, 2016 to be higher than the same period in the year ended June 30, 2015 due to recognition of revenue in connection with work performed under the GSK agreement, in relation to existing deferred revenue and future milestones.

Research and Development Expenses

Research and development expenses increased by 101% to £14.7 million for the year ended June 30, 2015 from £7.4 million for the year ended June 30, 2014. Our research and development expenses are highly dependent on the phases of our research projects and therefore fluctuate from year to year. Although it is difficult to project the levels of such spending due to the variety of factors affecting the related trials, we expect our total research and development expenses in the year ended June 30, 2016 to be higher than our expenses in our years ended June, 2014 and 2015 due to the ongoing advancement of our preclinical programs and clinical trials.

The increase in our research and development expenses in the year ended June 30, 2015 from the same period in 2014 was primarily due to an increase in two key drivers of our expenses:

- The increase in the average number of employees engaged in research and development from an average of 27 to 63. These costs include salaries, facilities, materials, equipment, depreciation of tangible fixed assets, and expenses for share-based compensation; and

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- An increase in subcontracted expenditures, including clinical trial expenses, CRO costs, and manufacturing expenses drive by increased recruitment in our clinical trials.

We have not historically tracked the internal costs of each research and development project since employees may be engaged in multiple projects at a time. In the year ended June 30, 2015, we employed an average of 13 employees working in our clinical and development teams, primarily responsible for development of our TCR therapeutic candidates targeting NY-ESO and MAGE-A10. The remainder of our scientific employees are engaged in developing our future pipeline.

Our subcontracted costs for the year ended June 30, 2015 were £5.6 million, of which £3.2 million related to our TCR therapeutic candidate targeting NY-ESO and the remaining £2.4 million related to other projects, including our MAGE-A10 TCR therapeutic candidate.

During the fiscal year ended June 30, 2016, we plan to increase the number of clinical trials we are running, both in new indications (including our MAGE-A-10 TCR therapeutic candidate) and as part of the GSK collaboration for our NY-ESO TCR therapeutic candidate. In order to commence these trials, we must incur in advance the costs of preclinical testing, vector production and other substances. The process optimization activities planned under the GSK collaboration will also require a large increase in the research and development expenses, which we expect will be funded by receipt of milestone payments from GSK. We expect to increase the number of staff employed in our research and development departments in order to invest in our future pipeline of TCR therapeutic candidates, develop our platform and manage clinical trials. This will significantly increase the related salaries and share-based compensation expenses, as well as require higher expenditures on facilities, materials and equipment.

General and Administrative Expenses

General and administrative expenses increased by 350% to £7.2 million for the year ended June 30, 2014 from £1.6 million in the same period in 2014. The increase of £5.6 million was due to:

- £1.8 million of increased personnel costs, primarily due to the addition of key management and other professionals to support our growth;

- £1.7 million of increased share-based payment expenses;

- £0.5 million of increased property costs; and

- £1.6 million of increased other corporate costs, including costs in relation to our Nasdaq listing, legal entity restructuring, consultants, additional audit costs and investor relations.

We expect that our general and administrative expenses will continue to increase, primarily due to the costs of operating as a public company, such as additional legal, accounting, and corporate governance expenses, including expenses related to compliance with the Sarbanes-Oxley Act, directors and officers insurance premiums, and investor relations. In addition, we were initially formed without our own administrative infrastructure and therefore relied on Immunocore, a company with whom we have a shared history, to provide certain administrative services to us under a facilities and services agreement. Over the past year we have put in place our own administrative infrastructure and therefore no longer rely on Immunocore to provide administrative services to us.

We also have a number of other agreements with Immunocore but we have always maintained separate financial statements and audit procedures. See Related Party Transactions Agreements with Immunocore Limited.

Other Income

Other income consists of grant income primarily generated through research and development grant programs offered by the U.K. and EU governments and income from Immunocore under a transitional services agreement. Grant income is recognized as we incur and pay for qualifying costs and services under the applicable grant.

Other income increased by 180% to £0.5 million for the year ended June 30, 2015 from £0.2 million for the year ended June 30, 2014 due to an increase in grant income. Grant income has increased due to an increase in qualifying costs and services on projects subject to U.K. grants.

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We expect that our other income in the year to June 30, 2016 will continue to increase due to a further increased in in qualifying costs and services on projects subject to U.K. and E.U grants.

Finance Income

Finance income increased to £0.3 million for the year ended June 30, 2015 from £0.0 million for the year ended June 30, 2014. Finance income consisted of bank interest on cash balances and short-term deposits and has increased due to an increase in cash balances.

We expect that our finance income for the year to June 30, 2016 will increase due an increase in interest income resulting from higher average cash balances and short-term deposits.

Finance Expense

Finance expense increased to £0.7 million for the year ended June 30, 2015 from £0.0 million for the year ended June 30, 2014. Finance expense consisted of foreign exchange losses on foreign currency transactions.

Taxation Credits

The research and development tax credit increased by 36% to £1.3 million for the year ended June 30, 2015 from £1.0 million in the year ended 30, June 2014. The increase was driven by the increase in our research and development expenditures; the increase in the proportion of those expenditures that is eligible for research and development tax credits.

The amount of tax credits we will receive is entirely dependent on the amount of eligible expenses we incur. As we expect our eligible expenses to be higher in the year ended June 30, 2016, the level of tax credits recoverable is anticipated to be higher in the year ended June 30, 2016 compared to the year ended June 30, 2015.

The amount of tax credits we will receive will depend on the amount of eligible expenses we incur. We expect our eligible expenses to be higher in our current fiscal year and therefore we anticipate the level of recoverable tax credits will be higher in the current fiscal year compared to the year ended June 30, 2015.

Comparison of Years Ended June 30, 2014 and 2013

The following table summarizes the results of our operations for the years ended June 30, 2014 and 2013, together with the changes to those items.

	Year Ended June 30,		Change	
	2014	2013	Increase/(Decrease)	
	£	£	£	%
	(in thousands, except for percentages)			
Revenue	**355**		**355**	**N/A**
Research and development expenses	(7,356)	(5,361)	(1,995)	37%
General and administrative expenses	(1,602)	(797)	(805)	101%
Other income	165	7	158	2257%
Operating loss	**(8,438)**	**(6,151)**	**(2,287)**	**37%**
Finance income	2	9	(7)	(78)%
Finance expense	(4)	(4)		N/A
Loss before tax	**(8,440)**	**(6,146)**	**(2,294)**	**37%**
Taxation credit	982	578	404	70%
Loss for the year	**(7,458)**	**(5,568)**	**(1,890)**	**34%**

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Revenue

Revenue increased from £0.0 for the year ended June 30, 2013 to £0.4 million for the year ended June 30, 2014 due to recognition of revenue under the collaboration and licensing agreement with GSK, which was entered into on May 30, 2014.

Research and Development Expenses

Research and development expenses increased by 37% to £7.4 million for the year ended June 30, 2014 from £5.4 million in the same period in 2013. Our research and development expenses are highly dependent on the phases of our research projects and therefore fluctuate from year to year.

The increase in our research and development expenses in the year ended June 30, 2014 from the same period in 2013 was primarily due to an increase in two key drivers of our expenses:

- The increase in the number of employees engaged in research and development from an average of 17 to 27. These costs include salaries, facilities, materials, equipment, depreciation of tangible fixed assets, and expenses for share-based compensation; and

- An increase in subcontracted expenditures, including clinical trial expenses, CRO costs, and manufacturing expenses drive by increased recruitment in our clinical trials.

We have not historically tracked the internal costs of each research and development project since employees may be engaged in multiple projects at a time. In the year ended June 30, 2014, we employed an average of 11 employees working in our clinical and development teams, primarily responsible for development of our TCR therapeutic candidates targeting NY-ESO and MAGE-A-10. The remainder of our scientific employees are engaged in developing our future pipeline.

Our subcontracted costs for the year ended June 30, 2014 were £3.2 million, which were substantially all related to our TCR therapeutic candidate targeting NY-ESO.

General and Administrative Expenses

General and administrative expenses increased by 101% to £1.6 million for the year ended June 30, 2014 from £0.8 million in the same period in 2013. This was primarily due to the addition of key management and other professionals, and related costs to support our growth.

Finance Income and Finance Expense

Finance income and finance expense were both less than £0.1 million for the years ended June 30, 2014 and 2013. Finance income consisted of bank interest on cash balances and short-term deposits. Finance expense consisted of bank interest on overdraft arrangements.

Taxation Credit

The research and development tax credit increased by 70% to £1.0 million for the year ended June 30, 2014 from £0.6 million in the same period in 2013. The increase was driven by the increase in our research and development expenditures; the increase in the proportion of those expenditures that is eligible for research and development tax credits; and an increase in the rate of tax credits from 11.0% to 14.5% that became effective on April 1, 2014.

B. Liquidity and Capital Resources.

Sources of Funds

Since our inception, we have incurred significant net losses and negative cash flows from operations, with the exception of the year ended June 30, 2014, when we incurred a net loss but generated positive cash flows from operations because we received payments under our collaboration and licence agreement with GSK. We incurred net losses of £13.7 million, £7.5 million and £5.6 million in the years ended June 30, 2015, 2014 and 2013, respectively and expect our losses to increase in future. We used £5.1 million of cash for operating activities for the year ended June 30, 2013, generated £21.9 million of cash from operating activities in the year ended June 30, 2014 and used £20.8 million of cash for operating activities for the year ended June 30, 2015. As of June 30, 2015, we had an accumulated deficit of £30.2 million.

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As of June 30, 2015, we had cash and cash equivalents of £145.7 million, in addition to current asset investments of £35.2 million. We therefore consider our total cash position to be £180.9 million, the sum of these two. Prior to the IPO, we financed our operations primarily through private placements of equity securities, government grants, research and development tax credits, and payments for collaborative research and development services. In the year ended June 30, 2015, we raised £63.6 million through the sale of Series A preferred shares before the deduction of fees of £3.0 million and subsequently raised a further £124.1 million in our IPO before deduction of underwriter fees of £8.7 million and other offering expenses of £1.2 million. In the year ended June 30, 2015, we received cash payments of £4.5 million from GSK upon the achievement of milestones under the GSK collaboration and license agreement. The total revenue recognized under the GSK collaboration in the year ended June 30, 2015 was £6.8 million. In the year ended June 30, 2014, we received an up-front payment of £25 million under our collaboration and license agreement with GSK. From inception to June 30, 2015, we have recognized £1.0 million of income in the form of government grants from the United Kingdom and the European Union, and we have recognized £3.5 million in the form of research and development tax credits.

We believe that our cash and cash equivalents as of June 30, 2015 of £145.7 million coupled with the £35.2 million of current asset investments will be sufficient to fund our operations, including currently anticipated research and development activities and planned capital spending, for the foreseeable future, including for at least the next 24 months.

If we obtain regulatory approval to advance any of our TCR therapeutic candidates into pivotal clinical trials or to commercialization, we will incur significant research and development expenses, and also commercialization expenses related to product sales, marketing, manufacturing and distribution. Accordingly, we will seek to fund our operations through milestone payments under our agreement with GSK and additional financings.

Cash Flows

The following table summarizes the results of our cash flows for the years ended June 30, 2015, 2014 and 2013.

	Year Ended June 30,			
	2015	**2015**	**2014**	**2013**
	$	**£**	**£**	**£**
		(in thousands)		
Net cash (used in)/from operating activities	(32,740)	(20,818)	21,860	(5,108)
Net cash used in investing activities	(60,288)	(38,334)	(851)	(105)
Net cash from financing activities	274,771	174,713	9,944	2,436
Cash and cash equivalents	229,089	145,666	30,105	(848)

Operating Activities

Net cash used in operating activities was £5.1 million for the year ended June, 30, 2013. The loss before taxation for the year ended June 30, 2013 was £6.1 million, which included noncash items of £0.1 million. The noncash items consisted primarily of equity-settled share-based

compensation expense. We also had a net cash inflow of £0.6 million from changes in operating assets and liabilities during the period. The significant items in the changes in operating assets and liabilities were an increase in trade payables and accruals by £0.7 million as a result of increased operating expenditures. In 2013, we also received a £0.3 million research and development tax credit relating to research and development activities performed in the previous year.

Net cash from operating activities was £21.9 million for the year ended June 30, 2014. This was significantly influenced by receipt of a payment of £25 million from GSK upon initiation of the collaboration and licensing agreement.

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The loss before taxation for the year ended June 30, 2014 was £8.4 million, which included noncash items of £0.5 million. The noncash items consisted primarily of depreciation expense on plant and equipment £0.1 million, equity-settled share-based compensation expense £0.2 million, and foreign exchange translation differences of £0.1 million. We also had a net cash inflow of £29.2 million from changes in operating assets and liabilities during the period. The significant items in the changes in operating assets and liabilities were an increase in deferred income in relation to the GSK collaboration and licensing agreement by £24.6 million and an increase in the VAT liability by £5.0 million, primarily as a result of VAT payable on the initial payment received from GSK. In 2014, we received a £0.6 million research and development tax credit relating to research and development activities performed in the previous year.

Net cash used in operating activities was £20.8 million for the year ended June 30, 2015. The loss before taxation for the year ended June 30, 2015 was £15.1 million, which included noncash items of £3.2 million. The noncash items consisted primarily of depreciation expense on plant and equipment £0.4 million and equity-settled share-based compensation expense £2.6 million. We also had a net cash outflow of £8.7 million from changes in operating assets and liabilities during the period due to a decrease in deferred income in relation to the GSK collaboration and licensing agreement by £2.3 million and a decrease in the VAT liability of £5.0 million, primarily as a result of VAT payable at June 30, 2014 on the initial payment received from GSK..

Cash (used in)/from operating activities was largely influenced by the GSK collaboration and licensing agreement initial payment of £25 million received in June 2014. This incurred 20% VAT of £5 million and therefore cash flows in relation to this initial payment were an inflow of £30 million in the year ending June 20, 2014 and an outflow of £5 million in the year ending June 30, 2015 in relation to the VAT liability. Stripping out the effect of this, the cash outflows from operating activities would have been £15.8 million and £8.2 million for the years ended June 30, 2015 and 2014 respectively. The increase in cash used in operations without the GSK initial payments was primarily the result of an increase in research and development costs due to the ongoing advancement of our preclinical programs and clinical trials, and an increase in general and administrative expenses.

Investing Activities

Net cash used in investing activities was £0.1 million, £0.9 million and £38.3 million for the years ended June 30, 2013, 2014 and 2015, respectively. These amounts included purchases of property and equipment of £0.1 million, £0.9 million and £3.1 million for the years ended June 30, 2013, 2014 and 2015, respectively, related predominantly to the expansion of our laboratory facilities in the United Kingdom. The net cash used in investing activities in the year ended June 30, 2015 also included the investment of £35.2 million in short-term cash deposits with maturities greater than three months but less than 12 months.

Financing Activities

Net cash from financing activities was £2.4 million, £9.9 million and £174.7 million for the years ended June 30, 2013, 2014 and 2015, respectively. Net cash from financing activities for the year ended June 30, 2015 consisted of proceeds of £60.6 million, after the deduction of fees of £3.0 million, from issuing 1,758,418 Series A Preferred Shares and proceeds of £114.2 million, after the deduction of fees of £9.9 million, from issuing 67,500,000 ordinary shares. The Preferred Shares were automatically converted to ordinary shares on a 1:1 basis immediately prior to the admission to trading of our ADSs on Nasdaq.

Net cash from financing activities for the year ended June 30, 2014 consisted of proceeds of £9.9 million from issuing 715,866 ordinary shares.

Net cash from financing activities for the year ended June 30, 2013 consisted of proceeds of £2.4 million from issuing 167,914 ordinary shares.

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

Full details of our research and development activities and expenditures are given in Item 4. Information on the Company - B. Business and Item 5. Operating and Financial Review and Prospects within this Annual Report.

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D. Trend Information

See Item 5. Operating and Financial Review and Prospects within this Annual Report.

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 other than operating leases as described under Contractual Obligations and Commitments below.

F. Tabular Disclosure of Contractual Obligations.

The following table summarizes our contractual commitments and obligations as of June 30, 2015.

		Payments Due by Period			
	Total	Less than 1 year	1 - 3 years	3 - 5 years	More than 5 years
			(£ in thousands)		
Operating lease obligations(1)(3)	3,771	914	1,579	1,194	85
Purchase obligations(2)(3)	1,633	1,633			
Total contractual cash obligations	5,404	2,547	1,579	1,194	85

(1) At June 30, 2015, operating lease obligations consisted of minimum lease payments under non-cancellable leases for laboratory and office property in Oxfordshire, U.K. and Philadelphia, USA.

(2) Purchase obligations include signed orders for capital equipment, which have been committed but not yet received at the balance sheet date, totaling £1,633,000, relating primarily to expansion of our laboratory space.

(3) In addition to the amounts disclosed above, the Group is in negotiations to enter into lease agreements in both the United Kingdom and United States to further expand the size of R&D operations and to develop a pilot manufacturing facility. As of the balance sheet date no lease agreements had been signed but the Group has indemnified the respective landlords for lease arrangement costs should the leases not be signed. There are currently no indicators that the Group will not enter into the lease arrangements. These lease agreements were both signed after the year end. These lease agreements have annual lease payments of £1.1 million and $1.6 million in the

United Kingdom and United States respectively, and can both be exited before the eleventh anniversary if the Group elects to do so.

G. Safe Harbor.

See the section titled Information Regarding Forward-Looking Statements at the beginning of this Annual Report.

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Item 6. Directors, Senior Management and Employees.

A. Directors and Senior Management.

The following table sets forth the names, ages, and positions of our executive officers and directors:

Name	Age	Position
Executive Officers		
James Noble	56	Chief Executive Officer and member of Board of Directors
Helen Tayton-Martin, Ph.D	48	Chief Operating Officer
Rafael Amado, M.D.	52	Chief Medical Officer
Adrian Rawcliffe	43	Chief Financial Officer
Gwendolyn Binder-Scholl, Ph.D	41	Executive Vice-President of Translational Sciences
Non-Employee Directors		
Jonathan Knowles, Ph.D.(3) (4)	67	Chairman of the Board of Directors
Lawrence M. Alleva(1) (4)	66	Non-Executive Director
Ali Behbahani, M.D.(3)	38	Non-Executive Director
Ian Laing(1)(2) (4)	68	Non-Executive Director
David M. Mott(1)(2)	50	Non-Executive Director
Elliott Sigal, Ph.D, M.D.(3)	63	Non-Executive Director
Peter Thompson, M.D.(2) (4)	56	Non-Executive Director

(1) Member of the Audit Committee.

(2) Member of the Compensation Committee.

(3) Member of the Corporate Governance and Nominating Committee.

(4) An independent director as such term is defined in Rule 10A-3 of the Exchange Act.

Executive Officers

James Noble. Mr. Noble has served as our full-time Chief Executive Officer since March 2014 and part-time CEO from July 2008 to March 2014 and is one of our co-founders. From July 2008 until March 2014, Mr. Noble was also

part-time CEO of Immunocore. Mr. Noble has 24 years of experience in the biotech industry. He has held numerous non-executive director positions, including at CuraGen Corporation, PowderJect Pharmaceuticals plc, Oxford GlycoSciences plc, Medigene AG, and Advanced Medical Solutions plc. Mr. Noble is also Deputy Chairman of GW Pharmaceuticals plc and was formerly a non-executive director of Immunocore . Mr. Noble qualified as a chartered accountant with Pricewaterhouse Coopers and spent seven years at the investment bank Kleinwort Benson Limited, where he became a director in 1990. He then joined British Biotech plc as Chief Financial Officer from 1990 to 1997. Mr. Noble was previously Chief Executive Officer of Avidex Limited, a privately held biotechnology company that was our predecessor, from 2000 to 2006. Mr. Noble holds an M.A. from the University of Oxford. Our Board believes Mr. Noble s qualifications to serve as a member of our Board include his financial expertise, his extensive experience in the biopharmaceutical industry and his years of experience in his leadership roles as a director and executive officer.

Helen Tayton-Martin, Ph.D. Dr. Tayton-Martin has served as our Chief Operating Officer since July 2008 and is one of our co-founders. She is responsible for our research and development planning oversight, and business development and commercial activities, including our strategic partnership with GSK. Dr. Tayton-Martin has 23 years of experience working within the pharma, biotech and consulting environment in disciplines across preclinical and clinical development, outsourcing, strategic planning, due diligence and business development. She is a co-founder of Adaptimmune, joining from Avidex Limited (subsequently Medigene) where she was responsible for commercial development of the soluble TCR programme in cancer and HIV therapy from 2005 to 2008. Dr. Tayton-Martin holds a Ph.D. in molecular immunology from the University of Bristol, U.K. and an M.B.A. from London Business School.

Rafael Amado, M.D. Dr. Amado has served as our Chief Medical Officer since March 2015 and has 12 years of experience within the biotech and pharma industries. Dr. Amado leads our clinical strategy and is responsible for our clinical trials across the U.S. and Europe under our strategic collaboration with GSK, as well as leading the development of our pipeline of wholly-owned research programs. He formerly served as Senior Vice President and Head of Oncology R&D at GSK, where he was responsible for integrating oncology R&D activities, from drug target identification to clinical development and registration globally. Dr. Amado joined GSK in 2008 as Vice President of Clinical Development, and served in positions of increasing responsibility, including Senior Vice President and Head of Oncology Clinical Development.

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He oversaw the development and registration globally of over fifteen novel indications across six products and led the development of a pipeline of products in novel areas of cancer biology. Prior to joining GSK, Dr. Amado was Executive Director of Therapeutic Oncology at Amgen from 2003 to 2008 where he was responsible for development activities of several assets. Dr. Amado trained as a Hematologist/Oncologist at the University of California, Los Angeles, where he remained as faculty for eight years until joining Amgen in 2003. He holds an M.D. from the University of Seville School of Medicine, and performed his residency in Internal Medicine at Michael Reese Hospital, a University of Chicago Affiliated Hospital, and his fellowship in Hematology/Oncology at the University of California, Los Angeles.

Adrian Rawcliffe. Mr. Rawcliffe has served as our Chief Financial Officer since March 2015 and leads our financial strategy, management and operations functions including financial compliance and risk management. He has 17 years of experience within the pharmaceutical industry and most recently served as Senior Vice President, Finance of GSK s North American Pharmaceuticals business. Mr. Rawcliffe joined GSK in 1998 and his other senior roles at the company included Senior Vice President Worldwide Business Development and R&D Finance, where he was responsible for all business development and finance activities for GSK s Pharmaceuticals R&D business and Managing Partner and President of SR One Ltd, GSK s venture-capital business. Mr. Rawcliffe qualified as a chartered accountant with PricewaterhouseCoopers and holds a B.Sc. degree in Natural Sciences from the University of Durham, U.K.

Gwendolyn Binder-Scholl, Ph.D. Dr. Binder-Scholl has served as our Executive Vice-President of Translational Sciences since May 2015 and formerly in roles including Executive Vice-President of Adaptimmune LLC, Head of Clinical and Regulatory Affairs and Vice President of Operations since March 2011. Dr. Binder-Scholl heads our Translational Science Group and her responsibilities are focused on optimizing the therapeutic potential of Adaptimmune s product through directed translational research across correlative clinical and manufacturing development. She has 14 years of industry and academic experience in cellular and gene therapy translational research and development, with prior roles including Director of Translational Research Operations at the University of Pennsylvania from 2006 to 2011 and Director of Scientific Affairs at Virxsys Corporation. Dr. Binder-Scholl is a biochemistry and molecular biology graduate of Wells College with a Ph.D. in cellular and molecular medicine from Johns Hopkins University.

Non-Employee Directors

Jonathan Knowles, Ph.D. Dr. Knowles has served as our Chairman since November 2013 and as a Non-Executive Director since July 2011. He was formerly President of Group Research and a Member of the Executive Committee at F.Hoffman-LaRoche Limited, Basel, Switzerland for 12 years. Dr. Knowles also served as a Board member at Genentech Inc. for 12 years, and as Chairman of the Genetech s Corporate Governance Committee, and was a Member of the Board of Chugai Pharmaceuticals, Tokyo, Japan, and has also formerly served as Chairman of the Hever Group and the EFPIA Research Directors Group. He was instrumental in creating the Innovative Medicines Initiative (IMI), a 5 Billion Euro public private partnership, and was the first Chairman of the Board of IMI. Prior to joining Roche in 1997, he was Research Director, Glaxo Wellcome Europe. Dr. Knowles is currently Chairman of Immunocore, and a director of several public and private companies including Herantis Pharma plc, Caris Life Sciences Ltd and Faron Ltd. He is a Trustee of Cancer Research UK, one of the world s leading cancer research organizations. Dr. Knowles is a Professor Emeritus at the École Polytechnique Fédérale de Lausanne, a Distinguished Professor in Personalized

Medicine at the University of Helsinki, Finland, holds a visiting chair at the University of Oxford, and is a visiting scholar of Pembroke College, Cambridge. Dr. Knowles holds a Ph.D. from the University of Edinburgh and a B.S. in Molecular Genetics from the University of East Anglia. Our Board believes Dr. Knowles s qualifications to serve as a member of our Board include his extensive experience in the pharmaceutical industry and his many years of experience in his leadership roles as a director and executive officer.

Lawrence M. Alleva. Mr. Alleva has served as a Non-Executive Director since March 2015. Mr. Alleva is a former partner with PricewaterhouseCoopers LLP (PwC), where he worked for 39 years from 1971 until his retirement in June 2010, including 28 years service as a partner. Mr. Alleva worked with numerous pharmaceutical and biotechnology companies as clients and, additionally, served PwC in a variety of office, regional and national practice leadership roles, most recently as the U.S. Ethics and Compliance Leader for the firm s Assurance Practice from 2006 until 2010. Mr. Alleva currently serves as a director for public companies Tesaro Inc. (NASDAQ: TSRO), Bright Horizons Family Solutions Inc. (NYSE: BFAM) and Mirna Therapeutics Inc. (NASDAQ: MIRN), and chairs the audit committee for those companies. He previously served on the board of GlobalLogic, Inc. through the sale of the company in 2013 and also chaired the audit committee. Mr. Alleva is a Certified Public Accountant (inactive).

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He received a B.S. degree in Accounting from Ithaca College and attended Columbia University s Executive MBA non-degree program. Our Board believes Mr.Alleva s qualifications to serve as a member of our Board include his financial expertise, his extensive experience working with public companies on corporate finance and accounting matters as a Certified Public Accountant (inactive), his experience serving as a director on other corporate boards and his experience in a senior leadership role at PwC.

Ali Behbahani, M.D. Dr. Behbahani has served as a Non-Executive Director since September 2014, initially in a capacity as a nominee of New Enterprise Associates 14 L.P., (NEA), one of our shareholders. Dr. Behbahani has been a Partner on the healthcare team at NEA since 2013, having worked for the fund since 2007, specializing in investments in the biopharmaceutical, medical device, specialty pharmaceutical and healthcare services sectors. He is also currently a member of the board of directors of Nevro Corp. He has previously worked as a consultant in business development at The Medicines Company and held positions as a Venture Associate at Morgan Stanley Venture Partners from 2000 to 2002 and as a Healthcare Investment Banking Analyst at Lehman Brothers from 1998 to 2000. Dr. Behbahani conducted basic science research in the fields of viral fusion inhibition and structural proteomics at the National Institutes of Health and at Duke University. He holds an M.D. degree from The University of Pennsylvania School of Medicine and an M.B.A. degree from The University of Pennsylvania Wharton School. Our Board believes Dr. Behbahani s qualifications to serve as a member of our Board include his financial expertise, his experience as a venture capital investor, his extensive experience in the healthcare industry and his years of experience in his leadership roles as a director and executive officer.

Ian Laing. Mr. Laing has served as a Non-Executive Director since December 2008 and is a founder shareholder of the Company. Having started his career in commercial property, Mr. Laing has been an active investor in life science and technology businesses for 25 years. He was previously a founder shareholder and non-executive director of Oxford Asymmetry International Plc (subsequently Evotec) from 1992 to 2000, Doctors.net.uk, Oxagen Limited, Oxford Semiconductor Limited and Phosphonics Limited. He is currently a non-executive director of several private companies including Aegate Limited, SQW Group Limited and Immunocore . Mr. Laing is a Trustee of the Nuffield Medical Trust and was formerly Deputy Chairman of London Business School and a non-executive director of the Oxford Radcliffe Hospitals NHS Trust. He is a Governor of the Royal Shakespeare Company and an Honorary Fellow of Green Templeton College and St. Edmund Hall in the University of Oxford. Mr. Laing holds a B.A. degree from the University of Oxford and an M.B.A. degree from London Business School. Our Board believes Mr. Laing s qualifications to serve as a member of our Board include his extensive experience as an investor and his years of experience in his leadership roles as a director.

David M. Mott. Mr. Mott has served as a Non-Executive Director since September 2014, initially in a capacity as a nominee of New Enterprise Associates 14 L.P., (NEA), one of our shareholders. Mr. Mott has served as a General Partner of NEA, an investment firm focused on venture capital and growth equity investments, since 2008, and leads its healthcare investing practice. He was formerly President and Chief Executive Officer of MedImmune LLC, a subsidiary of AstraZeneca Plc, and Executive Vice President of AstraZeneca Plc. From 1992 to 2008, Mr. Mott worked at MedImmune Limited and served in roles including Chief Operating Officer, Chief Financial Officer, President and Chief Executive Officer. Prior to joining MedImmune, Mr. Mott was a Vice President in the Health Care Investment Banking Group at Smith Barney, Harris Upham & Co., Inc. He is currently a member of the board of directors of Ardelyx, Epizyme and Tesaro, as well as several private companies, and has previously served on

numerous public and private company boards in the biopharmaceutical industry. Mr. Mott received a bachelor of arts degree from Dartmouth College. Our Board believes Mr. Mott s qualifications to serve as a member of our Board include his financial expertise, his experience as a venture capital investor, his extensive experience in the pharmaceutical industry and his years of experience in his leadership roles as a director and executive officer.

Elliott Sigal, M.D., Ph.D. Dr. Sigal has served as a Non-Executive Director since September 2014, and is a former Executive Vice President and member of the board of directors of Bristol-Myers Squibb. He joined BMS in 1997 as head of Applied Genomics, went on to head Discovery Research followed by clinical development and ultimately served as Chief Scientific Officer and President of R&D from 2004 until 2013. Dr. Sigal serves as a board member for the Mead Johnson Nutrition Company, Spark Therapeutics and the Melanoma Research Alliance. He also serves as a senior advisor to the healthcare team of NEA and consults for several biotechnology companies. Dr. Sigal holds an M.D. from the University of Chicago and trained in Internal Medicine and Pulmonary Medicine at the University of California, San Francisco, where he was on faculty from 1988 to 1992. He also holds a B.S., M.S., and Ph.D. in engineering from Purdue University. Our Board believes Dr. Sigal s qualifications to serve as a member of our Board include his extensive experience in the pharmaceutical industry and his years of experience in his leadership roles as a director and executive officer.

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Peter Thompson, M.D. Dr. Thompson has served as a Non-Executive Director since September 2014, initially in a capacity as a nominee of OrbiMed Private Investments V, L.P., one of our shareholders. Dr. Thompson has been a Private Equity Partner with OrbiMed since 2013 and was previously a Venture Partner since 2010. He co-founded and was Chief Executive Officer of Trubion Pharmaceuticals from 2002 to 2009, co-founded Cleave BioSciences and Corvus Pharmaceuticals, serves on the boards of several public and private companies, including Response BioMedical Corp since 2013, and was a senior executive of Chiron Corporation from 1995 to 1999 and Becton Dickinson from 1991 to 1995. Dr. Thompson is an Affiliate Professor of Neurosurgery at the University of Washington. He was a member of faculty at the National Cancer Institute, following his internal medicine training at Yale University, and is Board certified in internal medicine and medical oncology. Our Board believes Dr. Thompson s qualifications to serve as a member of our Board include his financial expertise, his experience as a venture capital investor, his extensive experience in the pharmaceutical industry and his years of experience in his leadership roles as a director and executive officer.

B. Compensation.

The following discussion provides the amount of compensation paid, and benefits in kind granted, by us and our subsidiaries to our directors and members of our executive committee for services in all capacities to us and our subsidiaries for the year ended June 30, 2015, as well as the amount contributed by us or our subsidiaries into money purchase plans for the year ended June 30, 2014 to provide pension, retirement or similar benefits to, our directors and member of our executive committee.

Directors and Executive Committee Compensation

Directors Compensation

For the year ended June 30, 2015, the table below sets forth the compensation paid to our directors, and in the case of Mr. Noble reflects the compensation paid for his services as our Chief Executive Officer.

Year Ended June 30, 2015 Directors Compensation (1)

Name	Salary/Fees £	Annual Bonus £	Benefit Excluding Pension £	Pension Benefit £	Total £
Jonathan Knowles, Ph.D					
Non-Executive Director Chairman					
James Noble (2)	260,000	200,000	1,117	13,000	474,117

Executive Director *Chief Executive Officer*		
Lawrence M. Alleva (3) (4)	6,678	6,678
Non-Executive Director		
Ali Behbahani, M.D.		
Non-Executive Director		
Ian Laing		
Non-Executive Director		
David M. Mott		
Non-Executive Director		
Elliott Sigal, Ph.D, M.D. (3) (5)	15,743	10,571
Non-Executive Director		
Peter Thompson, M.D.		
Non-Executive Director		

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(1) For the year ended June 30, 2015, the majority of compensation was set and paid in pounds sterling (£).

(2) The compensation for our Chief Executive Officer is determined to be effective from January 1 in each year. Therefore, the salary amount paid to Mr. Noble for the period from July 1, 2014 to June 30, 2015 represents the aggregate of a pro-rata amount in respect of his annual salary of £260,000 from July 1, 2014 through December 31, 2014 and a pro-rata amount in respect of his annual salary of £300,000 from January 1, 2015 through June 30, 2015. The amount for personal benefits represents medical and life insurance. The amount for pension benefit represents our contribution into a money purchase plan.

(3) For the purposes of this table, the fees paid in U.S. dollars to Mr. Alleva and Dr. Sigal have been translated into pounds sterling based on the U.S. dollar/pound sterling exchange rate in effect on June 30, 2015 ($1.5727 to £1).

(4) Amount represents fees of $10,503 paid to Mr. Alleva for services from March 5, 2015 to May 5, 2015. Effective from May 6, 2015, Mr. Alleva is no longer paid fees for his services.

(5) Amount represents fees of $24,759 paid to Dr. Sigal for services from September 23, 2014 to May 5, 2015. Effective from May 6, 2015, Dr. Sigal is no longer paid fees for his services.

Executive Committee Compensation

The compensation for each member of our executive committee, including our Chief Executive Officer, is comprised of the following elements: base salary, annual bonus, personal benefits and long-term incentives. The total amount of compensation paid and benefits in kind granted to the members of our executive committee, whether or not a director, for the year ended June 30, 2015 was £3.4 million.

Bonus Plans

The discussion set forth below describes each bonus plan pursuant to which compensation was paid to our executive director and to the other members of our executive committee for our last full year.

Our Chief Executive Officer is eligible for an annual bonus at the discretion of the Board and our other executive officers are eligible for an annual bonus at the discretion of the Compensation Committee. Bonus awards are reviewed at the end of each calendar year and any such awards are determined by the performance of the individual and the Company as a whole based upon the achievement of strategic objectives set at the beginning of the year or on the commencement of employment.

Outstanding Equity Awards, Grants and Option Exercise

During the year ended June 30, 2015, 15,354,577 new options to purchase ordinary shares were awarded to our executive officers and directors.

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Name	Type of plan (1)	Granted	Start date for vesting		Exercise price	First date of exercise of some or all options (2)	Date of expiry
Executive Officers							
James Noble	ATL Op	3,500,000	Dec. 19, 2014	£	0.3557	Dec. 19, 2015	Dec. 19, 2024
Chief Executive Officer							
Helen Tayton-Martin, Ph.D.	ATL Op	1,750,000	Dec. 19, 2014	£	0.3557	Dec. 19, 2015	Dec. 19, 2024
Chief Operating Officer							
Rafael Amado, M.D.	AT plc Op	3,600,000	March 16, 2015	£	0.5000	March 16, 2016	March 16, 2025
Chief Medical Officer							
Adrian Rawcliffe	AT plc Op	3,600,000	March 16, 2015	£	0.5000	March 16, 2016	March 16, 2025
Chief Financial Officer							
Gwendolyn Binder-Scholl, Ph.D.	AT plc Op	1,000,000	Dec. 19, 2014	£	0.3557	Dec. 19, 2015	Dec. 19, 2024
EVP, Translational Sciences							
Non-Executive Directors							
Jonathan Knowles, Ph.D	AT plc Op	175,806	May 11, 2015	£	1.82	May 11, 2015	May 11, 2015
Chairman							
Lawrence M. Alleva	AT plc Op	519,481	March 16, 2015	£	0.5000	March 16, 2016	March 16, 2025
Lawrence M.Alleva	AT plc Op	30,745	May 11, 2015	£	1.82	May 11, 2015	May 11, 2025
Ali Behbahani, M.D.	AT plc Op	155,682	May 11, 2015	£	1.82	May 11, 2015	May 11, 2025
Ian Laing	AT plc Op	159,875	May 11, 2015	£	1.82	May 11, 2015	May 11, 2025
David M. Mott	AT plc Op	163,229	May 11, 2015	£	1.82	May 11, 2015	May 11, 2025
Elliott Sigal, Ph.D, M.D.	AT plc Op	519,481	Mar 16, 2015	£	0.5000	March 16, 2016	March 16, 2025
Elliott Sigal, Ph.D, M.D.	AT plc Op	24,596	May 11, 2015	£	1.82	May 11, 2015	May 11, 2025
Peter Thompson, M.D.	AT plc Op	155,682	May 11, 2015	£	1.82	May 11, 2015	May 11, 2025

(1) ATL Op means the Adaptimmune Limited Share Option Scheme and AT plc Op means the Adaptimmune Therapeutics plc 2015 Share Option Scheme.

(2) All options granted to executive officers, 519,481 options granted to Mr. Alleva and 519,481 options granted to Dr. Sigal vest and become exercisable as follows: 25% on the first anniversary of the grant date and 75% in monthly instalments over the following 3 years. Additionally, in a change of control situation, any of the 3,600,000 share options held by each of Dr. Amado and Mr. Rawcliffe that are unvested will immediately vest and become exercisable whether or not his employment is also terminated. All options granted to non-executive directors (except for the options specified above to Mr. Alleva and Dr. Sigal) vested and became exercisable on May 11, 2015.

As of June 30, 2015, our directors held options to purchase 7,177,677 ordinary shares, and our directors and executive officers held options to purchase 18,912,677 ordinary shares. During the year ended June 30, 2015, none of our directors and executive officers exercised and sold any options over ordinary shares.

We periodically grant share options to employees and consultants to enable them to share in our successes and to reinforce a corporate culture that aligns their interests with that of our shareholders. Since June 30, 2012, we have granted options to purchase ordinary shares to 113 employees and consultants who are not directors.

Pension, Retirement and Similar Benefits

For the year ended June 30, 2015, we and our subsidiaries contributed a total of approximately £19,770 into money purchase plans to provide pension, retirement or similar benefits to our executive officers and directors.

Employment Agreements

James Noble

Mr. Noble has served as our Chief Executive Officer on a full-time basis since March 31, 2014, and previously on a part-time basis since July 2008. On April 24, 2015, Mr. Noble entered into a service agreement with Adaptimmune Therapeutics plc which provides that his service will continue until either party provides no less than six months written notice. Upon notice of termination, Adaptimmune Therapeutics plc may require Mr. Noble not to attend work for all or any part of the period of notice, during which time he will continue to receive his salary and other contractual entitlements.

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Adaptimmune Therapeutics plc may terminate Mr. Noble s employment with immediate effect at any time by notice in writing in certain circumstances, as described in his service agreement, including bankruptcy, criminal convictions, gross misconduct or serious or repeated breaches of obligations of his service.

Pursuant to Mr. Noble s service agreement, his base salary effective January 1, 2015, is £300,000 per annum (to be reviewed annually) and his agreement provides for access to Adaptimmune Limited s Group Personal Pension Scheme, permanent health insurance coverage and to a private healthcare scheme; and for the payment of a bonus of such amount, at such intervals and subject to such conditions as the Company may in its absolute discretion determine from time to time. For the year ending December 31, 2015, Mr. Noble is eligible for a discretionary bonus award of up to £200,000, subject to the achievement of certain performance criteria, and payable in two tranches. The first tranche of £100,000 was paid following Board approval in July 2015. The second tranche of up to £100,000 will be assessed by the Board at the end of the year.

Mr. Noble also serves as Deputy Chairman of GW Pharmaceuticals plc. His service agreement provides that, save for this engagement, his employment with Adaptimmune Therapeutics plc is, and shall remain, his sole and exclusive employment. His service agreement also contains provisions regarding confidentiality and proprietary information, including an express assignment of inventions to Adaptimmune Therapeutics plc, as well as non-competition and non-solicitation provisions. His service agreement also provides that for 12 months following termination of his employment with Adaptimmune Therapeutics plc, he will not entice, induce or encourage any customer or employee to end their relationship with Adaptimmune Therapeutics plc or any other of our members, solicit or accept business from customers or engage in competitive acts more fully described in his service agreement.

Helen Tayton-Martin, Ph.D.

Dr. Tayton-Martin has served as Chief Operating Officer since July 2008 and entered into a service agreement with Adaptimmune Limited on March 24, 2014. Her agreement provides that her services will continue until either party provides no less than six months written notice. Upon notice of termination, Adaptimmune Limited may require Dr. Tayton-Martin not to attend work for all or any part of the period of notice, during which time she will continue to receive her salary and other contractual entitlements. Adaptimmune Limited may terminate Dr. Tayton-Martin s employment with immediate effect at any time by notice in writing in certain circumstances, as described in her service agreement, including bankruptcy, criminal convictions, gross misconduct or serious or repeated breaches of obligations of her service.

Pursuant to Dr. Tayton-Martin s service agreement, her base salary effective January 1, 2015, is £225,000 per annum (to be reviewed annually) and her agreement provides for access to Adaptimmune Limited s Group Personal Pension Scheme, permanent health insurance coverage and to a private healthcare scheme; and for the payment of a bonus of such amount, at such intervals and subject to such conditions as the Company may in its absolute discretion determine from time to time. For the year ending December 31, 2015, Dr. Tayton-Martin is eligible for a discretionary bonus award of up to £90,000, subject to the achievement of certain performance criteria and payable in two tranches. The first tranche of £45,000 was paid following approval by the Compensation Committee in July 2015. The second tranche of up to £45,000 will be assessed by the Compensation Committee at the end of the year.

Dr. Tayton-Martin s service agreement contains provisions regarding confidentiality and proprietary information, including an express assignment of inventions to Adaptimmune Limited, as well as non-competition and non-solicitation provisions. Her service agreement also provides that for 12 months following termination of her employment with Adaptimmune Limited, she will not entice, induce or encourage any customer or employee to end their relationship with Adaptimmune Limited or any other of our members, solicit or accept business from customers or engage in competitive acts more fully described in her service agreement.

Rafael Amado, M.D.

Dr. Amado has served as our Chief Medical Officer since March 2015 and entered into an employment agreement with Adaptimmune LLC on February 18, 2015. His base salary effective March 16, 2015, is $418,200 per annum (to be reviewed annually) and he is eligible for an annual target bonus of 45% of his base salary, pro-rated for any part-year of employment. His agreement provided for the award of 3,600,000 share options as soon as practicable after his start date, which were granted on March 16, 2015, and access to equity plans maintained by Adaptimmune LLC and its affiliates, at the discretion of the Board or Compensation Committee. He is eligible for a period payment to defray the cost of Philadelphia city tax at an amount equating to 3.459% of his salary and bonus and has access to medical, dental and other employee plans that are maintained for employees in the United States.

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Dr. Amado s employment agreement can be terminated by either party without cause, provided that Dr. Amado is required to provide 60 days written notice. Adaptimmune LLC may terminate Dr. Amado s employment with immediate effect for cause, including material breach and gross negligence, and Dr. Amado may terminate his employment with immediate effect for good reason, including material diminution in his responsibilities or in his base salary, except for across-the-board salary reductions similarly affecting other senior management or as agreed with Dr. Amado. If his employment is terminated by the Company without cause or by Dr. Amado for good reason, he is eligible to receive a severance package that includes a severance payment equivalent to nine months of base salary and reimbursement of group health care coverage premiums for nine months after termination. In a change of control situation, any of Dr. Amado s 3,600,000 share options that are unvested will immediately vest and become exercisable whether or not his employment is also terminated.

Dr. Amado s agreement contains provisions regarding confidentiality and proprietary information, including an express assignment of inventions, as well as non-competition and non-solicitation provisions. His service agreement also provides that for 12 months following termination of his employment with Adaptimmune LLC, he will not compete with Adaptimmune LLC and its affiliates and will not solicit clients and employees of those companies or engage in competitive acts more fully described in his agreement.

Adrian Rawcliffe

Mr. Rawcliffe has served as our Chief Financial Officer since March 2015 and entered into an employment agreement with Adaptimmune LLC on February 20, 2015. His base salary effective March 16, 2015, is $425,000 per annum (to be reviewed annually) and he is eligible for an annual target bonus of 45% of his base salary, pro-rated for any part-year of employment. His agreement provides for the award of 3,600,000 share options as soon as practicable after his start date, which were granted on March 16, 2015, and access to equity plans maintained by Adaptimmune LLC and its affiliates, at the discretion of the Board or Compensation Committee. He is eligible for a period payment to defray the cost of Philadelphia city tax at an amount equating to 3.459% of his salary and bonus and has access to medical, dental and other employee plans that are maintained for employees in the United States.

Mr. Rawcliffe s employment agreement can be terminated by either party without cause, provided that Mr. Rawcliffe is required to provide 60 days written notice. Adaptimmune LLC may terminate Mr. Rawcliffe s employment with immediate effect for cause, including material breach and gross negligence, and Mr. Rawcliffe may terminate his employment with immediate effect for good reason, including material diminution in his responsibilities or in his base salary, except for across-the-board salary reductions similarly affecting other senior management or as agreed with Mr. Rawcliffe. If his employment is terminated by the Company without cause or by Mr. Rawcliffe for good reason, he is eligible to receive a severance package that includes a severance payment equivalent to nine months of base salary and reimbursement of group health care coverage premiums for nine months after termination. In a change of control situation, any of Mr. Rawcliffe s 3,600,000 share options that are unvested will immediately vest and become exercisable whether or not his employment is also terminated.

Mr. Rawcliffe s agreement contains provisions regarding confidentiality and proprietary information, including an express assignment of inventions, as well as non-competition and non-solicitation provisions. His service agreement also provides that for 12 months following termination of his employment with Adaptimmune LLC, he will not compete with Adaptimmune LLC and its affiliates and will not solicit clients and employees of those companies or engage in competitive acts more fully described in his agreement.

Gwendolyn Binder-Scholl, Ph.D.

Dr. Binder-Scholl, Executive Vice-President of Translational Sciences, entered into an employment agreement with Adaptimmune LLC on March 1, 2011. The agreement can be terminated by either party without cause on provision of no less than one month s written notice. Adaptimmune LLC may terminate Dr. Binder-Scholl s employment with immediate effect for cause, including bankruptcy, criminal convictions and gross negligence, and Dr. Binder-Scholl may terminate her employment with immediate effect for good reason, including demotion and the relocation of Adaptimmune LLC, following a change of control, to a location of 50 miles or more from Philadelphia. If her employment is terminated by the Company without cause or by Dr. Binder-Scholl for good reason, she is eligible to receive a severance payment equivalent to two months of her base salary.

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Pursuant to Dr. Binder-Scholl s agreement, her base salary effective May 1, 2015, is $300,000 per annum (to be reviewed annually), and her agreement provides for access to equity plans maintained by Adaptimmune LLC and its affiliates, at the discretion of the Board or Compensation Committee, and access to medical, dental and other employee plans that are maintained for employees in the United States. For the year ending December 31, 2015, Dr. Binder-Scholl is eligible for a discretionary bonus award of up to $90,000, subject to the achievement of certain performance criteria and payable in two tranches. The first tranche of $45,000 was paid following approval by the Compensation Committee in July 2015. The second tranche of up to $45,000 will be assessed by the Compensation Committee at the end of the year.

Dr. Binder-Scholl s agreement contains provisions regarding confidentiality and proprietary information, including an express assignment of inventions, as well as non-competition and non-solicitation provisions. Her service agreement also provides that for 12 months following termination of her employment with Adaptimmune LLC, she will not compete with Adaptimmune LLC and Adaptimmune Limited and will not solicit clients and employees of those companies or engage in competitive acts more fully described in her agreement.

Agreements with Non-Executive Directors

Jonathan Knowles, Ph.D.

On July 25, 2011, Adaptimmune Limited appointed Dr. Knowles as a Non-Executive Director and on November 12, 2013, he was appointed as Chairman with immediate effect. On May 14, 2014, Adaptimmune Limited entered into an appointment letter with Dr. Knowles. In February 2015, Dr. Knowles was appointed as a Non-Executive Director of Adaptimmune Therapeutics Limited and on April 22, 2015, Adaptimmune Therapeutics plc entered into an appointment letter with Dr. Knowles (to the exclusion of his earlier appointment letter) that relates to his service as the chairman and a member of our Board, and as the chairman of the Corporate Governance and Nominating Committee. The appointment letter provides that Dr. Knowles is not entitled to any director s fee and is entitled to reimbursement of reasonable and documented expenses incurred on company business and to directors and officers liability insurance. The appointment letter also provides for the award of options over 175,806 ordinary shares of the Company on the closing of the IPO, which were granted effective from May 11, 2015, and for an annual award of options, with such number to be determined by the directors, on each anniversary of May 11, 2015 during his period of appointment.

Dr. Knowles s appointment letter provides that his appointment will continue until either party provides no less than three months written notice and that he should be prepared to spend a minimum of 15 days per annum on company business. His appointment may be terminated in the circumstances described in his appointment letter, including bankruptcy, criminal convictions, gross misconduct or serious or repeated breaches of obligations of his service. Dr. Knowles s appointment letter contains provisions regarding confidentiality and does not contain non-competition and non-solicitation provisions.

From September 23, 2014, Dr. Knowles was deemed appointed as a representative of ordinary shareholders pursuant first to a shareholders agreement relating to Adaptimmune Limited and then, from February 23, 2015, to a replacement shareholders agreement relating to Adaptimmune Therapeutics Limited. Each shareholder s agreement included provisions dealing with removal from office. The latter shareholders agreement terminated upon admission of the ADSs to trading on Nasdaq and Dr. Knowles continues as a Director notwithstanding that termination.

Ian Laing

On December 2, 2008, Adaptimmune Limited appointed Mr. Laing as a Non-Executive Director and on May 14, 2014, Adaptimmune Limited entered into an appointment letter with Mr. Laing. In February 2015, Mr. Laing was appointed as a Non-Executive Director of Adaptimmune Therapeutics Limited and on April 22, 2015, Adaptimmune Therapeutics plc entered into an appointment letter with Mr. Laing (to the exclusion of his earlier appointment letter) that relates to his service as a member of our Board, and as a member of the Audit Committee and of the Compensation Committee. The appointment letter provides that Mr. Laing is not entitled to any director s fee and is entitled to reimbursement of reasonable and documented expenses incurred on company business and to directors and officers liability insurance. The appointment letter also provides for the award of options over 159,875 ordinary shares of the Company, which were granted effective from May 11, 2015, and for an annual award of options, with such number to be determined by the directors, on each anniversary of May 11, 2015during his period of appointment.

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Mr. Laing s appointment letter provides that his appointment will continue until either party provides no less than three months written notice and that he should be prepared to spend a minimum of 15 days per annum on company business. His appointment may be terminated in the circumstances described in his appointment letter, including bankruptcy, criminal convictions, gross misconduct or serious or repeated breaches of obligations of his service. Mr. Laing s appointment letter contains provisions regarding confidentiality and does not contain non-competition and non-solicitation provisions.

From September 23, 2014, Mr. Laing was deemed appointed as a representative of ordinary shareholders pursuant first to a shareholders agreement relating to Adaptimmune Limited and then, from February 23, 2015, to a replacement shareholders agreement relating to Adaptimmune Therapeutics Limited. Each shareholders agreement included provisions dealing with removal from office. The latter shareholders agreement terminated upon admission of our ADSs to trading on Nasdaq and Mr. Laing continues as a Director notwithstanding that termination.

Lawrence M. Alleva

On March 5, 2015, Adaptimmune Therapeutics Limited appointed Mr. Alleva as a Non-Executive Director and chairman of the Audit Committee and on March 16, 2015, Mr. Alleva was granted 519,481 options over ordinary shares of Adaptimmune Therapeutics Limited. On March 31, 2015, Adaptimmune Therapeutics Limited entered into an appointment letter with Mr. Alleva and on April 22, 2015, Adaptimmune Therapeutics plc entered into an appointment letter with Mr. Alleva (to the exclusion of his earlier appointment letter) that relates to his service as a member of our Board, and as a member and chairman of the Audit Committee. The appointment letter provides that Mr. Alleva is not entitled to any director s fee and is entitled to reimbursement of reasonable and documented expenses incurred on company business and to directors and officers liability insurance. The appointment letter also provides for the award of options over 30,745 ordinary shares of the Company, which were granted effective from May 11, 2015, and for an annual award of options, with such number to be determined by the directors, on each anniversary of May 11, 2015 during his period of appointment.

Mr. Alleva s appointment letter provides that his appointment will continue until either party provides no less than three months written notice and that he should be prepared to spend a minimum of 15 days per annum on company business. His appointment may be terminated in the circumstances described in his appointment letter, including bankruptcy, criminal convictions, gross misconduct or serious or repeated breaches of obligations of his service. Mr. Alleva s appointment letter contains provisions regarding confidentiality and does not contain non-competition and non-solicitation provisions.

Ali Behbahani, M.D.

In September 2014, Adaptimmune Limited appointed Dr. Behbahani as a Non-Executive Director. Dr. Behbahani was appointed by NEA upon the completion of our sale of Series A preferred shares. In February 2015, Dr. Behbahani was appointed as a Non-Executive Director of Adaptimmune Therapeutics Limited and on April 22, 2015, Adaptimmune Therapeutics plc entered into an appointment letter with Dr. Behbahani that relates to his service as a member of our Board, and as a member of the Corporate Governance and Nominating Committee. The appointment letter provides that Dr. Behbahani is not entitled to any director s fee and is entitled to reimbursement of reasonable and documented expenses incurred on company business and to directors and officers liability insurance. The appointment letter also provides for the award of options over 155,682 ordinary shares of the Company, which were granted effective from May 11, 2015, and for an annual award of options, with such number to be determined by the directors, on each anniversary of May 11, 2015during his period of appointment.

Dr. Behbahani s appointment letter provides that his appointment will continue until either party provides no less than three months written notice and that he should be prepared to spend a minimum of 15 days per annum on company business. His appointment may be terminated in the circumstances described in his appointment letter, including bankruptcy, criminal convictions, gross misconduct or serious or repeated breaches of obligations of his service. Dr. Behbahani s appointment letter contains provisions regarding confidentiality and does not contain non-competition and non-solicitation provisions.

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From September 23, 2014, Dr. Behbahani was an appointee of NEA pursuant first to a shareholders agreement relating to Adaptimmune Limited and then, from February 23, 2015, to a replacement shareholders agreement relating to Adaptimmune Therapeutics Limited. Each shareholders agreement included provisions dealing with removal from office. The latter shareholders agreement terminated upon admission of our ADSs to trading on Nasdaq and Dr. Behbahani continues as a Director notwithstanding that termination.

David M. Mott

In September 2014, Adaptimmune Limited appointed Mr. Mott as a Non-Executive Director. Mr. Mott was appointed by NEA upon the completion of our sale of Series A preferred shares. In February 2015, Mr. Mott was appointed as a Non-Executive Director of Adaptimmune Therapeutics Limited and on April 22, 2015, Adaptimmune Therapeutics plc entered into an appointment letter with Mr. Mott that relates to his service as a member of our Board, and as a member and chairman of the Compensation Committee and as a member of the Audit Committee. The appointment letter provides that Mr. Mott is not entitled to any director s fee and is entitled to reimbursement of reasonable and documented expenses incurred on company business and to directors and officers liability insurance. The appointment letter also provides for the award of options over 163,229 ordinary shares of the Company, which were granted effective from May 11, 2015, and for an annual award of options, with such number to be determined by the directors, on each anniversary of May 11, 2015 during his period of appointment.

Mr. Mott s appointment letter provides that his appointment will continue until either party provides no less than three months written notice and that he should be prepared to spend a minimum of 15 days per annum on company business. His appointment may be terminated in the circumstances described in his appointment letter, including bankruptcy, criminal convictions, gross misconduct or serious or repeated breaches of obligations of his service. Mr. Mott s appointment letter contains provisions regarding confidentiality and does not contain non-competition and non-solicitation provisions.

From September 23, 2014, Mr. Mott was an appointee of NEA pursuant first to a shareholders agreement relating to Adaptimmune Limited and then, from February 23, 2015, to a replacement shareholders agreement relating to Adaptimmune Therapeutics Limited. Each shareholder s agreement included provisions dealing with removal from office. The latter shareholders agreement terminated upon admission of our ADSs to trading on Nasdaq and Mr. Mott continues as a Director notwithstanding that termination.

Elliott Sigal, M.D., Ph.D.

In September 2014, Adaptimmune Limited appointed Dr. Sigal as a Non-Executive Director. Dr. Sigal was appointed upon the completion of our sale of Series A preferred shares. In February 2015, Dr. Sigal was appointed as a Non-Executive Director of Adaptimmune Therapeutics Limited and on March 16, 2015, he was granted 519,481 options over ordinary shares of the Company. On March 25, 2015, Adaptimmune Therapeutics Limited entered into an appointment letter with Dr. Sigal and on April 22, 2015, Adaptimmune Therapeutics plc entered into an appointment letter with Dr. Sigal (to the exclusion of his earlier appointment letter) that relates to his service as a member of our Board, and as a member of the Corporate Governance and Nominating Committee. The appointment letter provides that Dr. Sigal is not entitled to any director s fee and is entitled to reimbursement of reasonable and documented expenses incurred on company business and to directors and officers liability insurance. The appointment letter also provides for the award of options over 24,596 ordinary shares of the Company, which were granted effective from May 11, 2015, and for an annual award of options, with such number to be determined by the directors, on each anniversary of May 11, 2015 during his period of appointment.

Dr. Sigal s appointment letter provides that his appointment will continue until either party provides no less than three months written notice and that he should be prepared to spend a minimum of 15 days per annum on company business. His appointment may be terminated in the circumstances described in his appointment letter, including bankruptcy, criminal convictions, gross misconduct or serious or repeated breaches of obligations of his service. Dr. Sigal s appointment letter contains provisions regarding confidentiality. His appointment letter does not contain non-competition and non-solicitation provisions.

From September 23, 2014, Dr. Sigal was an independent Director pursuant first to a shareholders agreement relating to Adaptimmune Limited and then, from February 23, 2015, to a replacement shareholders agreement relating to Adaptimmune Therapeutics Limited. The latter shareholders agreement terminated upon admission of our ADSs to trading on Nasdaq and Dr. Sigal continues as a Director notwithstanding that termination.

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Peter Thompson, M.D.

In September 2014, Adaptimmune Limited appointed Dr. Thompson as a Non-Executive Director. Dr. Thompson was appointed by OrbiMed upon the completion of our sale of Series A preferred shares. In February 2015, Dr. Thompson was appointed as a Non-Executive Director of Adaptimmune Therapeutics Limited and on April 22, 2015, Adaptimmune Therapeutics plc entered into an appointment letter with Dr. Thompson that relates to his service as a member of our Board, and as a member of the Compensation Committee. The appointment letter provides that Dr. Thompson is not entitled to any director s fee and is entitled to reimbursement of reasonable and documented expenses incurred on company business and to directors and officers liability insurance. The appointment letter also provides for the award of options over 155,682 ordinary shares of the Company, which were granted effective from May 11, 2015, and for an annual award of options, with such number to be determined by the directors, on each anniversary of May 11, 2015 during his period of appointment.

Dr. Thompson s appointment letter provides that his appointment will continue until either party provides no less than three months written notice and that he should be prepared to spend a minimum of 15 days per annum on company business. His appointment may be terminated in the circumstances described in his appointment letter, including bankruptcy, criminal convictions, gross misconduct or serious or repeated breaches of obligations of his service. Dr. Thompson s appointment letter contains provisions regarding confidentiality and does not contain non-competition and non-solicitation provisions.

From September 23, 2014, Dr. Thompson was an appointee of OrbiMed pursuant first to a shareholders agreement relating to Adaptimmune Limited and then, from February 23, 2015, to a replacement shareholders agreement relating to Adaptimmune Therapeutics Limited. Each shareholders agreement included provisions dealing with removal from office. The latter shareholders agreement terminated upon admission of our ADSs to trading on Nasdaq and Dr. Thompson continues as a Director notwithstanding that termination.

Equity Compensation Plans

Summary

Through December 31, 2014, we granted options to purchase ordinary shares in Adaptimmune Limited under three option schemes: (i) the Adaptimmune Limited Share Option Scheme, (ii) the Adaptimmune Limited 2014 Share Option Scheme and (ii) the Adaptimmune Limited Company Share Option Plan. As part of our corporate reorganization in connection with our IPO, the holders of options granted under these schemes over ordinary shares of Adaptimmune Limited were granted equivalent options on substantially the same terms over ordinary shares of Adaptimmune Therapeutics plc (Replacement Options) in exchange for the release of these options. We do not intend to grant any further options under these schemes.

On March 16, 2015, we adopted two new option plans which provide for the grant of options over ordinary shares in Adaptimmune Therapeutics plc: (i) the Adaptimmune Therapeutics plc 2015 Share Option Scheme and (ii) the Adaptimmune Therapeutics plc Company Share Option Plan (the New Option Plans). On April 15, 2015, the rules of the New Option Plans were amended, effective from the admission to trading of our securities on Nasdaq on May 6, 2015, to provide that the maximum aggregate number of options which may be granted, following our IPO, under these plans and any incentive plans adopted by Adaptimmune, cannot exceed a scheme limit that equates to 8% of the initial fully diluted share capital of the Company immediately following our IPO plus an automatic annual increase of an amount equivalent to 4% of the

issued share capital on each 30 June (or such lower number as our Board, or an appropriate committee of the Board, may determine). The automatic increase is effective from July 1, 2016.

Vesting Dates of Options

Generally, the vesting dates for the Replacement Options under the Adaptimmune Limited option schemes are:

Options granted in 2009:	100% on the third anniversary of the grant date
Options granted in 2011, 2012, 2013 and April 2014:	25% on the first anniversary of the grant date and 75% in annual installments over the following three years
Options granted in December 2014:	25% on the first anniversary of the grant date and 75% in monthly installments over the following three years

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Generally, the vesting dates for the options that we have granted under the New Option Plans from March 16, 2015 to June 30, 2015 are 25% on the first anniversary of the grant date and 75% in monthly installments over the following three years. However, options granted to non-executive directors effective from May 11, 2015 vested and became exercisable immediately, but, as of the date of this Annual Report, none of these options has been exercised.

Adaptimmune Limited Share Option Scheme (Incorporating Management Incentive Options)

Our Adaptimmune Limited Share Option Scheme, or Adaptimmune Scheme, was adopted on May 30, 2008.

Enterprise Management Incentive (EMI) options (which are potentially tax-advantaged in the United Kingdom) may be granted (subject to the relevant conditions being met) under our Adaptimmune Scheme to our employees who are eligible to receive EMI options under applicable U.K. tax law. Unapproved options (which do not attract tax advantages) may be granted to our employees who are not eligible to receive EMI options, and to our directors and consultants.

Exercise Conditions. Options granted may be granted subject to performance targets or other exercise conditions which must be satisfied before exercise. These targets or conditions may be waived or amended by the Board provided that, in the case of a performance target, no amendment or variation may be made unless an event occurs in consequence of which the Board reasonably considers that the terms of the existing performance targets should be amended to ensure that the performance criteria will be a fairer measure of such performance, or that the performance condition will afford a more effective incentive to the participant and will be no more difficult to satisfy.

Leaver Provisions. Generally, options must be exercised while the participant is an employee, director or consultant of us or a subsidiary. However, in certain circumstances a participant may exercise his options within a period of ceasing to be so connected.

Takeovers and Corporate Events. If any person obtains control of us (as determined in accordance with specified U.K. tax law) as a result of making a general offer to acquire shares, any vested options may be exercised within four months after the time the person has obtained control and any conditions subject to which the offer is made have been satisfied. In addition, if such an offer is made, the Board has discretion to permit the exercise of all outstanding options, whether or not vested, within such time period as it may specify. To the extent they are not exercised, such options will lapse at the end of the relevant period for exercise. However, if another company obtains all of our shares as a result of a qualifying exchange of shares and participants are invited to release their options in consideration of the grant of equivalent options in the acquiring company, and fail to accept the invitation, their options will lapse.

Options which are not otherwise exercisable may, subject to certain conditions, be exercisable in connection with the demerger of a subsidiary of us. In the event of certain court sanctioned restructurings or amalgamations of us, options may be exercisable over such number of shares as the Board may determine during the period commencing with the date on which the court sanctions the compromise or arrangement and ending with the date on which it becomes effective. In the event of a proposal for a voluntary winding-up, except for the purpose of restructuring or amalgamation, options may be exercised within the period ending with the date on which we pass a resolution for voluntary winding up.

Adjustment of Awards. In the event that there is any variation in our share capital the Board may make such adjustments as it considers fair and reasonable to one or more of: the number of shares in respect of which options may be exercised; the option price and the number of shares which may be allotted following the exercise of options.

Transferability. No options under our Adaptimmune Scheme may be transferred, assigned, charged or otherwise disposed of (except on death to the participant s personal representatives) and will lapse immediately upon an attempt to do so. In addition, options that have been awarded will lapse immediately if the participant becomes bankrupt.

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Amendment. The Board may waive or amend the rules of our Adaptimmune Scheme as they deem desirable with the consent of our shareholders, provided that no modification or alteration shall be made which would abrogate or adversely affect the subsisting rights of participants without the prior consent of participants holding 75% of the shares then under option.

Termination. The Board may terminate our Adaptimmune Scheme, without prejudice to subsisting options granted under it.

Adaptimmune Limited 2014 Share Option Scheme (Incorporating Enterprise Management Incentive options)

Our Adaptimmune Limited 2014 Share Option Scheme, or Adaptimmune 2014 Scheme was adopted on April 11, 2014. EMI options may be granted (subject to the relevant conditions being met) under our Adaptimmune 2014 Scheme to our employees who are eligible to receive EMI options under applicable U.K. tax law. Unapproved options may be granted to our employees who are not eligible to receive EMI options and to directors.

Following entering into the GSK collaboration and license agreement in May 2014, we no longer qualified for EMI status because our assets exceed the maximum asset test of £30 million for EMI purposes. Therefore, since that date, no further EMI options were granted under our Adaptimmune Scheme or our Adaptimmune 2014 Scheme; however, unapproved options have been granted under those schemes since that date.

Exercise Conditions. Options granted under our Adaptimmune 2014 Scheme may not (subject to certain limited exceptions) be exercised prior to the earliest of the occurrence of a listing or takeover of us, the sale of the whole or substantially the whole of our business and assets, or the expiry of the period of 114 months commencing on the first day of the month in which the date of grant occurs (subject to a discretion on the part of the Board to allow exercise in other circumstances). In addition, options may be granted subject to vesting schedules or to performance targets which must be satisfied before exercise. Vesting schedules may be accelerated by the Board, and performance targets may be varied, provided that in the case of a performance target, no variation may be made unless an event occurs in consequence of which the Board reasonably considers that the terms of the existing performance targets should be so varied to ensure that the performance criteria will be a fairer measure of such performance, or that the performance condition will afford a more effective incentive to the participant and will be no more difficult to satisfy.

Leaver Provisions. Generally, options must be exercised while the participant is an employee or director of us or a subsidiary. However, in certain circumstances a participant may exercise his options within a period of ceasing to be so connected.

Takeovers and Corporate Events. If any person obtains control of us (as determined in accordance with specified U.K. tax law) as a result of making a general offer to acquire shares or pursuant to an agreement to acquire shares, any vested options may be exercised within 40 days after the time the person has obtained control and any conditions subject to which the offer is made have been satisfied. In addition, if such an offer is made or such an agreement is negotiated, the Board may specify a period for the exercise of options which would be vested as of the date of the change of control (and may additionally allow the exercise during that period of all outstanding options, whether or not vested). To the extent they are not exercised such options will lapse at the end of the relevant period for exercise. However, if another company obtains all of our shares as a result of a qualifying exchange of shares and participants are invited to release their options in consideration of the grant of equivalent options in the acquiring company, and fail to accept the invitation, their options will lapse.

In the event of a sale by of the whole or substantially the whole of our business and its assets, vested options may be exercised for the period of 40 days following that sale, and if unexercised will lapse at the end of that period, subject to a discretion on the part of the Board to allow exercise in advance of the sale.

In the event of a listing of Adaptimmune, the Board may specify certain restricted periods following the listing in which the exercise of options is allowed.

Adjustment of Awards. In the event that there is any variation in our share capital the Board may make such adjustments as it considers in its reasonable opinion to be fair and appropriate to the number and description of shares subject to each option and/or the option price.

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Transferability. No options under our Adaptimmune 2014 Scheme may be transferred, assigned or have any charge or other security interest created over them and will lapse immediately upon an attempt to do so. In addition, options that have been awarded will lapse immediately if the participant becomes bankrupt.

Amendment. The Board may amend, delete or add to the rules of our Adaptimmune 2014 Scheme in any respect as they deem desirable, provided that no amendment, deletion or addition shall be made which adversely affects the subsisting rights of participants without the prior consent of participants holding 75% of the shares under option.

Termination. The Board may terminate our Adaptimmune 2014 Scheme, without prejudice to subsisting options granted under it.

Adaptimmune Limited Company Share Option Plan

Our Adaptimmune Limited Company Share Option Plan, or Adaptimmune Limited CSOP, was adopted on December 16, 2014. The Adaptimmune Limited CSOP allowed the grant of options to our eligible employees prior to the acquisition of Adaptimmune Limited by Adaptimmune Therapeutics Limited pursuant to our corporate reorganization. The Adaptimmune Limited CSOP is a tax efficient option scheme and CSOP options were granted on December 19, 2014 and on December 31, 2014 to our part-time and full-time employees. None of the grants exceeds the maximum value of £30,000 per participant for the shares under the option, which is a CSOP compliance requirement.

Exercise Conditions. Options granted under the Adaptimmune Limited CSOP may not (subject to certain limited exceptions) be exercised prior to the earliest of the occurrence of a listing or takeover of us, the sale of the whole or substantially the whole of our business and assets, a court sanctioned compromise or arrangement affecting our shares or the expiry of the period of 114 months commencing on the first day of the month in which the date of grant occurs (subject to a discretion on the part of the Board to allow exercise in other circumstances). In addition, options may be granted subject to vesting schedules or to performance targets which must be satisfied before exercise. Vesting schedules may be accelerated by the Board, and performance targets may be varied, provided that no variation may be made unless an event occurs in consequence of which the Board reasonably considers that the terms of the existing performance targets should be so varied to ensure that the performance criteria will be a fairer measure of such performance, or that the performance condition will afford a more effective incentive to the participant and will be no more difficult to satisfy.

Leaver Provisions. Generally, options cease to vest when the participant is no longer an employee of us or a subsidiary and, in certain circumstances, will cease to be exercisable on the participant ceasing to be an employee unless the Board exercises discretion to allow exercise within a period of the date of cessation.

Takeovers and Corporate Events. If any person obtains control of us (as determined in accordance with specified U.K. tax law), as a result of making a general offer to acquire shares or pursuant to an agreement to acquire shares, any vested options may be exercised within 40 days after the time the person has obtained control and any conditions subject to which the offer is made have been satisfied. In addition, if such an offer is made or such an agreement is negotiated, the Board may specify a period for the exercise of options which would be vested as of the date of the change of control (and may additionally allow the exercise during that period of all outstanding options, whether or not vested). To the extent they are not exercised, such options will lapse at the end of the relevant period for exercise.

In the event of a sale of the whole or substantially the whole of our business and its assets, vested options may be exercised for the period of 40 days following that sale, and if unexercised will lapse at the end of that period, subject to a discretion on the part of the Board to allow exercise in advance of the sale. In the event of a court sanctioned compromised or arrangement applicable to or affecting the company s shares, options may be exercised within 40 days beginning with the date of court sanction, and to the extent they are not exercised, the options will lapse.

In the event of a listing of our Company, the Board may specify certain restricted periods following the listing in which the exercise of options is allowed.

Adjustment of Awards. In the event that there is any variation in our share capital the Board may make such adjustments as it considers in its reasonable opinion to be fair and appropriate to the number and description of shares subject to each option and/or the option price. Any such adjustment shall also comply with the requirements applicable to tax-advantaged CSOP options.

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Transferability. No options under the Adaptimmune Limited CSOP may be transferred, assigned or have any charge or other security interest created over them and will lapse immediately upon an attempt to do so. In addition, options that have been awarded will lapse immediately if the participant becomes bankrupt.

Amendment. The Board may amend the rules of the Adaptimmune Limited CSOP, provided that:

(a) no amendment may be made which would result in the tax advantages of the CSOP options being lost;

(b) no material amendment shall be made with a material adverse impact on subsisting options without the prior consent of participants holding 75% of the shares under option; and

(c) certain amendments which make the terms of options materially more generous, increase certain limits on participation or expand the class of potential participants may not be made without the approval of our shareholders.

Adaptimmune Therapeutics plc 2015 Share Option Scheme

Our Adaptimmune Therapeutics plc 2015 Share Option Scheme, or Adaptimmune 2015 Scheme was adopted on March 16, 2015. EMI options may be granted (subject to the relevant conditions being met) under the Adaptimmune 2015 Scheme to our employees who are eligible to receive EMI options under applicable U.K. tax law. Unapproved options (which do not have a preferential tax treatment) may also be granted to our employees, directors and consultants.

As noted above, we do not currently qualify for EMI status because our assets exceed the maximum asset test of £30 million for EMI purposes.

Plan Limit. The maximum number of shares for which awards may be granted under the Adaptimmune 2015 Scheme and all other incentive plans for employees, directors and consultants adopted by Adaptimmune or any of its subsidiaries (including the Adaptimmune Therapeutics plc CSOP) following our initial public offering cannot exceed the Scheme Limit . The Scheme Limit at any given time is the number of shares that is equal to (i) 8% of the Initial Fully Diluted Share Capital (described below) plus (ii) any Annual Increments (described below) by which the Scheme Limit has increased prior to that time. For the avoidance of doubt, awards made prior to our initial public offering shall not reduce the number of shares available under the Scheme Limit.

The Initial Fully Diluted Share Capital is (i) the issued share capital of Adaptimmune immediately following our initial public offering, plus (ii) the number of shares which would be issued if all options to acquire shares granted by Adaptimmune to employees, directors and consultants which were outstanding at the time of our initial public offering were exercised in full (and satisfied by the issue of shares).

On July 1 of each year, commencing with July 1, 2016, the Scheme Limit shall automatically increase by 4% of the issued share capital of Adaptimmune at the end of the immediately preceding June 30, or, in each case, such lower number as the Board may prior to that July 1 determine. Each such increase shall be an Annual Increment .

Shares subject to awards which (in whole or in part) have lapsed or otherwise become incapable of exercise (other than by reason of the satisfaction thereof) shall again become available for awards under the Scheme Limit (to the extent that the relevant award has lapsed or otherwise become incapable of exercise).

Exercise Conditions. Options granted under our Adaptimmune 2015 Scheme may be granted subject to vesting schedules or to performance targets which must be satisfied before exercise. Vesting schedules may be accelerated by the Board, and performance targets may be varied, provided that in the case of a performance target, no variation may be made unless an event occurs in consequence of which the Board reasonably considers that the terms of the existing performance targets should be so varied to ensure that the performance criteria will be a fairer measure of such performance, or that the performance condition will afford a more effective incentive to the participant and will be no more difficult to satisfy.

Leaver Provisions. Generally, options must be exercised while the participant is an employee or director of or a consultant to us or a subsidiary. However, in certain circumstances a participant may exercise his options within a period of ceasing to be so connected.

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Takeovers and Corporate Events. If any person obtains control of us (as determined in accordance with specified U.K. tax law) as a result of making a general offer to acquire shares or pursuant to an agreement to acquire shares, any vested options may be exercised within 40 days after the time the person has obtained control and any conditions subject to which the offer is made have been satisfied. In addition, if such an offer is made or such an agreement is negotiated, the Board may specify a period for the exercise of options which would be vested as of the date of the change of control (and may additionally allow the exercise during that period of all outstanding options, whether or not vested). To the extent they are not exercised such options will lapse at the end of the relevant period for exercise. However, if another company obtains all of our shares as a result of a qualifying exchange of shares and participants are invited to release their options in consideration of the grant of equivalent options in the acquiring company, and fail to accept the invitation, their options will lapse.

In the event of a sale by of the whole or substantially the whole of our business and its assets, vested options may be exercised for the period of 40 days following that sale, and if unexercised will lapse at the end of that period, subject to a discretion on the part of the Board to allow exercise in advance of the sale.

In the event of a listing of Adaptimmune, the Board may specify certain restricted periods following the listing in which the exercise of vested options is allowed.

Adjustment of Awards. In the event that there is any variation in our share capital the Board may make such adjustments as it considers in its reasonable opinion to be fair and appropriate to the number and description of shares subject to each option and/or the option price.

Transferability. No options under our Adaptimmune 2015 Scheme may be transferred, assigned or have any charge or other security interest created over them and will lapse immediately upon an attempt to do so. In addition, options that have been awarded will lapse immediately if the participant becomes bankrupt.

Amendment. The Board may amend, delete or add to the rules of our Adaptimmune 2015 Scheme in any respect as they deem desirable, provided that no amendment, deletion or addition shall be made which adversely affects the subsisting rights of participants without the prior consent of participants holding 75% of the shares under option.

Termination. The Board may terminate our Adaptimmune 2015 Scheme, without prejudice to subsisting options granted under it.

Adaptimmune Therapeutics plc Company Share Option Plan

Our Adaptimmune Therapeutics plc Company Share Option Plan, or Adaptimmune Therapeutics plc CSOP, was adopted on March 16, 2015. Options may be granted under the Adaptimmune Therapeutics plc CSOP to our eligible employees. The Adaptimmune Therapeutics plc CSOP is a tax efficient option scheme intended to comply with the requirements of Schedule 4 to the Income Tax (Earnings and Pensions) Act 2003 of the United Kingdom, which provides for the grant of company share option plan or CSOP options. Grants may not exceeds the maximum value of £30,000 per participant for the shares under the option, which is a CSOP compliance requirement.

Plan Limit. The maximum number of shares for which awards may be granted under the Adaptimmune Therapeutics plc CSOP and all other incentive plans for employees, directors and consultants adopted by Adaptimmune or any of its subsidiaries (including the Adaptimmune 2015 Scheme) following our initial public offering cannot exceed the Scheme Limit . The Scheme Limit at any given time is the number of shares that is equal to (i) 8% of the Initial Fully Diluted Share Capital (described below) plus (ii) any Annual Increments (described below) by which the Scheme Limit has increased prior to that time. For the avoidance of doubt, awards made prior to our initial public offering shall not reduce the number of shares available under the Scheme Limit.

The Initial Fully Diluted Share Capital is (i) the issued share capital of Adaptimmune immediately following our initial public offering, plus (ii) the number of shares which would be issued if all options to acquire shares granted by Adaptimmune to employees, directors and consultants which were outstanding at the time of our initial public offering were exercised in full (and satisfied by the issue of shares).

On July 1 of each year, commencing with July 1, 2016, the Scheme Limit shall automatically increase by 4% of the issued share capital of Adaptimmune at the end of the immediately preceding June 30, or, in each case, such lower number as the Board may prior to that July 1 determine. Each such increase shall be an Annual Increment .

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Shares subject to awards which (in whole or in part) have lapsed or otherwise become incapable of exercise (other than by reason of the satisfaction thereof) shall again become available for awards under the Scheme Limit (to the extent that the relevant award has lapsed or otherwise become incapable of exercise).

Exercise Conditions. Options granted under the Adaptimmune Therapeutics plc CSOP may be granted subject to vesting schedules or to performance targets which must be satisfied before exercise. Vesting schedules may be accelerated by the Board, and performance targets may be varied, provided that in the case of a performance target, no variation may be made unless an event occurs in consequence of which the Board reasonably considers that the terms of the existing performance targets should be so varied to ensure that the performance criteria will be a fairer measure of such performance, or that the performance condition will afford a more effective incentive to the participant and will be no more difficult to satisfy.

Leaver Provisions. Generally, options cease to vest when the participant is no longer an employee of us or a subsidiary and, in certain circumstances, will cease to be exercisable on the participant ceasing to be an employee unless the Board exercises discretion to allow exercise within a period of the date of cessation.

Takeovers and Corporate Events. If any person obtains control of us (as determined in accordance with specified U.K. tax law), as a result of making a general offer to acquire shares or pursuant to an agreement to acquire shares, any vested options may be exercised within 40 days after the time the person has obtained control and any conditions subject to which the offer is made have been satisfied. In addition, if such an offer is made or such an agreement is negotiated, the Board may specify a period for the exercise of options which would be vested as of the date of the change of control (and may additionally allow the exercise during that period of all outstanding options, whether or not vested). To the extent they are not exercised, such options will lapse at the end of the relevant period for exercise.

In the event of a sale of the whole or substantially the whole of our business and its assets, vested options may be exercised for the period of 40 days following that sale, and if unexercised will lapse at the end of that period, subject to a discretion on the part of the Board to allow exercise of options that would vest at the time of the sale in advance of the sale. In the event of a court sanctioned compromised or arrangement applicable to or affecting the company s shares, options may be exercised within 40 days beginning with the date of court sanction, and to the extent they are not exercised, the options will lapse.

In the event of a listing of our Company, the Board may specify certain restricted periods following the listing in which the exercise of options is allowed.

Adjustment of Awards. In the event that there is any variation in our share capital the Board may make such adjustments as it considers in its reasonable opinion to be fair and appropriate to the number and description of shares subject to each option and/or the option price. Any such adjustment shall also comply with the requirements applicable to tax-advantaged CSOP options.

Transferability. No options under the Adaptimmune Therapeutics plc CSOP may be transferred, assigned or have any charge or other security interest created over them and will lapse immediately upon an attempt to do so. In addition, options that have been awarded will lapse immediately if the participant becomes bankrupt.

Amendment. The Board may amend the rules of the Adaptimmune Therapeutics plc CSOP, provided that:

(a) no amendment may be made which would result in the tax advantages of the CSOP options being lost;

(b) no material amendment shall be made with a material adverse impact on subsisting options without the prior consent of participants holding 75% of the shares under option; and

(c) certain amendments which make the terms of options materially more generous, increase certain limits on participation or expand the class of potential participants may not be made without the approval of our shareholders.

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Limitations on Liability and Indemnification Matters

To the extent permitted by the Companies Act 2006, we shall indemnify our directors against any liability. We maintain directors and officers insurance to insure such persons against certain liabilities.

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

C. Board Practices.

Board Composition

Our business affairs are managed under the direction of our Board, which is currently composed of eight members. Seven of our directors (Dr. Knowles, Mr. Alleva, Dr. Behbahani, Mr. Laing, Mr. Mott, Dr. Sigal and Dr. Thompson) qualify as independent directors under Rule 5605(a)(2) of the Nasdaq Listing Rules.

Terms of Directors and Executive Officers

Each director is appointed subject to the provisions of our Articles of Association and their letter of appointment or service agreement. A director may be removed by an ordinary resolution passed by a majority of our shareholders. Our executive officers are selected by our Board and appointed under employment agreements or under service agreements, if they are also a director.

Committees of the Board of Directors and Corporate Governance

We have an audit committee, a compensation committee, and a corporate governance and nominating committee. Each of these committees has the responsibilities described below. Our Board may also establish other committees from time to time to assist in the discharge of its responsibilities.

Audit Committee

We are relying on the phase-in rules of the SEC and Nasdaq with respect to the independence of our Audit Committee. These rules require that all members of our Audit Committee must meet the independence standard for audit committee members within one year of the effectiveness of our registration statement, that is, by May 5, 2016.

Our Audit Committee is comprised of three of our non-executive directors, Mr. Alleva, Mr. Laing and Mr. Mott. Each of Mr. Alleva and Mr. Laing is an independent director as such term is defined in Rule 10A-3 under the Exchange Act. Mr. Alleva serves as chair of this committee. Our Board has determined that Mr. Alleva is an audit committee financial expert such term is defined in Item 16A of Form 20-F.

Our Audit Committee oversees and reviews our internal controls, accounting policies and financial reporting, and provides a forum through which our independent registered public accounting firm reports. Our Audit Committee is responsible for, among other things:

- overseeing the activities of our independent registered public accounting firm, including approving their appointment or removal and pre-approving all auditing and non-auditing services permitted to be performed by our independent auditors;

- discussing the annual audited financial statements with management and our independent auditors;

- annually reviewing and assessing the adequacy of our Audit Committee charter;

- meeting separately and periodically with management and our independent auditors;

- maintaining oversight over related person transactions to ensure that they are appropriately disclosed;

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- considering noteworthy questions of possible conflicts of interest involving directors and making recommendations to the Board regarding authorization of conflicts of interest; and

- reporting regularly to the Board.

Compensation Committee

Our Compensation Committee is comprised of three of our non-executive directors, Mr. Mott, Mr. Laing and Dr. Thompson, and each of Mr. Mott, Mr. Laing and Dr. Thompson is an independent director as such term is defined under Rules 5605(a)(2) and 5605(d)(2)(A) of the Nasdaq Stock Market, Marketplace Rules. Mr. Mott serves as chair of this committee.

Our Compensation Committee is responsible for reviewing, among other things, the performance of the senior executive officers and executive directors and setting the policy for their remuneration and the basis of their service and employment agreements with due regard to the interests of the shareholders. The compensation of the chief executive officer and the non-executive directors is a matter for the Board, although the Compensation Committee makes recommendations to the Board in that regard. The Compensation Committee also determines the allocation of awards under our share option schemes to our executive officers (with the exception of the chief executive officer), employees and consultants. It is a policy of the Compensation Committee that no individual participates in discussions or decisions concerning his own remuneration.

Corporate Governance and Nominating Committee

Our Corporate Governance and Nominating Committee is comprised of three of our non-executive directors, Dr. Behbahani, Dr. Knowles and Dr. Sigal, and each of the members is an independent director as such term is defined under Rules 5605(a)(2) of the Nasdaq Stock Market, Marketplace Rules. Dr. Knowles serves as chair of this committee and oversees the evaluation of the Board s performance. Dr. Knowles s performance as Chairman is reviewed by Dr. Sigal, taking into account feedback from other members of the Board. The Corporate Governance and Nominating Committee meets at least twice a year and reviews the structure, size and composition of the Board, supervising the selection and appointment process of directors, making recommendations to the Board with regard to any changes and using an external search consultant if considered appropriate. For new appointments, the committee makes a final recommendation to the Board, and the Board has the opportunity to meet the candidate prior to approving the appointment. Once appointed, the committee oversees the induction of new directors and provides appropriate training to the Board during the course of the year in order to ensure that they have the knowledge and skills necessary to operate effectively. The committee is also responsible for annually evaluating the performance of the Board, both on an individual basis and for the Board as a whole, taking into account such factors as attendance record, contribution during Board meetings and the amount of time that has been dedicated to Board matters during the course of the year. The committee is responsible for developing and recommending to the Board a set of corporate governance principles, and for reviewing the adequacy of such principles and recommending any proposed changes to the Board.

Code of Business Conduct and Ethics

Our Code of Business Conduct and Ethics is applicable to all of our employees, officers and directors and is available on our website at http://www.adaptimmune.com. We expect that any amendment to this code, or any waivers of its requirements, will be disclosed on our website. Information contained on, or that can be accessed through, our website is not incorporated by reference into this Annual Report, and you should not consider information on our website to be part of this Annual Report.

D. Employees.

The average number of employees by function and geographic location during our fiscal years ended June 30, 2015, 2014 and 2013 were as follows:

	2015	2014	2013
By Function:			
Research and development	63	27	17
Management and administrative			