Adaptimmune Therapeutics PLC
Form 10-K
February 27, 2019
Table of Contents

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 10-K

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

For the fiscal year ended December 31, 2018

OR

TRANSITION 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	Not Applicable
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

60 Jubilee Avenue, Milton Park Abingdon, Oxfordshire OX14 4RX United Kingdom (Address of principal executive offices)	(44) 1235 430000 (Registrant's telephone number, including area code)

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

Title of each class	Name of exchange on which registered
American Depositary Shares, each representing 6 Ordinary Shares, par value £0.001 per share	The NASDAQ Global Select Market

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

None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes No

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

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

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

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

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

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

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

As of June 30, 2018, the last business day of the registrant’s most recently completed second fiscal quarter, the aggregate market value of the registrant’s ordinary shares, par value £0.001 per share, held by non-affiliates was approximately $877,532,585.

As of February 26, 2019 the number of outstanding ordinary shares, par value £0.001 per share, of the Registrant is 628,148,866.

DOCUMENTS INCORPORATED BY REFERENCE

The following documents (or parts thereof) are incorporated by reference into the following parts of this Form 10-K: Certain information required by Part III of this Annual Report on Form 10-K is incorporated from our definitive proxy statement pursuant to Regulation 14A, to be filed with the Commission not later than 120 days after the close of our fiscal year ended December 31, 2018.

Table of Contents

GENERAL INFORMATION

In this Annual Report on Form 10 K ("Annual Report"), "Adaptimmune," the "Group," the "Company," "we," "us" and "our" Adaptimmune Therapeutics plc and its consolidated subsidiaries, except where the context otherwise requires. "Adaptimmune" and "SPEAR" are registered trademarks of Adaptimmune.

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 successfully advance our ADP-A2M10 (MAGE-A10), ADP-A2M4 (MAGE-A4) and ADP-A2AFP (AFP) products through clinical development and the timing within which we can recruit patients and treat patients in our clinical trials;
- our ability to successfully and reproducibly manufacture SPEAR T-cells in order to meet patient demand;
- our ability to further develop our commercial manufacturing process for our SPEAR T-cells, transfer such commercial process to third party contract manufacturers, if required, and for such third party contract manufacturers or ourselves to manufacture SPEAR T-cells to the quality and on the timescales we require;
- the scope and timing of performance of our ongoing collaboration with GSK;
- our ability to successfully advance our SPEAR T-cell technology platform to improve the safety and effectiveness of our existing SPEAR T-cell candidates and to submit Investigational New Drug Applications, or INDs, for new SPEAR T-cell candidates;
- the rate and degree of market acceptance of T-cell therapy generally, and of our SPEAR T-cells;
- government regulation and approval, including, but not limited to, the expected regulatory approval timelines for our SPEAR T-cells and the level of pricing and reimbursement for our SPEAR T-cells, if approved for marketing;
- the existence of any third party patents preventing further development of any of our SPEAR T-cells, including, any inability to obtain appropriate third party licenses, or enforcement of patents against us;
- our ability to obtain granted patents covering our SPEAR T-cells and to enforce such patents against third parties;
- volatility in equity markets in general and in the biopharmaceutical sector in particular;
- fluctuations in the price of materials and bought-in components;
- our relationships with suppliers, contract manufacturing organizations or CROs and other third-party providers including fluctuations in the price of materials and services, ability to obtain reagents particularly where such reagents are only available from a single source, and performance of third party providers;

Table of Contents

- increased competition from other companies in the biotechnology and pharmaceutical industries including where such competition impacts ability to recruit patients into clinical trials;
- claims for personal injury or death arising from the use of our SPEAR T-cell candidates;
- our ability to attract and retain qualified personnel; 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 Part I, Item 1A in this Annual Report and in our other filings with the Securities and Exchange Commission (the “SEC”). 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.

Table of Contents

Table of Contents

		Page
PART I		
Item 1.	Business	1
Item 1A.	Risk Factors	23
Item 1B.	Unresolved Staff Comments	74
Item 2.	Properties	74
Item 3.	Legal Proceedings	74
Item 4.	Mine Safety Disclosures	74
PART II		
Item 5.	Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities	74
Item 6.	Selected Financial Data	76
Item 7.	Management's Discussion and Analysis of Financial Condition and Results of Operations	78
Item 7A.	Quantitative and Qualitative Disclosures About Market Risk	96
Item 8.	Financial Statements and Supplementary Data	97
Item 9.	Changes in and Disagreements with Accountants on Accounting and Financial Disclosure	97
Item 9A.	Controls and Procedures	97
Item 9B.	Other Information	98
PART III		
Item 10.	Directors, Executive Officers and Corporate Governance	98
Item 11.	Executive Compensation	98
Item 12.	Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters	98
Item 13.	Certain Relationships and Related Transactions, and Director Independence	99

Item 14.	Principal Accounting Fees and Services	99
PART IV		
Item 15.	Exhibits, Financial Statement Schedules	99
Item 16.	Form 10-K Summary	101
Signatures		102

Table of Contents

Item 1. Business

Overview

We are a clinical-stage biopharmaceutical company focused on providing novel cell therapies to patients, particularly in solid tumors. Our comprehensive and proprietary SPEAR (Specific Peptide Enhanced Affinity Receptor) T-cell platform enables us to identify cancer targets, find and genetically engineer T-cell receptors ("TCRs"), and produce therapeutic candidates for administration to patients. Using our affinity engineered TCRs, we aim to become the first company to have a TCR T-cell approved for a solid tumor indication.

We have three SPEAR T-cells in clinical trials, ADP-A2M10 (MAGE-A10), ADP-A2M4 (MAGE-A4) and ADP-A2AFP (AFP). All SPEAR T-cells are currently exhibiting acceptable tolerability profiles with no evidence of off-target toxicities observed.

- Two Phase 1 clinical trials are ongoing with ADP-A2M10. The first clinical trial is in patients with non-small cell lung cancer ("NSCLC"). The second clinical trial is in patients with three cancer tumor types, urothelial, melanoma and head and neck cancers. Both trials have progressed to the expansion phase, with patients being treated with up to 10 billion transduced SPEAR T-cells.
- A Phase 1 clinical trial is ongoing with ADP-A2M4 in bladder, melanoma, head and neck, ovarian, NSCLC, synovial sarcoma, myxoid round cell liposarcoma ("MRCLS"), esophageal, and gastric cancers. This trial is now in the expansion phase with patients being treated with up to 10 billion transduced SPEAR T-cells.
- A Phase 1 clinical trial is ongoing with ADP-A2AFP in patients with hepatocellular carcinoma. The trial is in the dose escalation phase with patients receiving a target dose of 1 billion transduced SPEAR T-cells.

A fourth SPEAR T-cell, the NY-ESO SPEAR T-cell was transitioned to GlaxoSmithKline ("GSK") during 2018 following GSK's exercise of its option to obtain an exclusive global license to the NY-ESO SPEAR T-cell program in September 2017. GSK has assumed full responsibility for all development, manufacturing and commercialization activities for the NY-ESO SPEAR T-cell including progression of this SPEAR T-cell into further clinical trials.

We have our own manufacturing facility in the United States that routinely manufactures SPEAR T-cells to treat patients across a broad range of solid tumors. We also have dedicated vector manufacturing in the United Kingdom and we anticipate producing our first batch of vector to support pilot clinical trials in 2019, which will enable us to continue to develop enhancements and improvements with the aim of reducing the time taken to manufacture and supply patient product.

We continue to use our SPEAR T-cell platform to identify and validate further cancer targets (including targets which are closely related to a specific disease indication) to which SPEAR T-cells can be directed. We have a number of preclinical programs in progress.

We have a number of next generation and combination strategies designed to further enhance our SPEAR T-cells. In addition to our internal next generation programs, we also have collaborations with third parties intended to promote further next generation solutions. These include our collaboration with Universal Cells, Inc. ("Universal Cells") and our collaboration with Bellicum Pharmaceutical Inc. ("Bellicum"). With Universal Cells, we are looking to develop affinity engineered donor T-cells that are universally applicable to all patients. While these "off-the shelf cells" would be specific for a given Human Leukocyte Antigen ("HLA") type and target antigen, they would overcome the current limitation of autologous therapies that need to be manufactured specifically for each patient. The enhanced T-cell technology being developed involves selective engineering of cell surface proteins, without the use of nucleases, to develop these T-cell products. If successful, this will enable us to treat our patients with an off-the-shelf product. Our Bellicum collaboration was announced in December 2016 and under the collaboration, we are evaluating Bellicum's

1

Table of Contents

GoTCR technology (inducible MyD88/CD40 co-stimulation, or iMC) with our SPEAR T-cells for the potential to create enhanced T-cell therapeutics.

Business Strategy

Our strategic objective is to be a world leader in discovering, developing and commercializing TCR-based T-cell therapies that transform the clinical outcomes of patients with cancer. We have an ambition to have the first TCR T-cell approved for a solid tumor indication. In order to achieve our objectives, we are focused on the following strategies:

Advance our clinical studies for ADP-A2M10, ADP-A2M4 and ADP-A2AFP. We have three wholly owned SPEAR T-cells with open INDs covering multiple indications. We plan to advance these wholly-owned SPEAR T-cells during 2019 with the aim of providing initial clinical data for ADP-A2M10 and ADP-A2M4 during the first half of 2019. We are working with leading cancer centers including through our strategic alliance agreement with MD Anderson Cancer Center, to advance our SPEAR T-cells through clinical studies.

Continue to use our SPEAR T-cell platform to generate SPEAR T-cells for cancers with limited existing therapeutic approaches. We intend to continue to generate new SPEAR T-cells from our fully integrated technology platform, which enables the systematic identification and validation of suitable target peptides, T-cell cloning, engineering of TCRs and preclinical testing processes. We also continue to develop SPEAR T-cells to address targets from different HLA-types.

Continue to understand, further enhance and improve the effectiveness and persistence of our SPEAR T-cell therapies. We continue to evaluate and work to understand the mechanism of action of our SPEAR T-cells, in particular the best approaches for further enhancing the effectiveness and persistence of our SPEAR T-cells. We continue to further develop our SPEAR T-cells internally and through multiple collaborations including by exploring the addition of other components in our lentiviral vector, which would be expressed in the SPEAR T-cells alongside our engineered TCR.

Optimize and expand our process development and manufacturing capabilities to maintain our leadership position in the TCR space. We have a SPEAR T-cell manufacturing facility in the United States and dedicated vector manufacturing capability in the UK and we anticipate producing our first batch of vector to support pilot clinical trials in 2019. We will continue to expand our SPEAR T-cell and vector manufacturing capability during 2019 including optimization of the manufacture, supply, associated analytical expertise and quality systems for our SPEAR T-cell therapies. We also continue to work and develop an off-the-shelf product.

Expand our intellectual property portfolio. We intend to continue building on our technology platform, comprising intellectual property, proprietary methods and know-how in the field of TCRs and T-cells. These assets form the foundation for our ability to strengthen our product pipeline and to defend and expand our position as a leader in the field of T-cell therapies.

Our SPEAR T-cell Therapies

The Immune System and T-cells

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. T-cells naturally scan all other cells in the body for the presence of abnormal peptide fragments, such as those generated from

infectious agents. Recognition of this peptide-HLA complex takes place through the TCR expressed on the T-cells. However, binding of naturally occurring TCRs to cancer targets 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. Even when TCRs recognize cancer cells expressing novel proteins caused by mutations, elements of the immune system, or the cancer itself often suppress the T-cell response.

Table of Contents

Target Identification and Validation

Before developing any engineered T-cell or TCR, it is important to identify and validate a suitable target cancer peptide. The target must be expressed primarily only on the cancer cells of interest and with expression in normal non-cancerous tissue only where a risk to the patient would be deemed acceptable. Careful validation and identification of targets is important to ensuring that any engineered TCR is specific to the targeted cancer and does not bind to the same target on non-cancer cells, or that the TCR does not recognize a similar peptide derived from a protein in normal cells. Our target identification platform is focused on three approaches. First, we are using our platform to validate cancer testis antigens, for example the MAGE-A4 and MAGE-A10 antigens. Second, we are using our platform to identify non-cancer testis antigens which are closely related to a specific disease indication, for example the AFP antigen. Finally, we are identifying targets in the context of different HLA types ensuring that we can address a broad patient population for any given target across multiple HLA types.

Affinity Engineering

Following identification of a suitable target peptide, we identify TCRs that are capable of binding to that target peptide. We then engineer those identified TCRs to enhance and optimize their ability to target and bind to the cancer peptides, thereby enabling a highly targeted immunotherapy. The optimized TCR then undergoes extensive preclinical safety testing prior to administration to patients. Our SPEAR T-cell platform technology enables us to develop a pipeline of targets and TCR therapeutic candidates that we believe may be effective in a variety of cancer types that are unresponsive to currently available and experimental therapies. We have three wholly owned SPEAR T-cells currently in clinical trials (ADP-A2M10, ADP-A2M4 and ADP-A2AFP) and a pipeline of SPEAR T-cells in development, including SPEAR T-cells directed to peptides expressed in the context of different HLA-types.

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 self-inactivating (SIN) virus, known as SIN-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 a recognized HLA-peptide complex, they multiply and initiate the destruction of the targeted cancer cells.

Table of Contents

Our Wholly Owned Clinical Product Pipeline

ADP-A2M10

Phase 1 clinical trials are ongoing with ADP-A2M10 in NSCLC, urothelial, melanoma and head and neck cancers in the United States, Canada, the United Kingdom and Spain. These trials are first-in-human, open-label studies utilizing a modified 3+3 design with escalating target doses of 100 million (Cohort 1), 1 billion (Cohort 2), and 5 billion (Cohort 3) transduced SPEAR T-cells to evaluate safety, including dose limiting toxicities (DLTs). The first three safety cohorts are followed by an expansion phase with doses of up to 10 billion SPEAR T-cells. Patients are currently being enrolled in the expansion phase in both trials.

No evidence of off-target toxicity has been observed and as of December 31, 2018, most adverse events have been consistent with those typically experienced by cancer patients undergoing cytotoxic chemotherapy or other cancer immunotherapies. Data from the first two cohorts of the ADP-A2M10 clinical trials were presented at the European Society for Medical Oncology meeting (ESMO) in October 2018.

ADP-A2M4

A Phase 1 clinical trial is ongoing in nine solid tumor indications including urothelial, melanoma, head and neck, ovarian, NSCLC, esophageal, gastric cancers, synovial sarcoma and MRCLS. This trial is a first-in-human, open-label study utilizing a modified 3+3 design with escalating target doses of 100 million (Cohort 1), 1 billion (Cohort 2), and 5 billion (Cohort 3) transduced SPEAR T-cells to evaluate safety, including DLTs. The first three safety cohorts are followed by an expansion phase with doses of up to 10 billion SPEAR T-cells. Patients are currently being enrolled in the expansion phase of the trial.

No evidence of off-target toxicity has been observed in the initial safety cohorts of the trial and as of December 31, 2018, most adverse events have been consistent with those typically experienced by cancer patients undergoing cytotoxic chemotherapy or other cancer immunotherapies.

Data from the first two cohorts of the ADP-A2M4 clinical trial were presented at ESMO in October 2018.

Table of Contents

ADP-A2AFP

A Phase 1, open label, dose escalation trial is ongoing. This study is designed to evaluate the safety and anti-tumor activity of ADP-A2AFP in hepatocellular carcinoma ("HCC"). The trial is open in the United States, United Kingdom and Spain. The Phase 1 clinical trial includes a dose escalation utilizing a modified 3+3 design with escalating target doses of 100 million (Cohort 1), 1 billion (Cohort 2), and 5 billion (Cohort 3) transduced SPEAR T-cells to evaluate safety, including dose limiting toxicities (DLTs), followed by expansion phase with possible doses of up to 10 billion SPEAR T-cells to further explore safety and potential evidence of anti-tumor activity. The trial is currently enrolling patients within the second dose cohort, with patients receiving target doses of 1 billion cells. There were no dose limiting toxicity events or evidence of off-target toxicity observed in the first dose cohort.

NY-ESO SPEAR T-cell Therapy (transitioned to GSK)

On September 7, 2017, we announced that GSK had exercised its option under the strategic collaboration and license agreement with GSK (as amended from time to time, the "GSK Collaboration and License Agreement") to exclusively license the right to research, develop and commercialize the NY-ESO SPEAR T-cell. Following exercise of this option by GSK, the NY-ESO SPEAR T-cell program was transitioned to GSK in August 2018 at which point GSK assumed full responsibility for future research, development and potential commercialization of the NY-ESO T-cell therapy (now called GSK 3377794).

GSK nominated a second target program for the PRAME target antigen, which was announced on 9 January 2017. We have since completed all work under this collaboration program. The program led to the development of a final lead candidate SPEAR T-cell directed to a specific peptide from the PRAME antigen. We and GSK agreed that the collaboration should not continue due to the peptide, to which the lead candidate was directed, not reaching GSK criteria.

GSK have now nominated a third target program that will evaluate and develop new SPEAR T-cells. Adaptimmune and GSK are in the process of agreeing a collaboration program for this third target program.

GSK is entitled to nominate two further target programs under the GSK Collaboration and License Agreement, excluding our ongoing wholly-owned development programs.

Preclinical candidates

We continue to progress development of new SPEAR T-cells directed to new targets and to targets expressed in the context of HLA-types other than HLA-A2.

Next Generation Technology

We believe that there is potential to enhance the potency and durability of our SPEAR T-cells, for instance by adding additional active proteins by means of the lentiviral delivery system. These enhancements are designed to result in next generation SPEAR T-cells for future clinical programs. We have multiple development programs ongoing both internally and with third party collaborators to develop various enhancements to our SPEAR T-cells. For example, we

have development programs for:

- a dominant negative TGF-Beta ('dnTGFBRII') SPEAR T-cell designed to block immune suppression by TGF-Beta in certain tumor microenvironments,
- CD8 constructs that aim to promote epitope spreading, anti-tumor memory and tumor inflammation,
- phosphodiesterase constructs designed to enhance T-cell proliferation, and
- inducible IL-7 constructs that aim to enhance persistence of our SPEAR T-cells.

Table of Contents

Preclinical development is ongoing for a number of these programs with the aim of having the first next generation construct ready for IND submission during the second half of 2019.

Manufacturing Platform Development

Manufacturing Capability

We have our own SPEAR T-cell manufacturing capability at the Navy Yard in Philadelphia, Pennsylvania. Patient product manufacture for our wholly owned assets has started across a range of solid tumors. The Navy Yard facility is currently capable of manufacturing SPEAR T-cell product for up to 10 patients per month. This is scalable to 100 patients per month. We have dedicated vector manufacturing capability in the United Kingdom, with the first production of vector for pilot clinical trials expected in 2019. Control of our own manufacturing process enables us to improve and further develop our processes for manufacture of our SPEAR T-cells. We continue to work with our third party T-cell supplier to increase capacity for T-cell manufacture and are using a third party vector manufacturer for supply of vectors to support our ongoing clinical trials.

Manufacturing Improvements

We have the goal of reducing the time between apheresis of a patient and return of affinity enhanced SPEAR T-cells back to the patient. We have made a number of changes to our current SPEAR T-cell manufacturing process and are continuing to make changes. In particular, we have implemented rapid sterility testing within our Navy Yard facility. We have also developed a suspension vector manufacturing process with the first production run for early stage clinical trials expected in 2019.

Core Alliances and Collaborations

We have entered into core alliance or collaboration agreements with GSK (Collaboration and License Agreement), MD Anderson Cancer Center (collaboration designed to expedite the development of T-cell therapies for multiple types of cancer); Universal Cells (collaboration relating to gene editing and HLA-engineering technology); and Bellicum Pharmaceuticals Inc. (Co-Development and Co-Commercialization Agreement).

GSK Collaboration and License Agreement

We entered into the GSK Collaboration and License Agreement regarding the development, manufacture and commercialization of TCR therapeutic candidates in May 2014. The collaboration is for up to five programs. The first program was the NY-ESO SPEAR T-cell program, in relation to which GSK has now exercised its option to take an exclusive license. The second program related to development of a SPEAR T-cell to a peptide derived from the PRAME antigen. This program has now completed. We are in the process of agreeing the third target program with GSK.

Under the terms of the GSK Collaboration and License Agreement, the Company may be entitled to:

- development milestones of up to £18 million ($23 million) per product and HLA-type for the NY-ESO Program and up to £21.5 million ($27.3 million) per product and HLA-type for other programs (including the third target program);
- regulatory milestones of up to £36 million ($45.7 million) per product and HLA-type for the NY-ESO program and up to £40 million ($50.8 million) per product and HLA-type for other programs (including the third target program);

and

- commercialization milestones upon the first commercial sale of a product of up to £70.5 million ($89.5 million) per product and HLA-type for the NY-ESO Program and up to £80 million ($101.5 million) per product and HLA-type for other programs (including the third target program).

The development and regulatory milestones are per product milestones and are dependent on achievement of certain obligations, the nature of the product being developed, stage of development of product, territory in which an obligation is achieved and type of indication or indications in relation to which the product is being developed. In addition for any

Table of Contents

program, multiple products may be developed in the context of different HLA-types. As of December 31, 2018, we had achieved development milestones of $66.4 million.

For other programs (including the third target program) under the GSK Collaboration and License Agreement, an option fee is also payable of up to £6 million ($7.6 million) on exercise of the option by GSK, after which GSK is responsible for all development expenses.

For any product that is commercialized by GSK, the Company may receive tiered sales milestones up to £200 million ($253.8 million) per product and HLA-type and mid-single to low double-digit royalties on worldwide net sales of the applicable product. Royalties are payable while there is a jointly owned or solely owned valid patent claim covering the SPEAR T-cell in the country in which the relevant SPEAR T-cell 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.

On September 7, 2017 we announced that GSK had exercised its exclusive option for the NY-ESO SPEAR T-cell program. Transition of the program to GSK occurred during 2018. GSK has now assumed full responsibility for the NY-ESO SPEAR T-cell program including any ongoing clinical trials. As a result of the option exercise, Adaptimmune received £48 million (approximately $61 million) from GSK over the course of the transition period. This included development milestones of £18 million (approximately $23 million) and an option payment of £30 million (approximately $38 million), which also allows GSK to nominate two additional targets following completion of the transition. Successful continuation of development and subsequent commercialization of NY-ESO would trigger additional payments for development milestones, tiered sales milestones, and mid-single to low double-digit royalties on worldwide net sales.

Upon nomination of the third target program by GSK, we have granted to GSK an exclusive option to the nominated target which can be exercised up to four months after approval of an IND application in relation to a TCR therapeutic candidate directed against the nominated target. We are responsible for taking the third target program through preclinical testing and up to IND application filing. GSK is responsible for the IND filing itself should the preclinical testing and development be favorable.

Two other targets may be nominated by GSK at specified times under the GSK Collaboration and License Agreement, excluding any wholly-owned research programs already in progress by us. Upon nomination by GSK of any of these two additional targets, we will grant to GSK an exclusive option on each target, which can be exercised up to four months after approval of an IND application 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 any option (including the options for the NY-ESO SPEAR T-cell and third target programs), we will grant to (and have granted in relation to the NY-ESO SPEAR T-cell) GSK an exclusive worldwide license under intellectual property rights specific to the SPEAR T-cell developed under the relevant collaboration programs. GSK will, at its own expense, be fully responsible for all further development and commercialization of the relevant T-cell candidates. The licenses do not include a 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 T-cell therapeutics directed at the targets subject to outstanding options granted to GSK.

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 upon 60 days' written 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

Table of Contents

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 SPEAR T-cells in specified circumstances.

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 SPEAR T-cells 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 SPEAR T-cells and SPEAR 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 ("UKIPO") and/or 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 SPEAR T-cells or TCRs. 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, manufacturing processes and SPEAR T-cells.

As of December 31, 2018 we owned or jointly owned approximately 152 granted patents (of which 17 are U.S.-issued patents) and 338 pending patent applications (of which 43 are U.S. National patent applications). These patents and patent applications include claims directed to our SPEAR T-cells, our platform technology used to identify and generate engineered TCR therapeutic candidates, our next generation SPEAR T-cell technology and our manufacturing and process technology.

Product Patents

NY-ESO - We own granted patents covering the composition of matter of our NY-ESO SPEAR T-cell. The patent claims are directed to the NY-ESO SPEAR TCR 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.

ADP-A2M10 - We own patent applications covering the composition of matter of ADP-A2M10. 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 United Kingdom Intellectual Property Office ("UKIPO") and a patent application under the applicable Patent Co-operation Treaty has since been filed claiming priority from that United Kingdom patent application. National applications have been filed in all commercially relevant territories.

ADP-A2AFP - We own patent applications covering the composition of matter of ADP-A2AFP. As with our NY-ESO and ADP-A2M10 products, 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 UKIPO and a patent application under the applicable Patent Co-operation Treaty has since been filed claiming priority from that United Kingdom patent application. National applications have

been filed in all commercially relevant territories and claims have been allowed in Europe.

ADP-A2M4 - We own three patent applications covering the composition of matter of ADP-A2M4 and other related TCRs. As with our NY-ESO and ADP-A2M10 products, the patent application claims are directed to the engineered TCR therapeutic candidate and in particular the amino acid substitutions required for such engineered TCR

Table of Contents

therapeutic candidate. The initial priority patent applications were filed in the UKIPO and patent applications under the applicable Patent Co-operation Treaty have since been filed claiming priority from that United Kingdom patent application. National applications have been filed in all commercially relevant territories.

Platform Technology

We jointly own a number of platform technology patents and patent applications which are directed to certain aspects of the process that we use to engineer our SPEAR TCRs. These are jointly owned with Immunocore Limited ("Immunocore"), a company with whom, historically, we had a shared development history. 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.

Novel targets

We have filed 29 patent applications under the Patent Cooperation Treaty which cover peptides expressed on the tumor cell surface and the TCRs which recognize them. The applications as filed cover 872 peptides from 63 different target proteins. National applications have been filed in all commercially relevant territories.

TCR libraries

We have filed 10 patent applications which cover large libraries of TCR genes which we have generated and the method of their generation: these act as proprietary sources for screening for TCRs, which are the starting points for affinity engineering into clinical candidates. National applications have been filed in all commercially relevant territories

Manufacturing Process Patents and Patent Applications

We have know-how and patent applications relating to the manufacture of our SPEAR T-cells. For example, we have filed patent applications in commercially relevant territories, which claim priority from initial priority patent applications filed at the USPTO and UKIPO, which are directed to a particular modification to the lentiviral vector technology. We believe this modification enhances the safety profile of the lentiviral vector technology. This has been granted in the United States and allowed in Europe. Further patent applications have been filed on the manufacturing and quality control of our products

Preclinical and Next Generation Approaches

We have recently filed a priority generating patent application in relation to a gene which prevents our cytotoxic T-cells from being inhibited by the immunosuppressive tumor microenvironment. A patent application under the applicable Patent Co-operation Treaty has since been filed claiming priority from that United Kingdom patent application and a patent application was filed in the United States for accelerated prosecution under the Cancer Immunotherapy Pilot Program, and subsequently granted. We plan to file national applications claiming priority from

this in all commercially relevant territories. This is potentially relevant to all of our SPEAR T-cells in solid tumor indications and protects one of the next generation SPEAR T-cell products under development. Two further patent applications have been filed on modifications to the SPEAR T-cells enhancing their in vivo activity. We have also received a notice of grant for a European patent covering methods for predicting binding of a TCR to an off-target peptide utilizing proprietary alanine scanning processes.

Table of Contents

Exclusive License for Bead Products

In December 2012, we entered into two agreements, a license and a sub-license, with ThermoFisher Scientific Inc. ("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 Scientific 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.

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

Table of Contents

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.

On June 16, 2016, we entered into a supply agreement with ThermoFisher for the supply of the Dynabeads® CD3/CD28 technology. The Dynabeads® CD3/CD28 technology is used in our manufacturing process to isolate, activate and expand patient T-cells. The supply agreement runs until December 31, 2025. Under the supply agreement, we are required to purchase our requirements for CD3/CD28 magnetic bead product exclusively from ThermoFisher for a period of five years and there are also minimum purchasing obligations. ThermoFisher has the right to terminate the supply agreement for material breach or insolvency.

See “Risk Factors—Risks Related to Our Reliance Upon Third Parties—We rely heavily on ThermoFisher and the technology we license from them.”

Other Third-Party Intellectual Property Rights

Third-party patents do exist that purport to cover some or all of our current lentiviral vectors/systems 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 manufacturing 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.

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.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition, a strong emphasis on proprietary products and intellectual property. 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 SPEAR T-cells that we successfully develop and commercialize will compete with existing products and new products that may become available in the future.

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 (for instance PD 1/PD-L1 antibodies) 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 T cells. Other immunotherapies that are being actively investigated include: antibody-drug complexes, TCR-mimic antibodies, oncolytic viruses, cancer vaccines. A variety of

Table of Contents

cell-based autologous and allogeneic approaches are also being researched and developed, including but not limited to: CAR-T cell, TCR T-cell, GammaDelta T-cell, CAR-NK cell, NK cell, NKT cell and CTL.

- CAR-T in hematological malignancies: Engineered T-cell therapeutics have been identified using antibody recognition systems engineered into T cells, so-called CAR-T cells. A number of targets in hematological malignancies have been well characterized including, but not limited to: BCMA, CD4, CD5, CD19, CD22, CD20, CD33, CD38, CD70, CS1 and CD123. Two CD-19 directed CAR-T cell products have been approved by the U.S. Food and Drug Administration ("FDA") Kymriah™ (tisagenlecleucel) and Yescarta™ (axicabtagene ciloleucel) as well as by the European Medicines Agency (EMA) in the European Union. A number of companies and academic institutions are developing CAR-T cell products including but not limited to Allogene Therapeutics, Atara Bio, Autolus, Baylor College of Medicine, Bellicum Inc, bluebird bio, Celyad, Celgene, Cellectis, CRISPR Therapeutics, Fate Therapeutics, Intrexon, Janssen (JNJ with Nanjing Legend), Juno Therapeutics, Kite Pharma (Gilead), Mustang Bio, Novartis, Precigen, Refuge Biotechnologies Inc, Sorrento Therapeutics and Ziopharm Oncology.
- CAR-T in solid tumors: In addition to hematological malignancies, there are a growing number of pharmaceutical, biotechnology, and academic institutions researching and developing autologous and allogeneic CAR-T therapies in the solid tumor setting. These CAR-T cell therapies are at a variety of stages of preclinical and clinical development, as well as directed towards a broad target spectrum, including but not limited to: DLL3, EGFR, GD2, HER-2, IL13r 2, Lewis Y, L1-CAM, Mesothelin, MUC16, PSCA, PSMA and ROR1. Competitors include but are not limited to: Allogene Therapeutics, Amgen, Atara Bio, Aurora Biopharma, Avid Biotics / Xyphos, Baylor College of Medicine, Cell Medica, Bellicum, BioNTech, Carisma Therapeutics (formerly CARMA Therapeutics), Carsgen, Cellectis Therapeutics, Celyad, CRISPR Therapeutics, Endocyte, Fate Therapeutics, Formula Therapeutics, Fred Hutchinson Cancer Research Center, Helix BioPharma, Juno Therapeutics, MaxCyte, Memorial Sloan Kettering Cancer Center, Mustang bio, Poseida Therapeutics, Senti Biosciences, Sorrento Therapeutics, Symvivo, Targazyme and Tmunity.
- CARs & TCR-mimics targeting peptide-HLA complexes: Most CAR-T therapies in development are directed towards suitable antigen targets. Another area of development is the creation of CAR-T that selectively binds to the peptide-HLA (pHLA) complex (the natural binding site for endogenous TCR). Furthermore, competitors are also looking at pHLA antibodies or TCR mimic antibodies that can either be engineered in T-cells or developed as standalone antibody therapies in cancer indications (both hematologic malignancies and solid tumors). Targets of such pHLA CAR-T or TCR mimic antibodies include: AFP, CD19, BCMA, NY-ESO-1, p53 and WT1. A number of pharmaceutical, biotechnology, and academic institutions are researching and developing CARs & TCR-mimics targeting the peptide-HLA complex, including but not limited to: Adicet Bio / Regeneron, Altor Bioscience, Cancer Research Technology/CRUK, Eureka Therapeutics, Gritstone Oncology, Morphosys, Xencor and Ziopharm Oncology.
- TCR T-cells: TCR T-cells are being developed by competitors that are directed towards a multitude of targets including: AFP, CD20, HPV-16 E6/E7, KRAS, MAGE-A1, MAGE-A3, MAGE A3/A6, MART1, NRAS, NY-ESO-1, p53, PRAME, TGF RII frameshift antigen WT1, as well as personalized neoantigens. Juno Therapeutics (a Celgene Company) has developed an engineered TCR therapeutic candidate where the end TCR is purported to have enhanced affinity through stem-cell selection. Juno's candidate JTCR016 (WT1-specific TCR), in collaboration with Fred Hutchinson Cancer Research Center and the National Cancer Institute (NCI), is currently undergoing a Phase 1/2 trial in NSCLC and mesothelioma setting as well as a separate Phase 1/2 in AML. Medigene AG has reported development of a PRAME TCR therapeutic candidate (MDG1011), which has begun a Phase 1/2 clinical investigation in AML, MM and myelodysplastic syndromes. In addition to Juno there is a growing number of TCR companies that are adopting approaches to TCR affinity enhancement, for example Axis Therapeutics, Takara, Takara Bio, Fred Hutchinson Cancer Centre and Immatics. In addition other competitors include, but are not limited to: 3T, Adaptive Biotechnologies (with Genentech), AgenTus, Atreca, Baylor College, Bellicum, BioNTech, bluebird bio, Captain T cell, Cellular Biomedicine Group Inc, Cell Medica Ltd, GigaMune,

Table of Contents

GSK, Immunocellular Therapeutics, Immunocore, Intellia Therapeutics, Inc (with Ospedale San Raffaele), Juno Therapeutics, Kiromic, Kite Pharma (Gilead), Lion TCR LTD, MD Anderson Cancer Center, MediGene AG, NCI, Neon Therapeutics, Parker Institute, Roswell Park Cancer Institute, Scancell (with BioNTech), Tactiva Therapeutics, Takara Bio Inc, Takeda (T-CIRA), TCR x immunotherapies, T-Knife, Tmunity, University of Leiden, Zelluna (with Oslo University Hospital) and Ziopharm Oncology.

- Other cell-based approaches: In addition to adoptive cell therapy approaches aforementioned, our competitors are also investigating the potential of GammaDelta T-cell, CAR-Macrophages, CAR-NK cell, NK cell, NKT cell, CTLs, TILs, Marrow-infiltrating lymphocytes (MILs), Multi-tumor-associated antigen (TAA)-specific T-cells and virus-specific T-cells either preclinically or in a clinical setting (both hematologic malignancies and solid tumors). In this space there are a number of potential competitors, including, but not limited to: Adicet Bio, Atara Bio, Aurora BioPharma, Cell Medica, Cellular Biomedicine Group Inc, CytomX, Celgene, Fate Therapeutics, Fortress Biotech, Gadeta (with Kite Pharma), Gamma Delta Therapeutics (with Takeda), Gamida cell, Genocea, Glycostem Therapeutics, iCell Gene Therapeutics, Immatics, Iovance Biotherapeutics (formerly Lion Bio), KSQ Therapeutics, Multimmune, NantKwest, Sorrento Therapeutics, Marker Therapeutics, Tessa Therapeutics, TC Biopharm (with bluebird bio), Torque Therapeutics WindMIL Therapeutics and Ziopharm Oncology.

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 (“DOJ”), or other governmental entities.

FDA Approval Process

In the United States, therapeutic products, including drugs, biologics, and medical devices are subject to extensive regulation by the FDA. The Federal Food, Drug, and Cosmetic Act (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. Some biological products are subject to regulation under the FDC Act. Most biological products are approved for marketing under provisions of the Public Health Service Act (“PHSA”) via a Biologics License Application (“BLA”). The application process and requirements for approval of BLAs are generally similar to those for new drug applications (“NDAs”), and biologics are associated with generally similar, if not greater, 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 IND, which must become effective before human clinical testing may commence, and adequate and well-controlled clinical trials to

Table of Contents

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 not communicated deficiencies with 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 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.

In most cases, the FDA requires two adequate and well-controlled clinical trials to demonstrate the efficacy of the biologic. A single Phase 3 trial with other confirmatory evidence may be sufficient in some 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, compilation of data relating to the product's pharmacology, chemistry, manufacture, and controls as well as proposed labeling for the product. 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

Table of Contents

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 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, 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 ("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 ("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, may require submission and FDA approval of a BLA supplement before the change can be implemented. A BLA supplement for a new indication may require 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.

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.

Table of Contents

Expedited Pathways

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. These expedited programs include fast track designation, breakthrough therapy designation, accelerated approval, and priority review designation.

Fast Track Designation

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.

Benefits such as the ability to 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.

Accelerated Approval

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.

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.

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. Breakthrough Therapy Designation has all of the benefits of Fast Track designation as well as additional benefits such as FDA organizational commitment and intensive FDA guidance.

Table of Contents

The FDA may also award RMAT designation to regenerative medicine products. An RMAT designation is similar to breakthrough therapy designation and includes increased opportunities to meet with FDA officials and early meetings to discuss potential surrogate or intermediate endpoints. RMAT designation is available to regenerative medicine therapies where the therapy is intended to treat, modify, reverse or cure a serious or life-threatening disease or condition and the preliminary clinical evidence indicates that the therapy has the potential to address unmet medical needs for the disease or condition.

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 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 human 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 efficacy 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. Under the Best Pharmaceuticals for Children Act, or BPCA, a sponsor that qualifies for “pediatric exclusivity” is entitled to an additional six months of market exclusivity if it complies with a Written Request, or WR, issued by FDA for pediatric studies. The sponsor may apply to FDA to issue a WR. Pediatric exclusivity may apply to patent rights and to FDA regulatory exclusivity and operates by adding six months of exclusivity on to the end of the latest-expiring form of exclusivity. To qualify for pediatric exclusivity, at least one of those rights must still be currently in force at the time FDA approves the pediatric studies.

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

Table of Contents

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.

Biosimilars

The Biologics Price Competition and Innovation Act of 2009, or BPCIA, created an abbreviated approval pathway for biological products shown to be highly similar to or interchangeable with an FDA-licensed reference biological product. Under the BPCIA, a biological product may be deemed biosimilar to an FDA-approved biological product or reference biological product upon a showing that there are 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 generally 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. As of January 2019, the FDA had approved a total of 17 biosimilars, and seven of these had been launched into the U.St market.

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. Controversy over the appropriate manner of naming biosimilars has caused delay as well, with FDA currently calling for biosimilar names to have a random four-letter suffix appended to the name of the reference compound to which they refer. In addition, complexities of the regulatory provisions of the BPCIA, as well as the patent litigation provisions in the statute and accompanying litigation, have also led to a relatively slow pace of biosimilar approvals. FDA is taking steps to address these issues, most recently issuing the Biosimilars Action Plan, or BAP, to increase the speed and efficiency of biosimilar approvals and usage in the clinical setting.

A reference biologic is granted 12 years of marketing exclusivity from the time of first licensure of the reference product, and in addition 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.

Table of Contents

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 marketing approval through the pre-market approval (“PMA”) process 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.

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 finds the PMA application is approvable, 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

Table of Contents

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.

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 offeror/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

Table of Contents

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. In particular we have clinical trials ongoing in the United Kingdom and Spain and will be subject to regulations relating to performance of those clinical trials and manufacture and supply of our SPEAR T-cells and patient materials in the United Kingdom and Spain. 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 European Union, 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 application is then submitted to the EMA for approval by the European Commission. Finally, prior to any commercial supply, a pricing and reimbursement application is submitted to each relevant country's national or local health authority(ies).

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 Good Clinical Practice ("GCP") and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. However, the interpretation of these requirements may well differ from country to country.

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 European Union

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

Table of Contents

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 medicinal 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 scientific 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. For advanced therapy medicinal products (ATMPs), the scientific evaluation of MAA is primarily performed by the Committee for Advanced Therapies (CAT). The CAT prepares a draft opinion of each ATMP subject to a MAA which is sent for final approval to the CHMP.

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. Then, the European Commission grants or refuses the marketing authorization, following a procedure that involves representatives of the member states. The Commission's decision is in accordance with the CHMP's assessment except in very rare cases.

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 December 31, 2018, we had 430 employees. Of these employees, 337 were in research and development (including in manufacturing and operations, and quality control and quality assurance) and 93 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.

Table of Contents

Available Information

Access to our Annual Report on Form 10 K, Quarterly Reports on Form 10 Q, Current Reports on Form 8 K, and amendments to these reports filed with or furnished to the SEC, may be obtained through the investor section of our website at www.adaptimmune.com as soon as reasonably practical after we electronically file or furnish these reports. We do not charge for access to and viewing of these reports. Information in the investor section and on our website is not part of this Annual Report on Form 10 K or any of our other securities filings unless specifically incorporated herein by reference. In addition, the public may read and copy any materials that we file with the SEC at the SEC's Public Reference Room at 100 F Street, NE, Washington, D.C. 20549. Our filings with the SEC may be accessed through the SEC's website at www.sec.gov. All statements made in any of our securities filings, including all forward-looking statements or information, are made as of the date of the document in which the statement is included, and we do not assume or undertake any obligation to update any of those statements or documents unless we are required to do so by law.

Corporate Information

Adaptimmune Therapeutics plc was incorporated on December 3, 2014 and is a public limited company incorporated under the laws of England and Wales. Pursuant to a corporate reorganization, completed on April 1, 2015, Adaptimmune Therapeutics plc holds the entire issued share capital of Adaptimmune Limited. Prior to the corporate reorganization, our business was conducted by Adaptimmune Limited and its consolidated subsidiary. Adaptimmune Limited was incorporated on December 19, 2007. Subsequent to the corporate reorganization our business was conducted by Adaptimmune Therapeutics plc and its consolidated subsidiaries, including Adaptimmune Limited. Our registered and principal executive offices are located at 60 Jubilee Avenue, Milton Park, Abingdon, Oxfordshire OX14 4RX, United Kingdom, our general telephone number is (+44) 1235 430000 and our corporate website address is 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, located at 351 Rouse Boulevard, The Navy Yard, Philadelphia PA 19112, United States.

Item 1A. 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 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.

Table of Contents

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 SPEAR T-cells, including engaging in activities to manufacture and supply our SPEAR T-cells for clinical trials in compliance with current good manufacturing practice, or cGMP, conducting clinical trials of our SPEAR T-cells, 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 SPEAR T-cells.

For the years ended December 31, 2018, 2017 and 2016, we incurred net losses of $95.5 million, $70.1 million, and $71.6 million, respectively. As of December 31, 2018, we had accumulated losses of $318.5 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 SPEAR T-cells and their un-proven route to market. Our profitability is dependent upon the successful development, approval, and commercialization of our SPEAR T-cells, further development of the NY-ESO SPEAR T-cells by GSK (given the NY-ESO program has now been transitioned to GSK), achieving GSK milestones (for both the NY-ESO program and any future SPEAR T-cell programs under the GSK Collaboration and License Agreement) 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 funding.

We have never generated any revenue from sales of our SPEAR T-cells and our ability to generate revenue from sales of our SPEAR T-cells and become profitable depends significantly on our success in a number of factors.

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

- completing preclinical development and advancing our SPEAR T-cells to clinic;
- delivering on the clinical development strategy for our SPEAR T-cells;
- 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;
- demonstrating a favorable benefit (efficacy parameters): risk (safety) for our SPEAR T-cells that translate into a differentiated product of value for patients;
- obtaining data from clinical trials which are ongoing for SPEAR T-cells other than the NY-ESO SPEAR T-cell;
- obtaining regulatory approvals and marketing authorizations for our SPEAR T-cells 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;

Table of Contents

- developing sustainable and scalable manufacturing and supply processes for our SPEAR T-cells, including establishing and maintaining commercially viable supply relationships with third parties and establishing our own commercial manufacturing capabilities and infrastructure;
- developing a reliable and commercially viable/cost effective commercial manufacturing process to enable commercial supply of our SPEAR T-cells;
- launching and commercializing SPEAR T-cells for which we obtain regulatory approvals and marketing authorizations, either directly or with a collaborator or distributor;
- obtaining market acceptance, pricing and reimbursement of our SPEAR T-cells as viable treatment options;
- addressing any competing technological and market developments;
- identifying, assessing, acquiring and/or developing new SPEAR T-cells;
- 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 SPEAR T-cells is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved SPEAR T-cell. Our expenses could increase beyond expectations if 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 SPEAR T-cells, 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 SPEAR T-cell, 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 SPEAR T-cells, even if approved. If we are not able to generate revenue from the sale of any approved SPEAR T-cells, we may never become profitable.

If we fail to obtain additional financing, we may be unable to complete the development and commercialization of our SPEAR T-cells.

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

As of December 31, 2018, we had $68.4 million of cash and cash equivalents and $136.8 million of marketable securities. We expect to use these funds to advance and accelerate the clinical development of ADP-A2M10, ADP-A2M4 and ADP-A2AFP, to further develop and enhance our manufacturing capabilities and secure a commercially viable manufacturing platform for all of our SPEAR T-cells, to advance additional SPEAR T-cells into preclinical testing and progress such SPEAR T-cells 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, short-term deposits and marketable securities together with milestones 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 12 months. However, changing circumstances beyond our control, including changes to the scope and timing of the programs under the GSK collaboration, may cause us to increase our spending significantly faster than we currently

Table of Contents

anticipate. We may require additional capital for the further development and commercialization of our SPEAR T-cells and may need to raise additional funds sooner if we choose to expand more rapidly than we presently anticipate.

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 SPEAR T-cells 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 SPEAR T-cells 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 SPEAR T-cells 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 American Depositary Shares, or ADSs, to decline.

Risks Related to the Development of Our SPEAR T-cells

Our business is highly dependent on our existing SPEAR T-cell candidates including the NY-ESO SPEAR T-cell, the ADP-A2M10, ADP-A2M4 and ADP-A2AFP products, which will require significant additional clinical testing before we can seek regulatory approval and begin commercialization of any of our SPEAR T-cells.

There is no guarantee that any of our SPEAR T-cells 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 the NY-ESO SPEAR T-cell will be sufficient for GSK to plan one or more pivotal clinical trials and obtain regulatory approval or marketing authorization. Negative results in the NY-ESO SPEAR T-cell clinical program may also impact our ability to obtain regulatory approval for other SPEAR T-cells, either at all or within anticipated timeframes because, although the SPEAR T-cell may target a different cancer peptide, the underlying technology platform, manufacturing process and development process is the same for all of our SPEAR T-cells. Accordingly, a failure or delay in any one program may affect the ability to obtain regulatory approval to continue or conduct clinical programs for other SPEAR T-cells.

We may not be able to submit INDs, or the foreign equivalent outside of the United States, to commence additional clinical trials for other SPEAR T-cells 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 SPEAR T-cells 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 SPEAR T-cell. If results are not available when expected or problems are identified during SPEAR T-cell 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 SPEAR T-cells. Failure to submit further IND or the foreign equivalent and commence additional clinical programs will significantly limit our opportunity to generate revenue.

There is no guarantee that the FDA, or any other regulatory authority, will approve any IND (or equivalent application) for any of our future SPEAR T-cells, or for new indications for our SPEAR T-cells already in clinical

trials, or that amendments to existing protocols will not be required. For example, the FDA issued a partial clinical hold for the Company's proposed MRCLS trial with NY-ESO following review of the IND submitted for the trial. The FDA notification was not based on safety concerns. In its correspondence the FDA requested additional Chemistry Manufacturing and Controls, or CMC, and clinical information prior to the commencement of the proposed trial. An amendment to the ADP 0011 007 protocol for the trial was filed with the FDA which converted the trial into a pilot trial (rather than the previously proposed pivotal trial design with a futility phase) and this amended protocol was approved by the FDA resulting in a lift of the partial clinical hold. The start of the MRCLS trial was delayed as a result of the FDA

Table of Contents

issued partial clinical hold and there is no guarantee that any later MRCLS pivotal trial or further SPEAR T-cell trial will be approved by the FDA.

We are continuing to expand our clinical trial footprint in Europe. This requires gaining the approval of country specific review bodies for GMO application and Clinical Trial Application. As this is usually not a harmonized process, the requirements can vary considerably and delays can be incurred at a country level.

In the United States, some institutional review boards, or IRBs, have requested that the Sponsor obtain Investigational Device Exemptions (IDE) from the FDA for the validated clinical trial assay being used to select patients. This has delayed the initiation of some sites and limited the ability to obtain high risk biopsies until an IDE has been granted. We plan to proactively seek IDEs for our SPEAR T-cell assays where appropriate. IDE approval by the FDA is not guaranteed.

Our SPEAR T-cells being developed may have potentially fatal cross-reactivity to other peptides or protein sequences within the body.

One of our prior SPEAR T-cells, designed to target an HLA 1 restricted 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 terminated the program. We subsequently developed a preclinical safety testing program that identifies potential cross-reactivity risks but 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 SPEAR T-cells other than those for which INDs already exist 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 SPEAR T-cell. Detection of any cross-reactivity will halt or delay any ongoing clinical trials for any SPEAR T-cell and prevent or delay regulatory approval. Given that the underlying technology platform, manufacturing process and development process is similar for all of our TCR therapies, issues pertaining to cross-reactivity for one SPEAR T-cell may impact our ability to obtain regulatory approval for other SPEAR T-cells 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 HLA types) could also occur where the affinity-enhanced engineered TCR contained within our SPEAR T-cell binds to peptides presented by HLAs other than the HLA type for which the relevant TCR was developed. We have developed a preclinical screening process to identify allo-reactivity risk. Where any allo-reactivity risk is identified, patients with the allo-reactive alleles will be excluded from the trial. Any allo-reactivity or other cross-reactivity that impacts patient safety could materially impact our ability to advance our SPEAR T-cells into clinical trials or to proceed to market approval and commercialization. In addition, there is no guarantee that exclusion of patients with the identified 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 similar for all of our SPEAR T-cells, issues pertaining to allo-reactivity for one SPEAR T-cell may impact our ability to obtain regulatory approval for other SPEAR T-cells 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 SPEAR T-cells.

Use of our SPEAR T-cells to treat a patient requires the use of gene therapy technology, which involves combining a 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 SPEAR T-cells 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

Table of Contents

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 SPEAR T-cells to improve safety or effectiveness, may delay the clinical program, regulatory approval or commercialization, if approved at all, of any SPEAR T-cell. Consequently, this may have a material impact on our ability to receive milestone payments and/or generate revenue from our SPEAR T-cells.

In addition, given the novelty of our SPEAR T-cells, the end users and medical personnel require a substantial amount of education and training in their administration of our SPEAR T-cells. Regulatory authorities have very limited experience with commercial engineered cell therapies and SPEAR T-cells 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 SPEAR T-cell. To date, only a limited number of gene therapy products have been approved in the United States and European Union. Consequently, it is difficult to predict and evaluate what additional regulatory hurdles may apply to the development of our SPEAR T-cells and whether additional investment, time or resources will be required to overcome any such hurdles.

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.
- 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 SPEAR T-cells 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 NIH may be subject to review by the NIH Office of Biotechnology Activities' Recombinant DNA Advisory Committee, or RAC. The RAC review process can delay or impede the initiation of a clinical trial.

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.

In addition, results seen in third party clinical trials using other cell therapy products or combination products, for example CAR-T products, may impact on the further advancement of our clinical trials. Based on the data currently

Table of Contents

available to us in relation to our clinical trials there is no evidence that the type and severity of neurotoxicity events observed with CD19 directed CAR-T cell treatments, including the fatal events observed in the NCT02535364 trial, occur with our SPEAR TCRs and we do not therefore believe that any changes to our SPEAR T-cell clinical trial protocols are required. However there is no guarantee that the FDA or other regulatory authorities will agree with that position and further education and discussion with regulatory authorities may be required.

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 SPEAR T-cells.

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 SPEAR T-cell is not completely understood, which means that we cannot predict the long-term effects of treatment with our SPEAR T-cells. In addition it is not possible for any pre-clinical safety package to completely identify all potential safety risks.

We are aware that certain patients do not respond to our SPEAR T-cells and that other patients may relapse or cease to present the peptide being targeted by such SPEAR T-cells. 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 SPEAR T-cell.

Clinical trials are still in the early stages, and it is difficult to predict the results that will be obtained by us or our collaborator in ongoing clinical trials or the next phase or phases of any clinical program. It is also difficult to predict the way in which SPEAR T-cells will interact with third-party products used in combination clinical trials. For example, data seen in third party combination trials with KEYTRUDA® (pembrolizumab) has resulted in certain combination trials with pembrolizumab being placed on clinical hold by the FDA. Any undesirable side effects seen in combination trials may affect our ability or our collaborator's ability to continue with and obtain regulatory approval for any combination therapy, but may also impact our or our collaborator's ability to continue with and obtain regulatory approval for SPEAR T-cell therapies alone.

There is a significant risk at each stage of any clinical program that serious adverse events or low efficacy, as well as less favorable benefit:risk profiles, will prevent our SPEAR T-cells from proceeding further or will result in those programs being suspended or placed on hold (whether voluntarily or as a result of a regulatory authority requirement). For example, there is a risk that the target (or similar) peptide to which any SPEAR T-cell is directed may be present in both patients' cancer cells and other non-cancer cells and tissues. Should this be the case patients may suffer a range of side effects associated with the SPEAR T-cell binding to both the cancer cells and/or other cells and tissues and such side effects could cause patient death. The extent of these side effects will depend on which cells and tissues are affected as well as the degree to which the target (or similar) peptide is expressed in these cells and tissues. Further, following infusion of any of our SPEAR T-cells, there may be a transient inflammatory reaction of the disease to the treatment. Symptoms in any given subject would be dependent on the location and other characteristics of their tumor. For example, subjects with lung tumors may experience dyspnea and cardiac toxicities may be observed in patients with pre-existing cardiac or pericardial masses. These inflammatory reactions and related symptoms may be mild and self-limited, but can be severe and require medical intervention.

As of September 4, 2018, adverse events considered by investigators to be possibly related to either ADP-A2M4 or ADP-A2M10 and presented at ESMO in October 2018 include cytokine release syndrome ("CRS"), pyrexia, peripheral

edema, sinus tachycardia/tachycardia, increase in alanine aminotransferase, increase in amylase, increase in aspartate amino transferase, chills, delirium, dysphagia, dysphonia, hemoptysis, hyperhidrosis, hypotension, lymphopenia, leukopenia, neutropenia, pleural effusion, decreased appetite, fatigue, nausea, febrile neutropenia, thrombocytopenia, alopecia, encephalopathy, diarrhea, headache, hypoxia and tumor pain. As of September 4, 2018, serious adverse events seen in the ADP-A2M4 and ADP-A2M10 studies (whether considered related to the SPEAR T-cells or not) include CRS, dysponea, abdominal pain, cardiac arrest, progressive disease, haemoptysis, neutropenia, pneumonia, respiratory arrest, respiratory failure, sepsis, thrombocytopenia, pancytopenia, atrial fibrillation,

Table of Contents

hyponatraemia, muscular weakness, encephalopathy, syncope and pleural effusion. There were no dose limiting toxicity events or evidence of off-target toxicity observed in the first dose cohort of the ADP-A2AFP clinical trial.

Because each dose of SPEAR T-cells 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. Should the tracking process fail, whether at our own facility, a third party facility or at any point in the manufacturing and supply process, a patient could receive another patient's T-cells resulting in a patient fatality. We will need to invest in systems, such as bar coding, to ensure fail safe tracking. 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 and/or result in a patient fatality if a patient receives another patient's T-cells. The tracking systems required to ensure safe patient administration may also require increased administration to satisfy other regulatory requirements, for example data protection requirements in Europe. The need to ensure tracking systems are adequate and to comply with these additional regulatory requirements may result in delay to the start of trials or the need to obtain additional regulatory licenses or consents prior to starting such trials.

Validation of our SPEAR T-cells 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 SPEAR T-cells 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 SPEAR T-cells 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.

Our SPEAR T-cells and their application are not fully scientifically understood and are still undergoing validation and investigation.

Our SPEAR T-cells (including the impact of affinity modifying the T-cell receptors within such T-cells) and their potential associated risks are still under investigation. There is no guarantee that our SPEAR T-cells will work in the way we currently anticipate or that affinity modification of T-cell receptors will produce the anticipated enhancements in activity without also compromising the tolerability of the SPEAR T-cells. 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 SPEAR T-cells and is still being studied and investigated. This could delay regulatory approval, if any, for the relevant SPEAR T-cells. 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 SPEAR T-cells 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 SPEAR T-cell, such modified SPEAR T-cell 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 SPEAR T-cells. The occurrence of such events would 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 SPEAR T-cells 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

Table of Contents

and/or our ability to develop and isolate suitable TCRs for affinity enhancement could be significantly lower than projected or that no additional SPEAR T-cells suitable for further development can be identified. Any failure to identify and validate further target peptides will reduce the number of potential SPEAR T-cells that we can successfully develop, which in turn will reduce the commercial opportunities available to us and increase our reliance on our existing SPEAR T-cells.

In addition, there is no guarantee that our attempts to develop further SPEAR T-cells 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 SPEAR T-cell 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, TCRs or affinity-enhanced TCRs, our ability to submit INDs for further SPEAR T-cells may be delayed or never realized, which would have a materially adverse effect on our business. We have multiple research projects ongoing both internally and with third parties, for example Universal Cells Inc and Bellicum Inc. The outcomes of these research projects are uncertain and such research projects may or may not generate next generation SPEAR T-cells with profiles suitable for further development or progression into clinical trials.

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, screening of patients by the clinical sites, 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 SPEAR T-cells. The patient population in which any required peptide antigen is presented may be lower than expected which will increase the timescales required to find and recruit patients into the applicable clinical trial. Screening of a large number of patients is required to identify HLA and tumor antigen positive patients for most of our clinical trials. For example, it has taken longer to recruit patients into our NSCLC trials with both the NY-ESO SPEAR T-cell and ADP-A2M10 due to the low percentage expression of peptide antigen seen in the patient populations at the relevant clinical trial sites. With the NY-ESO SPEAR T-cell, presentation of the NY-ESO antigen occurs predominantly in certain sub-types of NSCLC and additional clinical sites may need to be initiated in order to identify patients with those certain NSCLC sub-types. With ADP-A2M10, presentation of the MAGE-A10 peptide antigen is seen in a lower number of patients than anticipated. This has delayed recruitment of patients into NSCLC trials for both therapies and has resulted in the Company incurring additional costs associated with the need to find and initiate additional clinical trial sites. It is also difficult to predict whether changes may be required to any clinical trial design as our clinical trials progress. For example, initial results from current Phase 1/2 clinical trials with the NY-ESO SPEAR T-cell have suggested that fludarabine is required as part of any patient pre-conditioning regimen. This has required amendment to protocol designs, which did not previously include fludarabine, to include fludarabine.

Our and our collaborator’s clinical trials will compete with other clinical trials that are in the same therapeutic areas as our SPEAR T-cells, 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 will conduct some of our clinical trials at the same clinical trial sites where competing trials are ongoing, which will reduce the number of patients who are available for our clinical trials at such clinical trial sites. Moreover, because our SPEAR T-cells 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. This may also mean we cannot recruit patients at a suitable time in their disease progression. In addition, in relation to any indication, the standard of care for patients in that indication may change or

further develop meaning that clinical sites are no longer prepared to continue with any clinical trial or require amendments to agreed protocols for clinical trials. Such circumstances can lead to the suspension of the relevant clinical trial at a site, inability to recruit further patients at that clinical site or a requirement to amend the protocol, all of which will delay or potentially halt progression of a SPEAR T-cell through clinical trials.

Table of Contents

Even if we are able to enroll a sufficient number of patients in our clinical trials, delays in patient enrollment may result, and have resulted 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 SPEAR T-cells.

Comparability studies related to the manufacturing of our SPEAR T-cells may be required ahead of any pivotal trial start date or ahead of use in the European Union or alternatively in connection with any changes made to our manufacturing process. The requirement to carry out such comparability studies may delay the uptake of any changed process, start of any pivotal trial or use of the relevant SPEAR T-cells in Europe. If the results from the comparability studies are not acceptable, this may further delay the start of such trials or changed process and require re-evaluation of the process used to manufacture of our SPEAR T-cells. For example, comparability studies are ongoing in relation to changes made to the process for manufacture of our NY-ESO SPEAR T-cells. The results from these comparability studies may impact the start date for any registrational study or impact what data can be used for any marketing application for the NY-ESO SPEAR T-cells. Failure in such comparability studies may also impact other studies in which the modified process is already being used.

We may not be able to develop or obtain approval for the analytical assays and companion diagnostics required for commercialization of our SPEAR T-cells.

Administration of our SPEAR T-cells requires the use of an immuno-chemistry or other screening assay in which patients are screened for the presence of the cancer peptide targeted by our SPEAR T-cells. 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 that are intended for use in selection of 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 approval or clearance to occur simultaneously with approval of the biologic product.

We expect that, for all of our SPEAR T-cells, 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 SPEAR T-cells. 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.

If we or our collaborators, or any third parties that we engage to assist us, are unable to successfully develop companion diagnostic assays for use with any SPEAR T-cells, 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 the relevant SPEAR T-cells 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 or our collaborators' ability to conduct further clinical trials or obtain regulatory approval.

Manufacturing and administering our SPEAR T-cells 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 SPEAR T-cells for clinical trials or for commercial purposes could be delayed or stopped.

The process of manufacturing and administering our SPEAR T-cells is complex and highly regulated. The manufacture of our SPEAR T-cells involves complex processes, including manufacture of a lentiviral delivery vector containing the gene for our affinity-enhanced engineered TCR. Administration of our SPEAR T-cells 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

Table of Contents

obtain the desired dose, and ultimately infusing the modified T cells back into the patient. As a result of the complexities, our manufacturing and supply costs are likely to be higher than those for more traditional manufacturing processes and the manufacturing process is less reliable and more difficult to reproduce.

Delays or failures in the manufacture of SPEAR T-cells (whether by us, any collaborator or our third party contract manufacturer) can result in a patient being unable to receive their SPEAR T-cells or a requirement to re-manufacture SPEAR T-cells which itself then causes delays in manufacture for other patients. Any delay or failure or inability to manufacture on a timely basis can adversely affect a patient's outcomes and delay the timelines for our clinical trials. Such delays or failure or inability to manufacture can result from:

- A failure in the manufacturing process itself for example by an error in manufacturing process (whether by us or our third party contract manufacturing organization), equipment or reagent failure (including failure in the bags the Company uses to freeze, differences in patient material, lack of sterility in starting materials), failure in any step of the manufacturing process, failure to maintain asceptic environment or asceptic processes, failure to maintain a GMP environment, failure in quality systems applicable to manufacture, contamination during process;

- A lack of reliability or reproducibility in the manufacturing process itself leading to variability in end manufacture of SPEAR T-cells. Should the process be unreliable, the relevant regulatory agency (for example the FDA in the United States) may place a hold on a clinical trial or request further information on the process which could in turn result in delays to the clinical trials;

- Variations in patient starting material resulting in less product than expected or product which is not viable or cannot be manufactured;

- Product loss or failure due to logistical issues including issues associated with the differences between patients' white blood cells or characteristics, interruptions to process, contamination, failure to supply patient apheresis material within required timescales (for example as a result of an import or export hold-up) or supplier error;

- Inability to obtain manufacturing slots from third party contract manufacturers or to have enough manufacturing slots (including those at our Navy Yard facility) to manufacture SPEAR T-cells for patients as and when those patients require manufacture;

- Inability to procure starting materials or to manufacture starting materials (including for vector manufacture), for example vector required for SPEAR T-cell manufacture;

- Inability to procure manufacturing slots from third party manufacturers (whether for SPEAR T-cell manufacture or for starting materials manufacture, including vector) at all or on a timely basis. Even where manufacturing slots are agreed in advance with third party manufacturers we cannot guarantee they will not be delayed or cancelled or that any manufacturing process will be successful;

- Loss of or close-down of any manufacturing facility used in the manufacture of SPEAR T-cells. For example, we will be manufacturing ADP-A2M10 and ADP-A2M4 at our Navy Yard manufacturing facility. Should there be an integrity breach of any asceptic processing areas at the facility (for example caused by contamination, direct physical harm or natural disaster) resulting in the close-down of that facility it may not be possible to find alternative manufacturing capability for ADP-A2M10 or ADP-A2M4 within the timescales required for ongoing clinical trials;

- Loss or contamination of patient starting material, requiring the starting material to be obtained again from the patient or the manufacturing process to be re-started; and

- A requirement to modify or make changes to any manufacturing process. Such changes may additionally require comparability testing which then may reduce the amount of manufacturing slots

Table of Contents

available for manufacture of patient SPEAR T-cells. Delays in our ability to make the required modifications or perform any required comparability testing within currently anticipated timeframes or that such modifications or comparability testing, 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 can also impact timelines for manufacture.

The requirements for manufacture and supply of SPEAR T-cells for clinical trials in Europe have additional complexities and the manufacture and supply of our SPEAR T-cells is raising issues which have not previously been regulated or observed by the relevant regulatory authorities. For example, supply of SPEAR T-cells for European clinical trials will either require manufacture of SPEAR T-cells in the United States or use of a new CMO in Europe. Where manufacture continues in the United States, there is a need to transfer patient product from clinical sites in Europe to the manufacturer in the United States, for the patient product to be converted into our end SPEAR T-cell product and then for that SPEAR T-cell product to be transported back to the site in Europe for administration to the patient. The supply and manufacturing chain required to achieve this is very complex and could be subject to failures at any point in the supply and manufacturing chain. Any inability to set up acceptable manufacturing and supply chains to enable treatment of patients in Europe could result in a delay to those trials starting in Europe or could result in a delay in patient treatment, requirement to re-apherese a patient or a requirement to re-manufacture patient material.

As our SPEAR T-cells 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, may not be transferable to third parties or able to be used at larger scales and could cause our SPEAR T-cells to perform differently or 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 or comparability tests to be conducted which may further delay the timeframes under which modified manufacturing processes can be used for any SPEAR T-cell. If SPEAR T-cells manufactured under the new process has a worse safety or efficacy profile than the prior investigational product or the process is less reproducible than the previous process, we may need to re-evaluate the use of that manufacturing process, which could significantly delay or even result in the halting 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, loss of product, and timely availability of reagents or raw materials or contract manufacturing services or facilities. A failure to develop such a commercially viable process within anticipated timescales may prevent or delay progression of our T-cell therapies into pivotal clinical trials and ultimately commercialization. In addition, we may ultimately be unable to reduce the expenses associated with our SPEAR T-cells to levels that will allow us to achieve a profitable return on investment. We have entered into an alliance with Universal Cells Inc. that, if successful, will enable us to treat patient populations with an off-the-shelf product. However, there is no guarantee that the research program with Universal Cells Inc. will be successful, will be carried out within the timescales currently anticipated or that even if successful it will result in a SPEAR T-cell that can be used to treat patients or that such SPEAR T-cell will allow us to achieve a profitable return on investment.

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 requirements at our Navy Yard manufacturing facility, the U.K. vector facility and at our third party contract manufacturing facilities.

Table of Contents

We may encounter difficulties in achieving quality control and quality assurance and may experience shortages in qualified personnel. We and our third party contract manufacturers are subject to inspections by the FDA and comparable agencies in other jurisdictions to confirm compliance with applicable regulatory requirements once the process has been approved. Any failure to follow cGMP or other regulatory requirements, reliably manufacture product or delay, interruption or other issues that arise in the manufacture, fill- finish, packaging, or storage of our SPEAR T-cells 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 SPEAR T-cells, including leading to significant delays in the availability of our SPEAR T-cells 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 SPEAR T-cells. Significant non-compliance could also result in the imposition of sanctions, including warning letters, fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approvals for our SPEAR T-cells, 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.

We now manufacture SPEAR T-cells at our Navy Yard manufacturing facility and intend to manufacture vector at the U.K. vector facility in the future. There is no guarantee that regulatory authorities will not raise non-compliance issues or that regulatory authorities may require us to make changes to the way in which either facility is operated. This may result in a delay in our ability to manufacture SPEAR T-cells at our own facility or inability to supply vector material for use in the SPEAR T-cell manufacturing process which delay may not be mitigated or mitigatable by third party contract manufacturing facilities. In addition, there is no guarantee that any SPEAR T-cells or vector produced in any of our facilities will be able to meet regulatory requirements or that we will be able to recruit and maintain sufficient staff to enable manufacture of products within required timescales. Any failure to meet regulatory requirements or produce SPEAR T-cells and vector according to regulatory requirements could result in delays to our clinical programs, potential side effects and even fatalities to patients and may result in withdrawal of regulatory approval for our manufacturing facility.

The outcome of clinical trials is uncertain and our clinical trials may fail to demonstrate adequately the safety and efficacy of any of our SPEAR T-cells which would prevent or delay regulatory approval and commercialization.

There is a risk in any clinical trial that side effects from our SPEAR T-cells will require a hold on, or termination of, our clinical programs or further adjustments to our clinical programs in order to progress our SPEAR T-cell. Our SPEAR T-cells are novel and unproven, and regulators will therefore require evidence that the safety profile of SPEAR T-cells is acceptable before permitting clinical trials to commence and evidence that the SPEAR T-cells are tolerable and effective before granting any regulatory approval. In particular, because our SPEAR T-cells are subject to regulation as biological products, we will need to demonstrate that they have an acceptable safety profile, are pure and are potent for use in each target indication. The SPEAR T-cell must demonstrate an acceptable benefit:risk profile in its intended patient population and for its intended use. The benefit:risk 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 SPEAR T-cells may not be sufficient to obtain regulatory approval unless we can also show an adequate duration of response.

The regulatory authorities (including the FDA) may issue a hold on our or our collaborators' clinical trials as a result of safety information and data obtained in third party clinical trials or in relation to third party products. Any such hold may require addressing by us and our collaborators and will inevitably delay progression of the clinical trials concerned, if such clinical trials progress at all.

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 SPEAR T-cells 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 might be required for regulatory approval. There may be other reasons why our early clinical trials are not

Table of Contents

predictive of results in 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 the NY-ESO SPEAR T-cell, 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 nearly 100% of the peripheral blood at day 14. As another example, in the synovial sarcoma trial using the NY-ESO SPEAR T-cell there has been one patient death considered to be related to treatment according to the investigator.

We expect there may be greater variability in results for our SPEAR T-cells 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 any products proceeding through clinical trials. SPEAR T-cells 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.

Certain of our clinical trials include dose escalation studies in which the dose of SPEAR T-cells administered to patients is varied or initial studies in which the pre-treatment regimen may be varied, for example a regimen with and without fludarabine. The outcome of such dose escalation or initial studies will inform the clinical study going forward. However, the need to carry out dose escalation or other initial studies may result in delays in data from such clinical programs while the most suitable dose or regimen is determined. For example, our current clinical trials include dose escalation and therefore efficacy data may not be obtained from initial patients treated at lower doses in such studies.

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 SPEAR T-cell 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 SPEAR T-cells. We cannot predict whether any of our SPEAR T-cells will satisfy regulatory requirements at all or for indications in which such SPEAR T-cells are currently being evaluated as part of any clinical programs.

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. 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 SPEAR T-cells 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 SPEAR T-cell has undesirable side effects, regulatory approval for such therapeutic may be delayed or suspended, or alternatively may be restricted to particular disease indications or patient populations 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 SPEAR T-cell can be used.

As of September 4, 2018, adverse events considered by investigators to be possibly related to either ADP-A2M4 or ADP-A2M10 and presented at ESMO in October 2018 include cytokine release syndrome (“CRS”), pyrexia,

Table of Contents

peripheral oedema, sinus tachycardia/tachycardia, increase in alanine aminotransferase, increase in amylase, increase in aspartate amino transferase, chills, delirium, dysphagia, dysphonia, haemoptysis, hyperhidrosis, hypotension, lymphopenia, leukopenia, neutropenia, pleural effusion, decreased appetite, fatigue, nausea, febrile neutropenia, thrombocytopenia, alopecia, encephalopathy, diarrhea, headache, hypoxia and tumor pain. As of September 4, 2018, serious adverse events seen in the ADP-A2M4 and ADP-A2M10 studies (whether considered related to the SPEAR T-cells or not) include CRS, dysponea, abdominal pain, cardiac arrest, progressive disease, haemoptysis, neutropenia, pneumonia, respiratory arrest, respiratory failure, sepsis, thrombocytopenia, pancytopenia, atrial fibrillation, hyponatraemia, muscular weakness, encephalopathy, syncope and pleural effusion.

In our SPEAR T-cell trials, CRS has been reported in subjects. A subset of these reported CRS events have been Grade 3 or 4 in severity. Subjects with more severe CRS symptoms have generally responded to treatment with the anti-IL6R antibody, tocilizumab. All our clinical trial protocols now allow for use of tocilizumab for treatment of cytokine release syndrome. Tocilizumab has been shown to control cytokine release syndrome likely without abrogating the anti-tumor response.

Any unacceptable toxicities arising in ongoing clinical programs could result in suspension or termination of those clinical programs. Any suspension or termination may affect other SPEAR T-cell programs 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 SPEAR T-cell, if at all, and require additional resources and financial investment to bring the relevant SPEAR T-cell to market.

In addition, the impact of SPEAR T-cells may vary from patient to patient and this may affect the number of patients who can be successfully treated with our SPEAR T-cells. 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 SPEAR T-cells.

Use of SPEAR T-cells in combination with other third party products or therapies, for example our Collaborator's use of the NY-ESO SPEAR T-cell in combination with Merck & Co., Inc.'s PD-1 inhibitor, KEYTRUDA® (pembrolizumab) in patients with multiple myeloma may increase or exacerbate side effects that have been seen with our SPEAR T-cells alone or may result in new side effects that have not previously been identified with our SPEAR T-cells alone. Any undesirable side effects seen in combination trials may affect our ability to continue with and obtain regulatory approval for the combination therapy, but may also impact our ability to continue with and obtain regulatory approval for SPEAR T-cell therapies alone.

Clinical trials are expensive, time-consuming, unpredictiable 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 SPEAR T-cells. 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 on the 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 SPEAR T-cells.

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. For example, low target peptide expression levels in the NY-ESO SPEAR T-cell and ADP-A2M10 programs adversely affected speed of patient recruitment. The ability to administer our SPEAR T-cells 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 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

Table of Contents

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 or our collaborators may find it difficult to enroll patients in our clinical trials. Identifying and qualifying patients, including testing of patients for appropriate target peptides and HLA type, to participate in clinical trials of our SPEAR T-cells are critical to our success. The patient population in which any required peptide antigen is presented may be lower than expected which will increase the timescales required to find and recruit patients into the applicable clinical trial. The timing of clinical trials depends on the speed at which we or our collaborators can recruit patients to participate in testing of the SPEAR T-cells. If patients are unwilling to participate in trials because of negative publicity from adverse events or for other reasons, including competitive clinical trials for similar patient populations, negative results seen in competitive third party clinical trials utilizing similar cell therapy products, 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 product development, delays in testing the effectiveness of our technology or termination of the clinical trials altogether. We or our collaborators 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. Successful execution of patient treatment and assessment of outcomes is affected by several factors including:

- eligibility criteria for the trial in question, in particular, presenting the correct HLA type and expression levels of the target antigen;
- ability to detect required expression levels of target antigens in any patient population;
- ability to detect required target antigens in any patient population and to set detection levels at an appropriate level to facilitate patient recruitment;
- severity of the disease under investigation and the type of patient being recruited into the clinical trial;
- design of the trial protocol;
- size of the patient population;
- perceived risks and benefits of the SPEAR T-cell under trial;
- novelty of the SPEAR T-cell and acceptance by oncologists;
- proximity and availability of clinical trial sites for prospective patients;
- availability of competing therapies and clinical trials and ability to obtain patient insurance coverage;
- efforts to facilitate timely enrollment in clinical trials and to provide manufactured product on a timely basis;
- patient referral practices of physicians;
- changes in the underlying standard of care applicable or treatments available for the relevant indication for which a patient is being treated; and

Table of Contents

- ability to monitor patients adequately during and after treatment, for example where patients decide not to attend follow-up appointments.

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.

Our SPEAR T-cells 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 or "reference" 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.

There is a risk that the FDA will not consider our SPEAR T-cells to be reference products for competing products, potentially creating the opportunity for generic-type biosimilar competition sooner than anticipated. Additionally, the period of regulatory exclusivity to which we might be entitled as a reference product would not apply to competitor companies pursuing regulatory approval via their own traditional BLA, rather than as a biosimilar 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 small-molecule non-biological drug 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 SPEAR T-cells 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 SPEAR T-cells.

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 SPEAR T-cell'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 SPEAR T-cells 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 SPEAR T-cells may be uncertain, complex, expensive and lengthy, and approval may not be obtained. For example, in relation to our NY-ESO SPEAR T-cell in synovial sarcoma, the FDA requested certain additional information be made available as part of the Company's application to conduct a pivotal study in synovial sarcoma, including a requirement to assess comparability between the manufacturing process used for the initial synovial sarcoma trials and the commercial-ready manufacturing process intended to be used in pivotal trials. The FDA also recommended that we file a SPA in relation to the design of the pivotal study. Such requirements and requests for additional information can delay the start of any pivotal or other trial and there is no guarantee that the

FDA will not continue to require further or additional information ahead of approving any trial whether from our collaborators for our NY-ESO SPEAR T-cells or from us for other SPEAR T-cells.

Table of Contents

We or our collaborators could also encounter delays if physicians encounter unresolved ethical issues associated with enrolling patients in clinical trials of our SPEAR T-cells in lieu of prescribing existing treatments that have established safety and efficacy profiles. Further, a clinical trial may be suspended or terminated by us, a collaborator, 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 SPEAR T-cell, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. If we or our collaborators experience termination of, or delays in the completion of, any clinical trial of our SPEAR T-cells, the commercial prospects for our SPEAR T-cells 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.

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 SPEAR T-cells.

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 SPEAR T-cells will depend on the data that are obtained in our ongoing clinical trials and in one or more future registration or pivotal clinical trials. We may attempt to seek approval on a per indication basis for our SPEAR T-cells 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 SPEAR T-cells. 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 SPEAR T-cells to market or the timeframes under which the relevant regulatory approvals can be obtained.

We have obtained breakthrough therapy status for our NY-ESO SPEAR T-cell for the treatment of certain patients with inoperable or metastatic synovial sarcoma who have received prior chemotherapy. Following exercise of the option over the NY-ESO SPEAR T-cell program by GSK, it is not known whether such breakthrough therapy status will continue or whether GSK will apply for and obtain any accelerated approval for the NY-ESO SPEAR T-cell. In addition, depending on the data that is obtained by us in our current and future clinical trials for our wholly owned SPEAR T-cells, we may seek breakthrough therapy or fast track designation or accelerated approval from the FDA for our SPEAR T-cells and equivalent accelerated approval procedures in other countries. However, given the novel nature of our SPEAR T-cells, 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 SPEAR T-cells involved. For example, clinical trials may be required in paediatric populations before any approval can be obtained, which can be time consuming and costly. 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 (including any

Table of Contents

trials specific to paediatric populations) that will be required for regulatory approval varies depending on the SPEAR T-cell, the disease or condition that the SPEAR T-cell is designed to address, the regulatory authority responsible for the approval process, and the regulations applicable to any particular SPEAR T-cell. Approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a SPEAR T-cell'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 SPEAR T-cells 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 SPEAR T-cells have a beneficial risk: benefit profile 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;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical programs or clinical trials;
- the data collected from clinical trials of our SPEAR T-cells 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 SPEAR T-cells; 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 SPEAR T-cells 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 SPEAR T-cell, which would result in significant harm to our business.

Obtaining and maintaining regulatory approval of our SPEAR T-cells in one jurisdiction does not mean that we will be successful in obtaining regulatory approval of our SPEAR T-cells in other jurisdictions.

Obtaining and maintaining regulatory approval of our SPEAR T-cells 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 SPEAR T-cell, comparable regulatory authorities in foreign jurisdictions must also approve the manufacturing, marketing and promotion of the SPEAR T-cell 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 SPEAR T-cell 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 SPEAR T-cells is also subject to approval.

Table of Contents

We or our collaborators may also submit marketing authorization applications in other countries. Regulatory authorities in jurisdictions outside of the United States have requirements for approval of SPEAR T-cells 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 SPEAR T-cells 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 SPEAR T-cells 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 SPEAR T-cells, but we may be unable to obtain such designations or, in the case of NY-ESO, maintain its breakthrough therapy designation or, obtain or maintain the benefits associated with such designations.

We obtained breakthrough therapy status in the United States and Europe for the NY-ESO SPEAR T-cell for the treatment of certain patients with inoperable or metastatic synovial sarcoma who have received prior chemotherapy. We may seek breakthrough therapy or fast track designations for our other SPEAR T-cells 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 SPEAR T-cell as a breakthrough therapy provides potential benefits that include more frequent meetings with the FDA to discuss the development plan for the SPEAR T-cell 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. There can be no assurance that we will receive breakthrough therapy designation for any SPEAR T-cell or any particular indication. Additionally, other treatments from competing companies may obtain the designations and impact our ability to develop and commercialize our SPEAR T-cells, which may adversely impact our business, financial condition or results of operation.

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 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

Table of Contents

may withdraw approval of our SPEAR T-cell or indication approved under the accelerated approval pathway if, for example:

- the trial or trials required to verify the predicted clinical benefit of our SPEAR T-cell 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 SPEAR T-cell is not shown to be safe or effective under the conditions of use;
- we fail to conduct any required post approval trial of our SPEAR T-cell with due diligence; or
- we disseminate false or misleading promotional materials relating to the relevant SPEAR T-cell.

Even if we receive regulatory approval of our SPEAR T-cells, 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 SPEAR T-cells.

Any regulatory approvals that we receive for our SPEAR T-cells will require surveillance to monitor the safety and efficacy of the SPEAR T-cell. The FDA may also require a risk evaluation and mitigation strategy in order to approve our SPEAR T-cells, 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 SPEAR T-cells, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export and recordkeeping for our SPEAR T-cells 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 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 SPEAR T-cells 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 SPEAR T-cells we develop for indications or uses for which they are not approved. Later discovery of previously unknown problems with our SPEAR T-cells, 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:

- 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;

Table of Contents

- 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 SPEAR T-cells. 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 any pivotal clinical trial we were able to obtain accelerated approval of any of our SPEAR T-cell, 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 SPEAR T-cells, but we may not be able to obtain or maintain such authorization.

As part of its marketing authorization process, the EMA may grant marketing authorizations for certain categories of medicinal products on the basis of less complete data than is normally required, when doing so may meet unmet medical needs of patients and serve the interest of public health. In such cases, it is possible for the Committee for Medicinal Products for Human Use, or CHMP, to recommend the granting of a marketing authorization, subject to certain specific obligations to be reviewed annually, which is referred to as a conditional marketing authorization. This may apply to medicinal products for human use that fall under the jurisdiction of the EMA, including those that aim at the treatment, the prevention, or the medical diagnosis of seriously debilitating diseases or life-threatening diseases and those designated as orphan medicinal products.

A conditional marketing authorization may be granted when the CHMP finds that, although comprehensive clinical data referring to the safety and 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 is still required.

Table of Contents

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 SPEAR T-cells 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 SPEAR T-cells.

We or our collaborators may not be able to obtain or maintain orphan drug exclusivity for our SPEAR T-cells.

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.

Orphan drug designation for the NY-ESO SPEAR T-cell for the treatment of soft tissue sarcoma was granted by the FDA in March 2016. Some of our other SPEAR T-cells or the indications which our SPEAR T-cells are used to treat 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.

Table of Contents

Orphan drug designation for the NY-ESO SPEAR T-cell for the treatment of soft tissue sarcoma, a solid tumor cancer has also been granted by the European Union. Orphan drug designation provides certain regulatory and financial incentives for companies to develop and market therapies that treat a life-threatening or chronically debilitating condition affecting no more than five in 10,000 persons in the European Union, and where no satisfactory treatment is available. The designation provides incentives for companies seeking protocol assistance and scientific advice from the EMA during the product development phase and a 10-year period of marketing exclusivity in the European Union following product approval.

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 SPEAR T-cell 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 or that we or GSK will not lose orphan drug designation for the NY-ESO SPEAR T-cell. Inability to obtain orphan drug designation for a specific SPEAR T-cell or loss of such designation for the NY-ESO SPEAR T-cell in the future would prevent any ability to take 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. The extent of market exclusivity which is obtained may also be affected if the indication for any relevant registration or pivotal trial is narrower than the orphan designation granted. 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 SPEAR T-cells 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 SPEAR T-cells 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 SPEAR T-cells 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 SPEAR T-cells or require us to undertake additional organizational changes to minimize the risk of further breach. A failure to comply may apply to any part of our business, for example to the processes used for manufacture of our SPEAR T-cells (including the reliability of the process) or to the processes used for treatment of patients (including tracking of patient product and supply of patient specific product).

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 hazardous and biological reagents and materials in our research and development at our U.K. site. We also use radioactive reagents and materials in our research and development in the United Kingdom. We have obtained the appropriate certification or ensured that such certification has been obtained as 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 employer’s 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.

Table of Contents

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 may 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.

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.

If we obtain marketing approval for our products in the United States, if at all, 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

Table of Contents

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 FCA 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;
- 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, 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

Table of Contents

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 within 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 approximately 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 approximately 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.

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 of 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 SPEAR T-cells

The market opportunities for our SPEAR T-cells 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 and our collaborators current clinical trials generally require that patients have received chemotherapy prior to enrollment. Depending upon the

outcome of current trials, we or our collaborators may conduct future clinical trials using SPEAR T-cells 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 SPEAR T-cells only receive third-line or second-line approval, the patient population to which we or our collaborators can supply our SPEAR T-cells will be significantly reduced, which may limit commercial opportunities

Table of Contents

In addition, our patient population may be derived from those who have previously failed checkpoint therapy, which may result in tumor resistance mechanisms which also impart resistance to SPEAR T-cell therapies.

Our estimates of the patient population that may be treated by our SPEAR T-cells is based on published information. This information may not be accurate in relation to our SPEAR T-cells 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 SPEAR T-cells. 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. Our current SPEAR T-cells have been developed for patients who are HLA A2 which will reduce the size of the patient population that can be treated unless we develop and receive regulatory approval for SPEAR T-cells 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 SPEAR T-cells, 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 sales force and will need to grow and develop the sales function and associated support network if we are to supply SPEAR T-cells on a commercial basis. As our SPEAR T-cells 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 SPEAR T-cell sales may be lower than if we had commercialized our SPEAR T-cells ourselves. We also face significant competition in our search for third parties to assist us with the sales and marketing efforts of our SPEAR T-cells. Such competition may also result in delay or inability to supply SPEAR T-cells to particular countries or territories in the world which in turn will restrict the revenue that can be obtained from any SPEAR T-cell. 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 SPEAR T-cell in the United States or elsewhere will have a materially adverse effect on our business and results of operations.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our SPEAR T-cells.

We face an inherent risk of product liability as a result of the clinical testing of our SPEAR T-cells and our ongoing manufacture of SPEAR T-cells and will face an even greater risk upon any commercialization. For example, we may be sued if any of our SPEAR T-cells 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 SPEAR T-cell. 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 SPEAR T-cells;

Table of Contents

- 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 SPEAR T-cells; 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 SPEAR T-cells. We currently hold £15.0 million in clinical trial insurance coverage in the aggregate per year, with a per trial limit of £5.0 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 SPEAR T-cells. 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.

Even if we obtain regulatory approval of our SPEAR T-cells, 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 SPEAR T-cells are accepted in the market, including:

- the clinical indications for which our SPEAR T-cells are approved;
- physicians, hospitals, cancer treatment centers and patients considering our SPEAR T-cells as a safe and effective treatment;
- the potential and perceived advantages of our SPEAR T-cells 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 SPEAR T-cells as well as competitive products;

Table of Contents

- 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 SPEAR T-cell 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, adverse publicity due to the ethical and social controversies surrounding the therapeutic use of embryonic stem cell or replication competent vector 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 SPEAR T-cells. If SPEAR T-cells are approved but fail to achieve market acceptance among physicians, patients, hospitals, cancer treatment centers or others in the medical community, we or our collaborators will not be able to generate significant revenue.

Even if our SPEAR T-cells 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 SPEAR T-cells, are more cost effective or render our SPEAR T-cells obsolete.

Coverage and reimbursement may be limited or unavailable in certain market segments for our SPEAR T-cells, which could make it difficult for us to sell our SPEAR T-cells profitably.

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

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 SPEAR T-cell from a government or other third-party payor is a time-consuming and costly process which could require us to provide to the payor supporting scientific,

Table of Contents

clinical and cost-effectiveness data for the use of our products. Even if we obtain coverage for a given SPEAR T-cell, 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 SPEAR T-cells unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our SPEAR T-cells.

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 SPEAR T-cells to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained.

We intend to seek approval to market our SPEAR T-cells in both the United States and in selected jurisdictions. If we obtain approval in one or more foreign jurisdictions for our SPEAR T-cells, we will be subject to rules and regulations in those jurisdictions.

In some foreign countries, particularly those in the European Union, 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 SPEAR T-cell. In addition, market acceptance and sales of our SPEAR T-cells will depend significantly on the availability of coverage and adequate reimbursement from third-party payors for our SPEAR T-cells 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 SPEAR T-cells, 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.

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 SPEAR T-cells, if we obtain regulatory approval;

Table of Contents

- our ability to set a price that we believe is fair for our SPEAR T-cells;
- 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 the NY-ESO SPEAR T-cell clinical program, which may also affect other SPEAR T-cells.

Commercialization of the NY-ESO SPEAR T-cell therapy and our own ability to commercialize other SPEAR T-cells 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 three further target programs in addition to the NY-ESO SPEAR T-cell and PRAME SPEAR T-cell programs 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 SPEAR T-cells. 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 GSK Collaboration and License Agreement or any specific license under the GSK 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 within which the NY-ESO SPEAR T-cell therapy can be further developed.

Any future development plan agreed upon between GSK and us, including the third target program, may be unsuccessful or fail to result in candidate therapies that are feasible for further development or commercialization. In particular, the PRAME SPEAR T-cell program (second target program) has terminated due to low presentation of peptide in certain indications and there is no guarantee that the third target program or any further program will be successful. In addition, milestone payments may not be paid or may be varied where any development plan is amended or 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.

There is no guarantee that any payments due on commercialization of products under the GSK Collaboration and License Agreement will be due or payable by GSK at any time or on the timeframes currently expected. In particular, GSK has now exercised its option to the NY-ESO SPEAR T-cell program and commercialization of the NY-ESO SPEAR T-cell is now the responsibility of GSK. The timing for commercialization of the NY-ESO SPEAR T-cell and the route to commercialization will be determined by GSK and we cannot guarantee that GSK will commercialize the NY-ESO SPEAR T-cell within expected timelines or at all. Any substantial delay in the progression of the NY-ESO SPEAR T-cell into pivotal or other clinical trials by GSK will impact the timing of payments received by us in relation to the NY-ESO SPEAR T-cell program.

In addition, any future development plans for SPEAR T-cells under the GSK Collaboration and License Agreement will be subject to change as a result of risks inherent with the development of any pharmaceutical, biological or gene therapy product. Changes may be agreed to expand or change the scope of the collaboration or the responsibilities of the parties under the collaboration. Changes to the development plans or collaboration agreement may impact the timing and extent of milestone payments made by GSK to us, the nature of the relationship with GSK or the scope of the collaboration with GSK.

GSK has the ability to influence or control certain decisions relating to the development of therapies covered by the GSK Collaboration and License Agreement. 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

Table of Contents

clinical programs. Under the GSK Collaboration and License 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 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. Given GSK has taken over the responsibility for the NY-ESO SPEAR T-cell program, decisions taken by GSK (with limited or no input from us) may impact on the development of our SPEAR T-cells outside of the collaboration program or may impact on the regulatory requirements applicable to such SPEAR T-cells.

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 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). 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.

The GSK collaboration programs relate to specific SPEAR T-cells 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 SPEAR T-cells could be significantly compromised.

We rely heavily on 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 SPEAR T-cells. 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.

Table of Contents

In June 2016, we entered into a supply agreement with ThermoFisher for the supply of the Dynabeads® CD3/CD28 technology. The supply agreement runs until December 31, 2025. Under the supply agreement we are required to purchase our requirements for CD3/CD28 magnetic bead product exclusively from ThermoFisher for a period of five years and there are also minimum purchasing obligations. Despite having negotiated this supply agreement there is no certainty that ThermoFisher will be able to continue to supply the Dynabeads® CD3/CD28 technology at the times or at the levels we require or that facilities used by ThermoFisher for the manufacture and supply of the Dynabeads® CD3/CD28 technology will continue to be available to us which could impact the timing of supply of SPEAR T-cells or ability to manufacture SPEAR T-cells.

ThermoFisher has the right to terminate the above described agreements for material breach or insolvency. On termination of the license agreements, the supply agreement will also automatically terminate. If ThermoFisher terminates the exclusive license, sub-license and supply agreements or otherwise refuses or is unable 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 SPEAR T-cells.

If the supply agreements with ThermoFisher is terminated or ThermoFisher is unable to supply the Dynabeads® CD3/CD28 technology for any reason, 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 SPEAR T-cells. 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 SPEAR T-cells and to develop next generation SPEAR T-cells, and we may have to rely on third parties to produce and process our SPEAR T-cells, if approved.

We currently rely on outside contract manufacturing organizations (“CMOs”) to manufacture, supply and process our SPEAR T-cells. If one or more of these CMOs become unable or unwilling to continue to manufacture our engineered SPEAR T-cells (including any raw or intermediate material required for the manufacture of our end engineered SPEAR T-cell therapy) 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 as a result we are 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 SPEAR T-cells after receipt of any applicable regulatory approval.
- We may not be able to obtain lentiviral delivery manufacturing slots with third party contract manufacturers within the timescales we require for supply of lentiviral delivery vector or to obtain agreed dates for such manufacturing

slots sufficiently in advance of the requirement for supply.

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

Table of Contents

- With any new manufacturing process or new CMO we will need to transfer the manufacturing process or new process to that CMO. Any delay in the development and transfer of these new processes to the third-party contract supplier or inability of the third-party contract supplier to replicate or carry out the transferred process at the appropriate level and quality or in a reproducible fashion will result in delays in our ability to progress clinical programs, further develop our SPEAR T-cells and obtain marketing approval for our SPEAR T-cells.
- Introduction of new raw material or intermediate material manufacturers, such as CMOs for vectors, may require comparability testing to be carried out to show that the manufacturing process and end material is comparable to the currently used manufacturing process and/or material. Any inability to show comparability or delay in comparability testing may result in delays to the supply of the affected materials and as a result delays to clinical trials.
- Contract manufacturers may not be able to execute our manufacturing procedures appropriately, or we may be unable to transfer our manufacturing processes to contract manufacturers successfully or without additional time and cost. Even where CMOs fail to manufacture our SPEAR T-cell products successfully, it may not be possible to achieve re-manufacture quickly or without expending resources or additional costs.
- Our future contract manufacturers may not perform as agreed, may be acquired by competitors 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 SPEAR T-cells. In addition, contract manufacturers may not manufacture within agreed timescales for manufacture and/or may cancel pre-agreed manufacturing slots, which would result in delays in manufacturing and could require us to find replacement manufacturers which may not be available to us on favorable terms or at all.
- 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.
- 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 SPEAR T-cells. Our third party manufacturers may use processes which infringe or potentially infringe third party intellectual property rights which may result in inability to use such processes going forward, an increase in the pricing of such processes or a need to change to a different process.
- Our third party manufactures may fail to perform testing and analysis services accurately, in a manner that can be interpreted or on a timely basis. This could delay or prevent release of our SPEAR T-cell product and as a result delay clinical trials and patient treatment.
- Our third-party manufacturers could breach or terminate their agreement with us.
- Our third-party manufacturers may cease to be able to do business with us (whether for insolvency or other reasons, including takeover, merger or acquisition) at a time when we are unable to source such manufacture elsewhere or at our own manufacturing facility.
- Increased costs, unexpected delays, equipment failures, lack of reproducibility, labor shortages, natural disasters, power failures and numerous other factors which are outside of our control or which may be imposed by our CMOs.

Certain raw materials or precursor materials used in the manufacture and supply of our SPEAR T-cells may come from sole source or limited source suppliers. For example, there are currently a limited number of third party

Table of Contents

manufacturers within the United States that can supply us with our lentiviral delivery vector, ThermoFisher is currently the only supplier of the Dynabeads® CD3/CD28 technology and PCT, LLC is currently the only manufacturer of our end SPEAR T-cell therapy. Should such suppliers be unable to supply or manufacture such raw materials or precursor materials either at all or within required timescales we may be unable to supply our SPEAR T-cells or such supply may be significantly delayed. Inability to obtain such raw materials or precursor materials may also necessitate changes in the manufacturing process used for supply of our SPEAR T-cells. Such changes to the manufacturing process may need to be developed internally or by a third party and may also require additional regulatory approvals to be obtained before they can be used for the manufacture and supply of our SPEAR T-cells for clinical trials.

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 SPEAR T-cells by the FDA or the commercialization of our SPEAR T-cells 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 SPEAR T-cells prior to delivery to patients. If these tests are not appropriately performed and test data is not reliable, patients could be put at risk of serious harm. For example if the HLA testing is not accurate then a patient without the correct HLA-type could be provided with incompatible SPEAR T-cells and as a result such patient could suffer severe side effects or fatality.

We also rely on certain third parties to assist us in the future development of SPEAR T-cells including next generation SPEAR T-cells and manufacture and supply of SPEAR T-cells for patient administration. For example, we have a research collaboration with Universal Cells Inc in which we are looking to develop affinity engineered donor T cells that are universally applicable to all patients. As with any research and development program there is no guarantee of the success of such program or that such program will be carried out by us or Universal Cells Inc within the timescales we currently anticipate.

We have a shared development history with Immunocore, and as a result jointly own certain intellectual property rights which are required for our ongoing business.

Our TCR technology was originally developed by Avidex, which 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 acquired the TCR technology for soluble TCRs from Medigene later in 2008 to develop soluble TCR proteins. Certain of our shareholders also hold shares in Immunocore.

Since January 1, 2018, the Company no longer considers Immunocore to be a related party due to several factors including the mutual termination of a target collaboration agreement with Immunocore that terminated effective March 1, 2017, our lack of common directors, and the decrease in Immunocore’s share ownership in 2017 to less than 5% of our ordinary shares. However, under the terms of that target collaboration agreement, we will continue to share a database of identified targets with Immunocore which resulted from the joint target identification efforts under that agreement.

In addition, many of the patents relating to our underlying core technology in TCR engineering, are co-owned by us and Immunocore pursuant to a separate assignment and license agreement. Under this agreement, both Immunocore and Adaptimmune utilize the jointly owned patents and know-how, with Adaptimmune focused on the treatment of patients with engineered SPEAR T-cells 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 SPEAR T-cells is targeting, and therefore compete directly with us.

Table of Contents

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 SPEAR T-cells.

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 SPEAR T-cells 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 any of our SPEAR T-cells 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.

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 SPEAR T-cells. As a result, our financial results and the commercial prospects for our SPEAR T-cells 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 SPEAR T-cells to market, if at all.

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

The manufacture of our SPEAR T-cells 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 SPEAR T-cells.

Some of the materials used in the manufacture and processing of our SPEAR T-cells 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 SPEAR T-cells and progress SPEAR T-cells 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. In addition, where any raw

Table of Contents

material or precursor material (including, for example, lentiviral delivery vector, medium or other essential raw material) is currently supplied by one or a few vendors, replacing such raw material or precursor or finding alternative vendors may not be possible or may significantly impact on the timescales for manufacture and supply of our SPEAR T-cells. Even where alternative materials or precursors or alternative vendors are identified, such alternative materials, precursors or vendors will need to be properly assessed, validated and qualified and additional regulatory approvals may also need to be obtained all of which could result in significant delays to the supply of our SPEAR T-cells or an inability to supply SPEAR T-cells within anticipated timescales, if at all.

Risks Related to Our Intellectual Property

Our SPEAR T-cells 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 SPEAR T-cells 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 SPEAR T-cells 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 SPEAR T-cells and the extent of commercialization possible in relation to such SPEAR T-cells.

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 SPEAR T-cells 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 ADSs.

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 SPEAR T-cells. 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 SPEAR T-cells 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 SPEAR T-cells 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

Table of Contents

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 additional years to cover an FDA-approved product, with the limitation that the total patent life for the product with the patent term extension may not exceed 14 years from the product's approval date. The actual length of the extension will depend on the amount of patent term lost while the product was undergoing regulatory review, which includes a testing phase and an agency approval phase. 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.

Any loss of, or failure to obtain, patent protection could have a material adverse impact on our business. Enforcement of patents may also be cost prohibitive and we may be unable to prevent competitors from entering the market with products that are similar to or the same as our SPEAR T-cells. This is particularly the case where third parties are using T-cell therapies falling within the scope of our patents in clinical trials. It may not be possible to enforce our patents against such third parties during the course of those clinical trials.

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.. 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 SPEAR T-cells or have additional, material adverse effects upon our business, results of operations and financial condition.

Table of Contents

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 SPEAR T-cells or reengineer or rebrand our SPEAR T-cells, 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 SPEAR T-cells, we have not conducted a full freedom-to-operate search or analysis for such SPEAR T-cells, and we may not be aware of patents or pending or future patent applications that, if issued, would block us from commercializing our SPEAR T-cells. Thus, we cannot guarantee that we can successfully commercialize SPEAR T-cells in a way that will not infringe any third party’s intellectual property.

Licenses may be required from third parties in relation to any SPEAR T-cells developed or commercialized by us.

We may identify third-party intellectual property rights that are required to enable the further development, commercialization, manufacture or development of our SPEAR T-cells. 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 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.

As we change, develop and modify our manufacturing processes we may identify further third-party patents covering those developments and modifications. We cannot guarantee that we will be able to obtain licenses under these third-party patents or other intellectual property rights and as a result we may not be able to undertake the developments of modifications that we wish, either at all or in the timescales we require. This could ultimately impact our ability to deliver commercial T-cell products at the cost required.

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.

Table of Contents

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 SPEAR T-cells 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 SPEAR T-cells, the defendant could counterclaim that the patent protecting our SPEAR T-cell, 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 SPEAR T-cells. 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 SPEAR T-cells. 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 SPEAR T-cells.

Filing, prosecuting and defending patents on our SPEAR T-cells 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

Table of Contents

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.

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 Business Officer, Dr. Rafael Amado, our President of Research and Development, William Bertrand, our Chief Operating Officer, and Adrian Rawcliffe, our Chief Financial 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 nine months' notice periods in the case of Mr. Noble and Dr. Tayton-Martin; mutual three months' or two months' notice periods in the case of senior managers and mutual one-month notice periods for all other employees. In the United States, the employment agreements provide for at-will employment except that, under their employment agreements, Dr. Amado, Mr. Rawcliffe and Mr. Bertrand must provide 60 days' written notice for termination without cause. This means that any of our employees in the United States, except for Dr. Amado, Mr. Rawcliffe and Mr. Bertrand, 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.

Table of Contents

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

As of December 31, 2018, we had 430 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:

- identifying, recruiting, integrating, maintaining, and motivating additional employees;
- managing our internal development efforts effectively, including the clinical and FDA review process for our SPEAR T-cells, 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 SPEAR T-cells 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 SPEAR T-cells and, accordingly, may not achieve our research, development, and commercialization goals.

Expansion of our business has necessitated a move in premises both in the United Kingdom and in the United States. While the move in the United States has occurred, work is still ongoing to enable the operation of these premises as a manufacturing facility. The move in the United Kingdom occurred in the second quarter of 2017. The move required transfer of all equipment, cell lines, tissues and materials to the new premises and re-validation and calibration of equipment. Any failure to properly validate or calibrate equipment or any destruction of materials transferred to the new premises may result in additional delays to the work carried out in the United Kingdom.

We have opened a manufacturing facility of our own which may result in increased costs being incurred by the company

During 2017, we opened a manufacturing facility for our SPEAR T-cell products within our Navy Yard facility in Philadelphia, Pennsylvania and have started manufacturing SPEAR T-cells for use in our clinical trials. As a company we have never previously operated our own manufacturing facility or manufactured SPEAR T-cells ourselves. We cannot guarantee that we will be successful in developing SPEAR T-cell manufacturing capability at all or within the currently planned timescales or resource levels or that the regulatory authorities, in particular the FDA, will continue to approve our ability to manufacture SPEAR T-cells at the Navy Yard facility.

Our ability to successfully manufacture our own SPEAR T-cells at the Navy Yard facility within a reasonable period of time and within currently projected costs is dependent on a number of factors including:

- our ability to recruit the required employees at a suitable level and experience and within required timescales and to maintain employment of such required employees;

Table of Contents

- our ability to obtain regulatory approval for the facility and for the manufacture of SPEAR T-cells at the facility and to satisfy regulatory authorities on an ongoing basis;
- our ability to manufacture SPEAR T-cells reliably and reproducibly and to timescales sufficient to support required patient administration;
- our ability to manufacture SPEAR T-cells in compliance with the applicable regulatory requirements, including requirements applicable in both the United States and European Union;
- our ability to develop internal quality controls and processes sufficient to enable manufacture and supply of SPEAR T-cells at our Navy Yard facility;
- our ability to establish comparability with currently used manufacturing processes and for such comparability data to be accepted by the appropriate regulatory authorities; and
- our ability to be able to fund the ongoing development including equipment requirements necessary for successful manufacture of SPEAR T-cells at our facility.

Any delay or failure in manufacture at our facility could result in delays to the supply of SPEAR T-cells for our clinical programs. Should any of our third party manufacturers also cease to be able to supply SPEAR T-cells at a time where our own manufacturing facility is unable to produce SPEAR T-cells for use in our clinical programs or is unable to produce SPEAR T-cells at the required level, then we will be unable to support such clinical programs until alternative manufacturing capability is secured.

We are in the process of increasing the number of manufacturing slots available at our Navy Yard facility. The cost of developing, out-fitting and operating a larger manufacturing facility may also be greater than currently anticipated and we may require additional capital for the completion of the upscaling of the manufacturing facility which may result in the need for us to raise additional funds earlier than expected.

We cannot guarantee that we will be successful in manufacturing SPEAR T-cells at all or in a manner that complies with regulatory requirements. For example, there is a risk that any SPEAR T-cells we manufacture are contaminated or are otherwise incorrectly manufactured resulting in injury or death to any patient receiving those SPEAR T-cells. Such failure could result in a halt being placed on manufacture at our Navy Yard facility. We may also face difficulties in properly tracking and administering our SPEAR T-cells to patients, again potentially resulting in injury or death to any patient receiving those SPEAR T-cells.

We may also be unable to support use of our own manufacturing facility together with third party suppliers and become the sole supply for our SPEAR T-cells. Any inability to supply SPEAR T-cells at the required levels and to the required specifications, will result in delays to clinical trials and may result in holds being applied to such clinical trials.

We expect to face intense competition, which may be 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 SPEAR T-cells through the regulatory process and commercialization. Smaller or early-stage companies and academic sites 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 SPEAR T-cells. Competing companies may also compete for resources including staff, materials and third party CMOs and CROs. We

66

Table of Contents

expect any competition to increase further as SPEAR T-cells and CAR-T technologies progress further in particular in the following areas and from the following companies or other companies developing similar products.

- CAR-T in hematological malignancies: Engineered T-cell therapeutics have been identified using antibody recognition systems engineered into T cells, so-called CAR-T cells. A number of targets in hematological malignancies have been well characterized including, but not limited to: BCMA, CD4, CD5, CD19, CD22, CD20, CD33, CD38, CD70, CS1 and CD123. Two CD-19 directed CAR-T cell products have been approved by the FDA Kymriah™ (tisagenlecleucel) and Yescarta™ (axicabtagene ciloleucel) as well as by the EMA in the European Union. A number of companies and academic institutions are developing CAR-T cell products including but not limited to Allogene Therapeutics, Atara Bio, Autolus, Baylor College of Medicine, Bellicum Inc, bluebird bio, Celyad, Celgene, Cellectis, CRISPR Therapeutics, Fate Therapeutics, Intrexon, Janssen (JNJ with Nanjing Legend), Juno Therapeutics, Kite Pharma (Gilead), Mustang Bio, Novartis, Precigen, Refuge Biotechnologies Inc, Sorrento Therapeutics and Ziopharm Oncology.
- CAR-T in solid tumors: In addition to hematological malignancies, there are a growing number of pharmaceutical, biotechnology, and academic institutions researching and developing autologous and allogeneic CAR-T therapies in the solid tumor setting. These CAR-T cell therapies are at a variety of stages of preclinical and clinical development, as well as directed towards a broad target spectrum, including but not limited to: DLL3, EGFR, GD2, HER-2, IL13r 2, Lewis Y, L1-CAM, Mesothelin, MUC16, PSCA, PSMA and ROR1. Competitors include but are not limited to: Allogene Therapeutics, Amgen, Atara Bio, Aurora Biopharma, Avid Biotics / Xyphos, Baylor College of Medicine, Cell Medica, Bellicum, BioNTech, Carisma Therapeutics (formerly CARMA Therapeutics), Carsgen, Cellectis Therapeutics, Celyad, CRISPR Therapeutics, Endocyte, Fate Therapeutics, Formula Therapeutics, Fred Hutchinson Cancer Research Center, Helix BioPharma, Juno Therapeutics, MaxCyte, Memorial Sloan Kettering Cancer Center, Mustang bio, Poseida Therapeutics, Senti Biosciences, Sorrento Therapeutics, Symvivo, Targazyme and Tmunity.
- CARs & TCR-mimics targeting peptide-HLA complexes: Most CAR-T therapies in development are directed towards suitable antigen targets. Another area of development is the creation of CAR-T that selectively bind to the peptide-HLA (pHLA) complex (the natural binding site for endogenous TCR). Furthermore, competitors are also looking at pHLA antibodies or TCR mimic antibodies that can either be engineered in T-cells or developed as standalone antibody therapies in cancer indications (both hematologic malignancies and solid tumors). Targets of such pHLA CAR-T or TCR mimic antibodies include: AFP, CD19, BCMA, NY-ESO-1, p53 and WT1. A number of pharmaceutical, biotechnology, and academic institutions are researching and developing CARs & TCR-mimics targeting the peptide-HLA complex, including but not limited to: Adicet Bio / Regeneron, Altor Bioscience, Cancer Research Technology/CRUK, Eureka Therapeutics, Gritstone Oncology, Morphosys, Xencor and Ziopharm Oncology.
- TCR T-cells: TCR T-cells are being developed by competitors that are directed towards a multitude of targets including: AFP, CD20, HPV-16 E6/E7, KRAS, MAGE-A1, MAGE-A3, MAGE A3/A6, MART1, NRAS, NY-ESO-1, p53, PRAME, TGF RII frameshift antigen WT1, as well as personalized neoantigens. Juno Therapeutics (a Celgene Company) has developed an engineered TCR therapeutic candidate where the end TCR is purported to have enhanced affinity through stem-cell selection. Juno's candidate JTCR016 (WT1-specific TCR), in collaboration with Fred Hutchinson Cancer Research Center and the National Cancer Institute (NCI), is currently undergoing a Phase 1/2 trial in NSCLC and mesothelioma setting as well as a separate Phase 1/2 in AML. Medigene AG has reported development of a PRAME TCR therapeutic candidate (MDG1011), which has begun a Phase 1/2 clinical investigation in AML, MM and myelodysplastic syndromes. In addition to Juno there is a growing number of TCR companies that are adopting approaches to TCR affinity enhancement, for example Axis Therapeutics, Takara, Takara Bio, Fred Hutchinson Cancer Centre and Immatics. In addition other competitors include, but are not limited to: 3T, Adaptive Biotechnologies (with Genentech), AgenTus, Atreca, Baylor College, Bellicum, BioNTech, bluebird bio, Captain T cell, Cellular Biomedicine Group Inc, Cell Medica Ltd, GigaMune, GSK, Immunocellular

Table of Contents

Therapeutics, Immunocore, Intellia Therapeutics, Inc (with Ospedale San Raffaele), Juno Therapeutics, Kiromic, Kite Pharma (Gilead), Lion TCR LTD, MD Anderson Cancer Center, MediGene AG, NCI, Neon Therapeutics, Parker Institute, Roswell Park Cancer Institute, Scancell (with BioNTech), Tactiva Therapeutics, Takara Bio Inc, Takeda (T-CIRA), TCR x immunotherapies, T-Knife, Tmunity, University of Leiden, Zelluna (with Oslo University Hospital) and Ziopharm Oncology.

- Other cell-based approaches: In addition to adoptive cell therapy approaches aforementioned, our competitors are also investigating the potential of GammaDelta T-cell, CAR-Macrophages, CAR-NK cell, NK cell, NKT cell, CTLs, TILs, Marrow-infiltrating lymphocytes (MILs), Multi-tumor-associated antigen (TAA)-specific T cells and virus-specific T-cells either preclinically or in a clinical setting (both hematologic malignancies and solid tumors). In this space there are a number of potential competitors, including, but not limited to: Adicet Bio, Atara Bio, Aurora BioPharma, Cell Medica, Cellular Biomedicine Group Inc, CytomX, Celgene, Fate Therapeutics, Fortress Biotech, Gadeta (with Kite Pharma), Gamma Delta Therapeutics (with Takeda), Gamida cell, Genocea, Glycostem Therapeutics, iCell Gene Therapeutics, Immatics, Iovance Biotherapeutics (formerly Lion Bio), KSQ Therapeutics, Multimmune, NantKwest, Sorrento Therapeutics, Marker Therapeutics, Tessa Therapeutics, TC Biopharm (with bluebird bio), Torque Therapeutics WindMIL Therapeutics and Ziopharm Oncology.

Although Immunocore is focused on soluble TCRs rather than engineered SPEAR T-cells, 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.

Table of Contents

The results of the United Kingdom's referendum on withdrawal from the European Union ("Brexit") may have a negative effect on global economic conditions, financial markets and our business.

The United Kingdom is currently negotiating the terms of its exit from the European Union ("Brexit") scheduled for March 29, 2019. In November 2018, the U.K. and the European Union agreed upon a draft withdrawal agreement ("Withdrawal Agreement") that sets out the terms of the U.K.'s departure, including commitments on citizen rights after Brexit, a financial settlement from the U.K., and a transition period from March 29, 2019 through December 31, 2020 to allow time for a future trade agreement to be agreed. On January 15, 2019, the draft Withdrawal Agreement was rejected by the U.K. Parliament creating significant uncertainty about the terms (and timing) under which the U.K. will leave the European Union. If no agreement can be reached and the U.K. leaves the European Union with no agreement ("hard Brexit"), there will be a period of considerable uncertainty particularly in relation to United Kingdom financial and banking markets, the regulatory process in Europe and movement of goods and people between U.K. and European Union. As a result of this uncertainty, financial markets could experience volatility which could adversely affect the market price of our ADSs. We may also face new regulatory costs and challenges that could have a material adverse effect on our operations. In this regard, the EMA has already issued a notice reminding marketing authorization holders of centrally authorized medicinal products for human and veterinary use of certain legal requirements that need to be considered as part of Brexit, such as the requirement for the marketing authorization holder of a product centrally approved by the European Commission to be established in the European Union, and the requirement for some activities relating to centrally approved products, such as batch release and pharmacovigilance, to be performed by entities or individuals in the European Union. In the absence of any clear indication that any agreed form of Withdrawal Agreement will contain a contrary requirement, we are already in the process of ensuring that any impact on our operations is limited. Depending on the terms of Brexit, the United Kingdom could lose the benefits of global trade agreements negotiated by the European Union on behalf of its members, which may result in increased trade barriers which could make our doing business worldwide more difficult. In addition, currency exchange rates in the pound sterling and the euro with respect to each other and the U.S. dollar have already been adversely affected by Brexit. Should this foreign exchange volatility continue it could cause volatility in our financial results.

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 SPEAR T-cells on a commercial basis or for use in clinical programs.

Table of Contents

We are exposed to risks related to currency exchange rates.

We conduct a significant portion of our operations within the United Kingdom in both U.S. dollars and pounds sterling and our arrangements with GSK are denominated in pounds sterling. Changes in currency exchange rates have had and could have a significant effect on our operating results. Exchange rate fluctuations between the U.S. dollar and local currencies create risk in several ways, including the following: weakening of the pound sterling may increase the cost of overseas research and development expenses and other costs outside the United Kingdom; strengthening of the U.S. dollar may decrease the value of any future revenues denominated in other currencies. Effects of exchange rates on transactions and cash deposits held in a currency other than the functional currency of a subsidiary 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 ADSs 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 the Company was classified as a PFIC for U.S. federal income tax purposes for the U.S. taxable year ended December 31, 2018. There can be no assurance, however, that we will not be considered to be a PFIC for this taxable year or any particular year in the future because PFIC status is factual in nature, depends upon factors not wholly within our control, generally cannot be determined until the close of the taxable year in question and is determined annually.

If we are a PFIC, U.S. holders of our ADSs 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 ADSs may be able to mitigate some of the adverse U.S. federal income tax consequences described above with respect to owning the ADSs 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.

Investors should consult their own tax advisors regarding all aspects of the application of the PFIC rules to our ordinary shares.

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;

Table of Contents

- 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 SPEAR T-cells;
- 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 SPEAR T-cells, if approved for marketing, 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 the Nasdaq Global Select Market, or 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.

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.

Table of Contents

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. Sales of a substantial number of our ADSs in the public market could occur at any time. Moreover, certain shareholders have rights under an investors rights agreement dated as of February 23, 2015, subject to certain conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other shareholders. In addition, we have registered an aggregate of 66,999,747 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 December 31, 2018, an aggregate of 47,678,481 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 capital in the future.

We incur increased costs as a result of being a public company whose ADSs are publicly traded in the United States and our management must devote substantial time to public company compliance.

As a U.S. public company whose ADSs trade on Nasdaq, we have incurred and will continue to incur significant legal, accounting, insurance and other expenses. We are subject to the reporting requirements of the Exchange Act, which requires, among other things, that we file with the SEC annual, quarterly and current reports with respect to our business and financial condition and must comply with the Nasdaq listing requirements and other applicable securities rules and regulations. In addition, the Sarbanes-Oxley Act, as well as rules subsequently adopted by the SEC and the Nasdaq to implement provisions of the Sarbanes-Oxley Act, impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. Further, pursuant to the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010, the SEC has adopted and will adopt additional rules and regulations, such as mandatory “say on pay” voting requirements, that we must comply with. We expect the rules and regulations applicable to public companies to substantially increase our legal and financial compliance costs and to 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. To the extent these requirements divert the attention of our management and personnel from other business concerns, they could have a material adverse effect on our business, financial condition and results of operations. The increased costs will increase our net loss and may require us to reduce costs in other areas of our business. 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.

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.

We must maintain effective internal control over financial reporting in order to accurately and timely report our results of operations and financial condition. In addition, as a U.S. public company, the Sarbanes-Oxley Act of 2002, or the

Sarbanes-Oxley Act, requires, among other things, that we assess the effectiveness of our disclosure controls and procedures and the effectiveness of our internal control over financial reporting at the end of each fiscal year. Pursuant to Section 404 of the Sarbanes-Oxley Act, we are required to furnish a report by our management on our internal control over financial reporting, and we are required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. The rules governing the standards that must be met for our management to assess our internal control over financial reporting pursuant to Section 404 of the Sarbanes-Oxley Act are complex and require significant documentation, testing and possible remediation. These stringent standards require

Table of Contents

that our audit and finance committee be advised and regularly updated on management's review of internal control over financial reporting.

Our compliance with applicable provisions of Section 404 requires that we incur substantial accounting expenses and expend significant management attention and time on compliance-related issues as we implement additional corporate governance practices and comply with reporting requirements. If we fail to staff our accounting and finance function adequately or maintain internal control over financial reporting adequate to meet the requirements of the Sarbanes-Oxley Act, our business and reputation may be harmed. Moreover, if we are not able to comply with the applicable requirements of Section 404 in a timely manner, we may be subject to sanctions or investigations by regulatory authorities, including the SEC and Nasdaq. Furthermore, if we are unable to conclude that our internal control over financial reporting is effective or if our independent registered public accounting firm identifies deficiencies in our internal control over financial reporting that are deemed to be material weaknesses, we could lose investor confidence in the accuracy and completeness of our financial reports, the market price of our ADSs could decline, and we could be subject to sanctions or investigations by the SEC, Nasdaq or other regulatory authorities. Failure to implement or maintain effective internal control systems required of U.S. public companies could also restrict our access to the capital markets. The occurrence of any of the foregoing would also require additional financial and management resources.

U.S. investors may have difficulty enforcing civil liabilities against our company, our directors, officers and members of senior management.

We are incorporated under the laws of England and Wales. The rights of holders of our 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 organized in, for example, Delaware. Some of our directors, officers and members of senior management reside outside the United States, and a substantial portion of our assets and all or a substantial portion of the assets of such persons are located outside the United States. As a result, it may be difficult for you to serve legal process on us or our directors and executive officers or have any of them appear in a U.S. court. The United States and the United Kingdom do not currently have a treaty providing for the recognition and enforcement of judgments, other than arbitration awards, in civil and commercial matters. The enforceability in the United Kingdom of any judgment of a U.S. federal or state court will depend on the particular facts of the case as well as the laws and any treaties in effect at the time, including conflicts of laws principles (such as those bearing on the question of whether a U.K. court would recognize the basis on which a U.S. court had purported to exercise jurisdiction over a defendant). In this context, there is doubt as to the enforceability in the United Kingdom, in original actions or in actions for enforcement of judgments of U.S. courts, of civil liabilities based solely on the federal securities laws of the United States. In addition, awards for 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 likely be considered punitive if it did not seek to compensate the claimant for loss or damage suffered and was intended to punish the defendant.

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 to an offer for, among other things, a public company whose registered office is in the United Kingdom 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.

In July 2018, the Takeover Panel confirmed that, based on our current circumstances, we are not subject to the Takeover Code. As a result, our shareholders are not entitled to the benefit of certain takeover offer protections provided under the Takeover Code. We believe that this position is unlikely to change at any time in the near future but, in

Table of Contents

accordance with good practice, we will review the situation on a regular basis and consult with the Takeover Panel if there is any change in our circumstances which may have a bearing on whether the Takeover Panel would determine our place of central management and control to be in the United Kingdom.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

The following table summarizes the facilities we lease as of December 31, 2018, including the location and size of the facilities, and their primary use.

Location	Approximate Square Feet	Primary Usage	Lease Expiration Dates
Abingdon, Oxfordshire, United Kingdom	67,140	Corporate headquarters , Research, Development, Process development, Manufacturing, Administration	October 2041
Abingdon, Oxfordshire, United Kingdom	46,017	Manufacturing, Process Development, Research	October 2041
Philadelphia, Pennsylvania, United States	47,700	Manufacturing, Process Development, Research	October 2031
Stevenage, Hertfordshire, United Kingdom	2,642	Administration	December 2023

As of December 31, 2018, all of the above sites were utilized by the Company with the exception of our facilities in Abingdon, Oxfordshire, of 46,017 sq ft, which are not currently occupied after completion of external works in November 2018.

We believe that our existing facilities are adequate for our near-term needs, but we expect to need additional space as we grow and expand our operations. We believe that suitable additional or alternative office, laboratory, and manufacturing space will be available as required in the future on commercially reasonable terms.

Item 3. Legal Proceedings

As of December 31, 2018, we were not a party to any material legal proceedings.

Item 4. Mine Safety Disclosures

Not applicable

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Table of Contents

Holders of Common Stock

The Company's ADSs each represent six ordinary shares of Adaptimmune Therapeutics plc. The ADSs have been listed on Nasdaq since May 6, 2015 and are traded under "ADAP". As of February 22, 2019, there were approximately 27 holders of record of our ordinary shares, par value £0.001 per share, and seven holders of record of our ADSs. The closing sale price per ADS on Nasdaq on February 22, 2019 was $4.57.

Dividends

Since our inception, we have not declared or paid any dividends on our ordinary shares. We intend to retain any earnings for use in our business and do not currently intend to pay dividends on our ordinary shares.

The payment of dividends by Adaptimmune Therapeutics plc is governed by English law. The declaration and payment of any future dividends will be at the discretion of our board of directors and will depend upon our results of operations, cash requirements, financial condition, contractual restrictions, restrictions imposed by our indebtedness, any future debt agreements or applicable laws and other factors that our board of directors may deem relevant.

Performance Graph

This performance graph shall not be deemed "filed" for purposes of Section 18 of the Exchange Act, or incorporated by reference into any of our filings under the Securities Act or the Exchange Act, except as shall be expressly set forth by specific reference in such filing.

Table of Contents

The following graph shows the cumulative total stockholder return of an investment of $100 in cash at market close on May 6, 2015 (the first day of trading of our ADSs) through December 31, 2018 for (1) our ADSs, (2) the NASDAQ Composite Index (U.S.) and (3) the NASDAQ Biotechnology Index.

Recent Sales of Unregistered Securities

We did not sell any unregistered securities during the year ended December 31, 2018.

Information about Our Equity Compensation Plans

Information regarding our equity compensation plans is incorporated by reference in Item 12 of Part III of this Annual Report on Form 10-K.

Item 6. Selected Financial Data

The selected statements of operations data for the years ended December 31, 2018, 2017 and 2016, six months ended December 31, 2015 and the years ended June 30, 2015 and 2014 and the selected balance sheet data as of December 31, 2018, 2017, 2016 and 2015 and June 30, 2015 and 2014 are derived from our financial statements appearing elsewhere in this Annual Report.

On January 1, 2018, the Company adopted new accounting guidance on revenue recognition, which has been codified within Accounting Standard Codification Topic 606, Revenue from Contracts with Customers (“ASC 606”). The comparative financial information for the years ended December 31, 2017 and 2016, six months ended December 31, 2015 and the years ended June 30, 2015 and 2014 and the selected balance sheet data as of December 31, 2017, 2016 and 2015 and June 30, 2015 and 2014 has not been restated and is prepared in accordance with the previous accounting guidance.

Table of Contents

The following selected financial data (in thousands, except for share and per share amounts) should be read in conjunction with the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and the financial statements and related notes appearing elsewhere in this Annual Report. Our historical results are not necessarily indicative of the results that can be expected in the future.

	Year ended December 31, 2018	Year ended December 31, 2017	Year ended December 31, 2016	Six months ended December 31, 2015	Year ended June 30, 2015	Year ended June 30, 2014
Statements of Operations Data(2):						
Revenue	$ 59,505	$ 37,833	$ 14,198	$ 8,979	$ 9,871	$ 825
Research and development	(98,269)	(87,388)	(63,789)	(25,472)	(24,137)	(9,575)
General and administrative	(43,601)	(31,106)	(23,208)	(9,917)	(10,375)	(2,771)
Total operating expenses	(141,870)	(118,494)	(86,997)	(35,389)	(34,512)	(12,346)
Operating loss	(82,365)	(80,661)	(72,799)	(26,410)	(24,641)	(11,521)
Interest income	2,849	2,230	1,110	489	504	—
Other income (expense), net	(15,501)	8,744	1,002	2,866	2,323	(5)
Loss before tax	(95,017)	(69,687)	(70,687)	(23,055)	(21,814)	(11,526)
Income taxes	(497)	(451)	(892)	55	(244)	(75)
Loss for the year	(95,514)	(70,138)	(71,579)	(23,000)	(22,058)	(11,601)
Deemed dividends	—	—	—	—	(14,735)	
Net loss attributable to ordinary shareholders	$ (95,514)	$ (70,138)	$ (71,579)	$ (23,000)	$ (36,793)	$ (11,601)
Basic and diluted loss per share	$ (0.16)	$ (0.13)	$ (0.17)	$ (0.05)	$ (0.17)	$ (0.08)
Weighted average number of shares outstanding(1)	584,338,942	527,637,086	424,713,997	424,711,900	214,704,593	148,335,529

	December 31, 2018	December 31, 2017	December 31, 2016	December 31, 2015	June 30, 2015	June 30, 2014
Balance Sheet Data(2):						
Cash and cash equivalents	$ 68,379	$ 84,043	$ 158,779	$ 194,263	$ 229,046	$ 51,179
Short-term deposits	—	—	22,694	54,620	55,292	—
Marketable securities — available-for-sale debt securities	136,755	124,218	—	—	—	—
Total assets	276,736	281,147	234,515	285,821	300,653	55,735
Total liabilities	29,851	78,163	68,373	50,828	41,650	52,778
Total stockholders' equity	246,885	202,984	166,142	234,993	259,003	2,957

(1) Adjusted to reflect a 1 for 100 stock split effective February 2015.

(2) On April 1, 2015, the Company completed a corporate reorganization. Prior to the corporate reorganization, our business was conducted by Adaptimmune Limited and its consolidated subsidiary. Subsequent to the corporate reorganization, our business was conducted by Adaptimmune Therapeutics plc and its consolidated subsidiaries, including Adaptimmune Limited. The historical consolidated financial statements of Adaptimmune Limited and consolidated 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.

Table of Contents

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

The following discussion contains management's discussion and analysis of our financial condition and results of operations and should be read together with "Selected Financial Data" and the historical consolidated financial statements and the notes thereto included in "Financial Statements and Supplementary Data". This discussion contains forward-looking statements that reflect our plans, estimates and beliefs and involve numerous risks and uncertainties, including but not limited to those described in the "Risk Factors" section of this Annual Report. Actual results may differ materially from those contained in any forward-looking statements. You should carefully read "Special Note Regarding Forward-Looking Statements" and "Risk Factors."

Overview

We are a clinical-stage biopharmaceutical company focused on providing novel cell therapies to patients, particularly in solid tumors. Our comprehensive and proprietary SPEAR (Specific Peptide Enhanced Affinity Receptor) T-cell platform enables us to identify cancer targets, find and genetically engineer T-cell receptors ("TCRs"), and produce therapeutic candidates for administration to patients. Using our affinity engineered TCRs, we aim to become a fully integrated cell therapy company and to be the first company to have a TCR T-cell that we have developed approved for a solid tumor indication.

We have three SPEAR T-cells in clinical trials, ADP-A2M10 (MAGE-A10), ADP-A2M4 (MAGE-A4) and ADP-A2AFP (AFP). All SPEAR T-cells are currently exhibiting acceptable tolerability profiles with no evidence of off-target toxicities observed.

- Two Phase 1 clinical trials are ongoing with ADP-A2M10. The first clinical trial is in patients with NSCLC. The second clinical trial is in patients with three cancer tumor types, urothelial, melanoma and head and neck cancers. Both trials have progressed to the expansion phase, with patients being treated with up to 10 billion transduced SPEAR T-cells.
- A Phase 1 clinical trial is ongoing with ADP-A2M4 in bladder, melanoma, head and neck, ovarian, NSCLC, synovial sarcoma, MRCLS, esophageal, and gastric cancers. This trial is now in the expansion phase with patients being treated with up to 10 billion transduced SPEAR T-cells.
- A Phase 1 clinical trial is ongoing with ADP-A2AFP in patients with hepatocellular carcinoma. The trial is in the dose escalation phase with patients receiving a target dose of 1 billion transduced SPEAR T-cells.

A fourth SPEAR T-cell, the NY-ESO SPEAR T-cell was transitioned to GlaxoSmithKline ("GSK") during 2018 following GSK's exercise of its option to obtain an exclusive global license to the NY-ESO SPEAR T-cell program in September 2017. GSK has assumed full responsibility for all development, manufacturing and commercialization activities for the NY-ESO SPEAR T-cell including progression of this SPEAR T-cell into further clinical trials.

Recent events since December 31, 2018

Dose escalation to the second dosing cohort in the ADP-A2AFP clinical trial was announced on January 7, 2019.

GSK have nominated a third target program. Adaptimmune and GSK are in the process of agreeing a collaboration program for this third target program.

Financial operations overview

On January 1, 2018, the Company adopted new accounting guidance on revenue recognition, which has been codified within Accounting Standard Codification Topic 606, Revenue from Contracts with Customers ("ASC 606").

78

Table of Contents

The comparative financial information for the years ended December 31, 2017 and 2016 and as of December 31, 2017 has not been restated and is prepared in accordance with the previous accounting guidance.

Revenue

Revenue arises from the GSK Collaboration and License Agreement. The contract consists of multiple performance obligations, including the transition of the NY-ESO SPEAR T-cell program to GSK, the pre-clinical development of a second target, PRAME, and the NY-ESO License.

The aggregate transaction price consists of an upfront payment of $42.1 million in June 2014, development milestones achieved of $66.4 million, an option exercise fee of $39.8 million.

The transaction price is allocated to the performance obligation and recognized as or when the Company satisfies the performance obligation. The Company satisfies the performance obligations relating to the transition of the NY-ESO SPEAR T-cell program and the development of a second target, PRAME, over time and recognizes revenue based on an estimate of the percentage of completion of the project determined based on the costs incurred on the project as a percentage of the total expected costs.

The performance obligation relating to the NY-ESO License was recognized at a point-in-time, upon commencement of the license in September 2018.

Research and Development Expenses

Research and development expenses consist principally of the following:

- salaries for research and development staff and related expenses, including 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 associated with the development of a process to manufacture and supply our lentiviral vector and SPEAR T-cells for use in clinical trials;
- costs to develop manufacturing capability at our U.S. facility for manufacture of SPEAR T-cells for use in clinical trials;
- costs relating to facilities, materials and equipment used in research and development;
- costs of acquired or in-licensed research and development which does not have alternative future use;
- amortization and depreciation of property, plant and equipment and intangible assets used to develop our SPEAR T-cells; and
- share-based compensation expenses;

offset by:

· reimbursements from government grants; and
· reimbursable tax and expenditure credits from the U.K. government.

Table of Contents

Research and development expenditures are expensed as incurred.

Research and development expenditure is presented net of reimbursements from reimbursable tax and expenditure credits from the U.K. government. 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 ("SME R&D Tax Credit Scheme"), 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 approximately 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 for which we do not receive income. Subcontracted research expenditures are eligible for a cash rebate of up to approximately 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.

Expenditures incurred in conjunction with the GSK Collaboration and License Agreement are not qualifying expenditures under the SME R&D Tax Credit Scheme but certain of these expenditures can be reimbursed through the U.K. research and development expenditure credit scheme (the "RDEC Scheme"). Under the RDEC Scheme tax relief is given at 12% of allowable R&D costs.

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. The duration, costs, and timing of clinical trials and development of our SPEAR T-cells 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 rates;
- future clinical trial results;
- significant and changing government regulation;
- the timing and receipt of any regulatory approvals; and
- supply and manufacture of lentiviral vector and SPEAR T-cells for clinical trials.

For further detail please see Part I — Item 1A Risk Factors — Risks Related to the Development of our SPEAR T-cells of this Annual Report.

A change in the outcome of any of these variables may significantly change the costs and timing associated with the development of that SPEAR T cell. 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;

Table of Contents

- professional fees for auditors, lawyers and other consulting expenses;
- costs of facilities, communication, and office expenses;
- information technology expenses;
- amortization and depreciation of property, plant and equipment and intangible assets not related to research and development activities; and
- share-based compensation expenses.

Other Income (Expense), net

Other income (expense), net comprises foreign exchange gains (losses). We are exposed to foreign exchange rate risk because we currently operate in the United Kingdom and United States. Our revenue from the GSK Collaboration and License Agreement is denominated in pounds sterling and is generated by our U.K.-based subsidiary, which has a pounds sterling functional currency. As a result, these sales are subject to translation into U.S. dollars when we consolidate our financial statements. Our expenses are generally denominated in the currency in which our operations are located, which are the United Kingdom and United States. However, our U.K.-based subsidiary incurs significant research and development costs in U.S. dollars and, to a lesser extent, Euros. Our U.K. subsidiary with a pound sterling functional currency held our investments in marketable securities until May 2018, which are predominately denominated in U.S. dollars. The entire change in the fair value of a foreign currency-denominated security, including the change due to foreign exchange, was included in other comprehensive income. At the end of May 2018, our investments in marketable securities were transferred to our U.K. subsidiary with a U.S. dollar functional currency, which reduced the potential for foreign exchange gains or losses arising on these investments.

Our results of operations and cash flows will be subject to fluctuations due to changes in foreign currency exchange rates, which could harm our business in the future. We seek to minimize this exposure by maintaining currency cash balances at levels appropriate to meet foreseeable expenses in U.S. dollars and pounds sterling. To date, we have not used hedging contracts to manage exchange rate exposure, although we may do so in the future.

Taxation

We are subject to corporate taxation in the United Kingdom and the United States. We incur tax losses and tax credit carryforwards in the United Kingdom. No deferred tax assets are recognized on our U.K. losses and tax credit carryforwards because there is currently no indication that we will make sufficient taxable profits to utilize these tax losses and tax credit carryforwards. Unsurrendered U.K. tax losses and tax credit carryforwards can be carried forward to be offset against future taxable profits, however this is restricted to an annual £5 million allowance in each standalone company or group and above this allowance, there will be a 50% restriction in the profits that can be covered by losses brought forward. There are accumulated tax loss carry forwards and tax credit carryforwards in the United Kingdom amounting to $175.6 million and $0.6 million as of December 31, 2018. These tax losses and tax credit carryforwards do not expire.

We benefit from reimbursable tax credits in the United Kingdom through the SME R&D Tax Credit Scheme as well as the RDEC Scheme which are presented as a deduction to research and development expenditure.

Our subsidiary in the United States has generated taxable profits due to a Service Agreement between our U.S. and U.K. operating subsidiaries and is subject to U.S. federal corporate income tax of 21% for the year ended December 31, 2018. In December 2017, various U.S. tax reforms were enacted in the U.S., which reduced the corporate tax rate for our U.S. subsidiary to from 34% for the year ended December 31, 2017 to 21% for the year ended December 31, 2018. Due to its activity in the United States, and the sourcing of its revenue, the U.S. subsidiary is not currently subject to any state or local income taxes.

Table of Contents

We also benefit from tax credits arising through the Credit for Increasing Research Activities ("Research Tax Credit") under the U.S. Internal Revenue Code and the U.S. Orphan Drug Credit. There are accumulated tax credit carryforwards in the United States amounting to $4.2 million as of December 31, 2018. These tax credit carryforwards expire after 20 years.

In the future, if we generate taxable income in the United Kingdom, we may benefit 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 of 10%. As we have many different patents covering our products, future upfront fees, milestone fees, product revenues, and royalties may be taxed at this favorably low tax rate.

U.K. 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 relevant sales invoices and is payable to the U.K. tax authorities. Similarly, VAT paid on purchase invoices paid by Adaptimmune Limited and Adaptimmune Therapeutics plc is reclaimable from the U.K. tax authorities.

Results of Operations

We are reporting herein results for the year ended December 31, 2018, 2017 and 2016. On January 1, 2018, the Company adopted new accounting guidance on revenue recognition, which has been codified within Accounting Standard Codification Topic 606, Revenue from Contracts with Customers ("ASC 606"). The comparative financial information for the years ended December 31, 2017 and 2016 have not been restated and is prepared in accordance with the previous accounting guidance.

Comparison of Year Ended December 31, 2018 and 2017

The following table summarizes the results of our operations for the years ended December 31, 2018 and 2017, together with the changes to those items (in thousands):

	Year ended December 31, 2018	2017	Increase/decrease		
Revenue	$ 59,505	$ 37,833	$ 21,672	57	%
Research and development expenses	(98,269)	(87,388)	(10,881)	12	%
General and administrative expenses	(43,601)	(31,106)	(12,495)	40	%
Total operating expenses	(141,870)	(118,494)	(23,376)	20	%
Operating loss	(82,365)	(80,661)	(1,704)	2	%
Interest income	2,849	2,230	619	28	%
Other (expense) income, net	(15,501)	8,744	(24,245)	(277)	%
Loss before income taxes	(95,017)	(69,687)	(25,330)	36	%
Income taxes	(497)	(451)	(46)	10	%
Loss for the period	$ (95,514)	$ (70,138)	$ (25,376)	36	%

Revenue

Revenue increased by $21.7 million to $59.5 million in the year ended December 31, 2018 compared to $37.8 million for the year months ended December 31, 2017. Revenue comprises the following (in thousands):

	Year ended December 31, 2018	2017	Increase/decrease		
Development revenue	$ 20,391	$ 37,833	$ (17,442)	(46)	%
License revenue	39,114	—	39,114	NM	
	$ 59,505	$ 37,833	$ 21,672	57	%

Table of Contents

Revenue arises from the GSK Collaboration and License Agreement. Development revenue relates to performance under the NY-ESO SPEAR T-cell transition program and the PRAME pre-clinical development program. License revenue relates to NY-ESO License.

Revenue for the year ended December 31, 2018 has been recognized under ASC 606 which is effective January 1, 2018. Revenue in the ended December 31, 2017 has been recognized under the previous guidance. Development revenue in the year ended December 31, 2018 under the previous guidance would be $28.7 million and license revenue would be $39.1 million.

Development revenue for the year ended December 31, 2018 has decreased by 46% compared to the year ended December 31, 2017 due to the NY-ESO program having transferred to GSK on July 23, 2018. The development revenue for the year ended December 31, 2017 also benefited from cumulative revenue amortization of $17.5 million in September 2017 due to a reduction in the estimate of the period over which we would be delivering services to GSK in relation to the NY-ESO SPEAR T-cell development program.

License revenue was $39.1 million in the year ended December 31, 2018 compared to nil in the year ended December 31, 2017. License revenue is recognized upon commencement of the NY-ESO License which occurred in the third quarter of 2018.

We anticipate that there will be no significant revenues in the year ended December 31, 2019 arising from the NY-ESO SPEAR T-cell transition program or the PRAME pre-clinical development program due to the completion of both programs in 2018.

Research and development expenses

Research and development expenses increased by 12% to $98.3 million for the year ended December 31, 2018 from $87.4 million for the year ended December 31, 2017. Our research and development expenses comprise the following (in thousands):

	Year ended December 31, 2018	2017	Increase/decrease		
Salaries, materials, equipment, depreciation of property, plant and equipment and other employee-related costs(1)	$ 60,590	$ 47,087	$ 13,503	29	%
Subcontracted expenditure	41,580	41,505	75	0	%
Manufacturing facility expenditure	4,848	2,820	2,028	72	%
Share-based compensation expense	8,340	5,669	2,671	47	%

Payments for in-process research and development	210	1,033	(823)	(80)	%
Reimbursements for research and development tax and expenditure credits and government grants	(17,299)	(10,726)	(6,573)	61	%
	$ 98,269	$ 87,388	$ 10,881	12	%

(1) These costs are not analyzed by project since employees may be engaged in multiple projects at a time.

The increase in our research and development expenses of $10.9 million for the year ended December 31, 2018 compared to the year ended December 31, 2017 was primarily due to the following:

- an increase of $13.5 million in salaries, materials, equipment, depreciation of property, plant and equipment and other employee-related costs, primarily due to the increase in the average number of employees engaged in research and development from 260 to 320
- an increase of $0.1 million in subcontracted expenditures, including clinical trial expenses, contract research organization (CRO) costs and contract manufacturing expenses due to the transition of our NY-

Table of Contents

ESO SPEAR T-cell program to GSK and the commencement of manufacturing at our U.S. facility in Philadelphia;

- an increase in expenditure of $2.0 million on manufacturing at our U.S. facility in Philadelphia due to manufacturing for clinical trials commencing at our U.S. facility in January 2018 and development of a dedicated vector manufacturing capability in Stevenage, Hertfordshire, UK; and
- an increase of $2.7 million in share-based compensation expense due to an increase in the number of employees and the grant-date fair value of share options;

offset by:

- an increase in reimbursements for research and development tax and expenditure credits and government grants of $6.6 million due to an increase in eligible R&D expenditure.

Our subcontracted costs for the year ended December 31, 2018 were $41.5 million, compared to $41.5 million in the same period of 2017, of which $3.6 million related to our NY-ESO SPEAR T-cells, $23.0 million related to process development for our SPEAR T-cell platform and the remaining $14.9 million related to our wholly owned pipeline, including ADP-A2M4, ADP-A2M10 and ADP-A2AFP. The subcontracted costs for our NY-ESO SPEAR T-cells has reduced compared to the prior year due to the transition of the program to GSK.

Our research and development expenses are highly dependent on the phases and progression of our research projects and future clinical trial results and therefore fluctuate from period to period.

General and administrative expenses

General and administrative expenses increased by 40% to $43.6 million for the year ended December 31, 2018 from $31.1 million in the same period in 2017.

The net increase of $12.5 million was primarily due to a $7.7 million increase in personnel costs and share-based compensation expense, due to the addition of key management and other professionals to support our growth, a $2.7 million increase in costs associated with supporting and maintaining our IT infrastructure, a $0.9 million in legal, accounting and professional fees and a $0.7 million increase in depreciation and amortization.

Interest income

Interest income was $2.8 million for the year ended December 31, 2018 compared to $2.2 million for the year ended December 31, 2017. Interest income primarily relates to interest on cash, cash equivalents and available-for-sale debt securities.

Other income (expense), net

Other income (expense), net was an expense of $15.5 million for the year ended December 31, 2018 compared to an income of $8.7 million for the year ended December 31, 2017. Other income (expense), net primarily relates to unrealized foreign exchange gains and losses on cash and cash equivalents, intercompany loans and short-term deposits held in U.S. dollars by our U.K. subsidiary. The movement in other income (expense), net is primarily due to movements in exchange rates and an increase in net foreign currency balances.

Income taxes

Income taxes was $0.5 million for the year ended December 31, 2018 and 2017. Income taxes arise in the United States. The Company incurs losses in the United Kingdom.

Table of Contents

Comparison of Year Ended December 31, 2017 and 2016

The following table summarizes the results of our operations for the years ended December 31, 2017 and 2016, together with the changes to those items (in thousands):

	Year ended December 31, 2017	2016	Increase/decrease		
Revenue	$ 37,833	$ 14,198	$ 23,635	166	%
Research and development expenses	(87,388)	(63,789)	(23,599)	37	%
General and administrative expenses	(31,106)	(23,208)	(7,898)	34	%
Total operating expenses	(118,494)	(86,997)	(31,497)	36	%
Operating loss	(80,661)	(72,799)	(7,862)	11	%
Interest income	2,230	1,110	1,120	101	%
Other income, net	8,744	1,002	7,742	773	%
Loss before income taxes	(69,687)	(70,687)	1,000	(1)	%
Income taxes	(451)	(892)	441	(49)	%
Loss for the period	$ (70,138)	$ (71,579)	$ 1,441	(2)	%

Revenue

We recognize non-contingent milestones earned under the GSK Collaboration and License Agreement using a proportional performance method over an estimate of the period which we will be delivering services to GSK. When a milestone is achieved, the total non-contingent consideration, including the milestone, is recognized over the period we are delivering services to GSK, resulting in an adjustment to the cumulative revenue amortization in the period the milestone is achieved and higher revenue amortization in future periods. Any changes in the estimate of the period over which we are delivering services to GSK will also result in an adjustment to the cumulative revenue amortization in the period the estimate is revised.

Revenue increased by 166% to $37.8 million for the year ended December 31, 2017 from $14.2 million for the year ended December 31, 2016. On September 7, 2017, GSK exercised its option to the NY-ESO SPEAR T-cell program and further amended the GSK Collaboration and License Agreement. Upon the exercise of the NY-ESO option, the estimate of the period over which we will be delivering services to GSK in relation to the NY-ESO SPEAR T-cell development program has significantly reduced, resulting in an increase in cumulative revenue amortization of $17.5 million in 2017. The increase in revenue in the year ended December 31, 2017 compared to the year ended December 31, 2016 is primarily due to cumulative revenue amortization recognized on exercise of the NY-ESO option and additional revenue amortization on milestone payments achieved in the year.

Table of Contents

Research and development expenses

Research and development expenses increased by 37% to $87.4 million for the year ended December 31, 2017 from $63.8 million for the year ended December 31, 2016. Our research and development expenses comprise the following (in thousands):

	Year ended December 31, 2017	2016	Increase/decrease	
Salaries, materials, equipment, depreciation of property, plant and equipment and other employee-related costs(1)	$ 47,087	$ 40,348	$ 6,739	17 %
Subcontracted expenditure	41,505	23,560	17,945	76 %
Manufacturing facility expenditure	2,820	—	2,820	N/A
Share-based compensation expense	5,669	4,186	1,483	35 %
Payments for in-process research and development	1,033	3,000	(1,967)	(66) %
Reimbursements for research and development tax and expenditure credits and government grants	(10,726)	(7,305)	(3,421)	47 %
	$ 87,388	$ 63,789	$ 23,599	37 %

(1) These costs are not analyzed by project since employees may be engaged in multiple projects at a time.

The increase in our research and development expenses of $23.6 million for the year ended December 31, 2017 compared to the year ended December 31, 2016 was primarily due to the following:

- an increase of $6.7 million in salaries, materials, equipment, depreciation of property, plant and equipment and other employee-related costs, primarily due to the increase in the average number of employees engaged in research and development from 210 to 260;
- an increase of $18.0 million in subcontracted expenditures, including clinical trial expenses, contract research organization (CRO) costs and manufacturing expenses driven by increased recruitment in our clinical trials, initiation of clinical trials for ADP-A2M4, ADP-A2M10 and ADP-A2AFP, and an increase in manufacturing process development activities;
- operating expenditure of $2.8 million on developing our manufacturing capabilities at our U.S. facility in Philadelphia; and
- an increase of $1.5 million in share-based compensation expense for employee and nonemployee share options;

offset by:

- a decrease of $2.0 million in payments made to Universal Cells for in-process research and development; and
- an increase in reimbursements for research and development tax and expenditure credits and government grants of $3.4 million.

Our subcontracted costs for the year ended December 31, 2017 were $41.5 million, compared to $23.6 million in the same period of 2016, of which $13.4 million related to our NY-ESO SPEAR T-cells, $7.8 million related to process development for our SPEAR T-cell platform and the remaining $20.3 million related to our wholly owned pipeline, including ADP-A2M4, ADP-A2M10 and ADP-A2AFP.

Table of Contents

General and administrative expenses

General and administrative expenses increased by 34% to $31.1 million for the year ended December 31, 2017 from $23.2 million in the same period in 2016.

The net increase of $7.9 million was primarily due to a $4.9 million increase in personnel costs and share-based compensation expense, due to the addition of key management and other professionals to support our growth, a 1.2 million increase in costs associated with supporting and maintaining our IT infrastructure and a $1.2 million increase in depreciation and amortization.

Interest income

Interest income was $2.2 million for the year ended December 31, 2017 compared to $1.1 million for the year ended December 31, 2016. Interest income primarily relates to interest on cash, cash equivalents and available-for-sale debt securities. Interest income has increased due to cash generated from our two equity offerings completed in March and April 2017, which has been invested in marketable securities.

Other income, net

Other income, net was $8.7 million for the year ended December 31, 2017 compared to $1.0 million for the year ended December 31, 2016. Other income (expense), net primarily relates to unrealized foreign exchange gains and losses on cash and cash equivalents, intercompany loans and short-term deposits held in U.S. dollars by our U.K. subsidiary. Other income, net has increased primarily due to unrealized foreign exchange gains arising on intercompany loans, which is partially offset by unrealized foreign exchange losses on cash balances, which are lower in the year ended December 31, 2017 because we invested approximately $80 million of cash and cash equivalents into marketable securities in the year ended December 31, 2017. The unrealized foreign exchange gains (losses) arising on marketable securities are recognized within other comprehensive income.

Income taxes

Income taxes decreased by 49% to $0.5 million for the year ended December 31, 2017 from $0.9 million for the year ended December 31, 2016. Income taxes arise in the United States. The decrease in income taxes is due to the Company initiating an assessment in the fourth quarter of 2017 of the benefit from U.S. Research Tax Credits and Orphan Drug Credits. Based on this preliminary assessment, the Company has estimated that it will benefit from U.S. Research Tax Credits and Orphan Drug Credits of $0.5 million for the year ended December 31, 2017, of which $0.3 million can be used to offset taxes in the year ended December 31, 2017 and has been recognized in the fourth quarter of 2017. The Company incurs losses in the United Kingdom.

Liquidity and Capital Resources

Sources of Funds

Since our inception, we have incurred significant net losses and negative cash flows from operations. We financed our operations primarily through sales of equity securities, cash receipts under our GSK Collaboration and License Agreement, government grants and research and development tax and expenditure credits. From inception through to December 31, 2018, we have raised:

- $513.5 million, net of issue costs;
- $148.3 million upfront fees, milestones and exercise fees under our GSK Collaboration and License Agreement;

· $2.8 million of income in the form of government grants; and

Table of Contents

· $24.6 million in the form of U.K. research and development tax credits and receipts from the U.K. RDEC Scheme.

We use a non-GAAP measure, Total Liquidity, which is defined as the total of cash and cash equivalents, short-term deposits and marketable securities, to evaluate the funds available to us in the near-term. A description of Total Liquidity and reconciliation to cash and cash equivalents, the most directly comparable U.S. GAAP measure, are provided below under “Non-GAAP measures”.

As of December 31, 2018, we had cash and cash equivalents of $68.4 million and Total Liquidity of $205.1 million. We believe that our Total Liquidity will be sufficient to fund our operations, based upon our currently anticipated research and development activities and planned capital spending, through to late 2020.

Cash Flows

The following table summarizes the results of our cash flows for the years ended December 31, 2018, 2017 and 2016 (in thousands).

	Year ended December 31, 2018	Year ended December 31, 2017	Year ended December 31, 2016
Net cash used in operating activities	$ (104,388)	$ (54,315)	$ (48,168)
Net cash (used in) provided by investing activities	(17,457)	(126,081)	17,755
Net cash provided by financing activities	102,690	103,568	17
Cash, cash equivalents and restricted cash	72,476	88,296	162,796

Operating Activities

Year ended December 31, 2018 compared to December 31, 2017

Net cash used in operating activities increased by $50.1 million to $104.4 million for the year ended December 31, 2018 from $54.3 million for the year ended December 31, 2017. Net cash used in operating activities is significantly impacted by the timing of milestone payments received from GSK under the GSK Collaboration and License Agreement. In the year ended December 31, 2018, we received $30.2 million of milestone payments from GSK compared to $38.2 million in the year ended December 31, 2017. After taking into account the GSK milestone payments and the associated VAT, the increase in cash used in operations 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.

Year ended December 31, 2017 compared to December 31, 2016

Net cash used in operating activities increased by $6.1 million to $54.3 million for the year ended December 31, 2017 from $48.2 million for the year ended December 31, 2016. Net cash used in operating activities is significantly impacted by the timing of milestone payments received from GSK under the GSK Collaboration and License Agreement. In the year ended December 31, 2017, we received $38.2 million of milestone payments from GSK compared to $19.8 million in the year ended December 31, 2016. After taking into account the GSK milestone payments and the associated VAT, the increase in cash used in operations 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.

Components of cash flows from operating activities

Net cash used in operating activities of $104.4 million for the year ended December 31, 2018 comprised a net loss of $95.5 million and $45.3 million of adverse changes in operating assets and liabilities offset by noncash items of $36.5 million and. The noncash items consisted primarily of depreciation expense on plant and equipment of

Table of Contents

$7.2 million, share-based compensation expense of $16.2 million, a realized loss on marketable securities of $2.5 million and unrealized foreign exchange losses of $9.7 million.

Net cash used in operating activities of $54.3 million for the year ended December 31, 2017 comprised a net loss of $70.1 million offset by noncash items of $8.6 million and a $7.2 million beneficial changes in operating assets and liabilities. The noncash items consisted primarily of depreciation expense on plant and equipment of $5.0 million, share-based compensation expense of $10.8 million and a realized loss on marketable securities of $0.6 million, partially offset by unrealized foreign exchange gains of $8.6 million.

Net cash used in operating activities of $48.2 million for the year ended December 31, 2016 comprised a net loss of $71.6 million offset by noncash items of $10.9 million and a $12.5 million beneficial changes in operating assets and liabilities. The noncash items consisted primarily depreciation expense on plant and equipment of $3.1 million and equity-settled share-based compensation expense of $8.8 million, partially offset by unrealized foreign exchange gains of $1.3 million.

Investing Activities

Net cash from investing activities was a cash outflow of $17.5 million and $126.1 million for the years ended December 31, 2018 and 2017, respectively, and a cash inflow of $17.8 million for the year ended December 31, 2016. These amounts included purchases of property and equipment of $3.9 million, $24.6 million, $11.5 million for the year ended December 31, 2018, 2017 and 2016, respectively, and acquisition of intangibles of $0.8 million, $0.4 million, $1.3 million for the years ended December 31, 2018, 2017 and 2016, respectively. The purchases of property, plant and equipment for the year ended December 31, 2017 and 2016 related predominantly to the expansion of our laboratory facilities in the United Kingdom and the United States.

The net cash used in investing activities also included:

- investment in short-term deposits with maturities greater than three months but less than 12 months of $18.0 million and $42.8 million for the year ended December 31, 2017 and 2016, respectively; and
- investment in marketable securities with maturities greater than three months but less than 12 months of $150.8 million and $153.3 million in the year ended December 31, 2018 and 2017, respectively;

offset by

- cash inflows from maturity of short-term deposits of $40.6 million and $73.4 million in the years ended December 31, 2017 and 2016, respectively; and
- cash inflows from maturity or redemption of marketable securities with maturities greater than three months but less than 12 months of $138.0 million and $29.1 million in the year ended December 31, 2018 and 2017, respectively.

Financing Activities

Net cash provided by financing activities was $102.7 million, $103.6 million, $17,000 for the years ended December 31, 2018, 2017 and 2016, respectively.

Net cash provided by financing activities for the year ended December 31, 2018 consisted of $99.7 million, net of issuance costs of $0.3 million, raised through a registered direct offering in September 2018 and proceeds from exercise of share options of $3.0 million.

Net cash provided by financing activities for the year ended December 31, 2017 consisted of $61.4 million net of issuance costs of $4.5 million raised through a follow-on public offering in March 2017, $41.8 million net of issuance

89

Table of Contents

costs of $0.2 million raised through a registered direct offering in April 2017 and proceeds from exercise of share options of $401,000.

Net cash provided by financing activities for the year ended December 31, 2016 consisted of proceeds from exercise of share options of $17,000.

Non-GAAP Measures

Total Liquidity (a non-GAAP financial measure)

Total Liquidity (a non-GAAP financial measure) is the total of cash and cash equivalents, short-term deposits and marketable securities. Each of these components appears in the consolidated balance sheet. The U.S. GAAP financial measure most directly comparable to Total Liquidity is cash and cash equivalents as reported in the consolidated financial statements, which reconciles to Total Liquidity as follows (in thousands):

	December 31, 2018	December 31, 2017
Cash and cash equivalents	$ 68,379	$ 84,043
Marketable securities	136,755	124,218
Total Liquidity	$ 205,134	$ 208,261

We believe that the presentation of Total Liquidity provides useful information to investors because management reviews Total Liquidity as part of its management of overall liquidity, financial flexibility, capital structure and leverage. The definition of Total Liquidity includes marketable securities, which are highly-liquid and available to use in our current operations.

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 in Note 9 of the consolidated financial statements included in Item 15 of this Annual Report.

Contractual Obligations

The following table summarizes our contractual commitments and obligations as of December 31, 2018 (in thousands):

	Payments due by period				
	Total	Less than 1 year	1 - 3 years	3 - 5 years	More than 5 years
Operating lease obligations(1)	$ 31,958	$ 3,682	$ 7,423	$ 7,081	$ 13,772
Purchase obligations(2)(3)	25,849	13,213	12,636	—	—
Total contractual cash obligations	$ 57,807	$ 16,895	$ 20,059	$ 7,081	$ 13,772

(1) Operating lease obligations primarily consists of minimum lease payments under non-cancellable leases for laboratory and office property in Oxfordshire, U.K. and Philadelphia, U.S.

(2) Purchase obligations include signed orders for capital equipment, clinical materials and contract manufacturing, which have been committed but not yet received and committed funding under the MD Anderson strategic alliance. The timing of the payments may vary depending on the rate of progress of development and clinical trial enrollment rates.

Table of Contents

(3) Future clinical trial expenses have not been included within the purchase commitments because they are contingent on enrollment in clinical trials and the activities required to be performed by the clinical sites.

Operating lease obligations

In May 2017, we entered into an agreement for the lease of a building at Milton Park, Oxfordshire, U.K. The lease term expires on October 23, 2041, with termination options exercisable by us on the fifth anniversary of the lease commencement date and at approximately five yearly intervals thereafter. The related lease commitments are included in the table above.

Purchase obligations

On September 26, 2016, we announced that we had entered into a multi-year strategic alliance with MD Anderson designed to expedite the development of T-cell therapies for multiple types of cancer. We and MD Anderson are collaborating on a number of studies including clinical and preclinical development of our SPEAR T-cell therapies targeting NY-ESO and MAGE-A10 and we will collaborate on future clinical stage first and second generation SPEAR T-cell therapies such as ADP-A2M4 across a number of cancers, including bladder, lung, ovarian, head and neck, melanoma, synovial sarcoma, esophageal and gastric cancers. Under the terms of the agreement, we have committed at least $19.6 million to fund studies. The Company made an upfront payment of $3,412,000 to MD Anderson in the year ended December 31, 2017 and milestone payments of $2,325,000 in the year ended December 31, 2018. Payment of this funding is contingent on mutual agreement to study orders under the alliance agreement and the performance of set milestones by MD Anderson. The timing and amount of future payments is uncertain. These milestones are included within ‘Purchase obligations’ above.

On June 16, 2016, we entered into a supply agreement with ThermoFisher for the supply of the Dynabeads® CD3/CD28 technology. The Dynabeads® CD3/CD28 technology is designed to isolate, activate and expand human T-cells, and is being used in the manufacturing of our affinity enhanced T-cell therapies. The supply agreement runs until December 31, 2025. Under the supply agreement, we are required to purchase our requirements for CD3/CD28 magnetic bead product exclusively from ThermoFisher for a period of five years and there are also minimum purchasing obligations (which have been included in the purchase obligations above). ThermoFisher has the right to terminate the supply agreement for material breach or insolvency.

Other obligations

On November 25, 2015, we entered into a Research Collaboration and License Agreement relating to gene editing and HLA-engineering technology with Universal Cells. We paid an upfront license fee of $2.5 million to Universal Cells. A milestone payment of $3.0 million was made in February 2016 and further milestone payments of $0.9 million in 2017. We are obligated to make further payments of up to $43.5 million if certain development and product milestones are achieved. Universal Cells would also receive a profit-share payment for the first product, and royalties on sales of other products utilizing its technology. Future payments are not reflected in the table above because the timing of the payments is uncertain.

In 2012, we entered into a series of license and sub-license agreements with Life Technologies Corporation, part of ThermoFisher that provide us with a field-based exclusive license under certain intellectual property rights owned or controlled by ThermoFisher. We paid upfront license fees of $1.0 million relating to the license and sublicense agreements and has an obligation to pay minimum annual royalties (in the 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 and a low single-digit running royalty payable on the net selling price of each licensed product. Future payments are not reflected in the table above because the timing and amount of the payments are uncertain.

Critical Accounting Policies and Significant Judgments and Estimates

We have prepared our consolidated financial statements in accordance with U.S. GAAP. Our preparation of these consolidated financial statements requires us to make estimates, assumptions and judgments that affect the reported

Table of Contents

amounts of assets, liabilities, expenses and related disclosures at the date of the consolidated financial statements, as well as revenue and expenses during the reporting periods. We evaluate our estimates and judgments on an ongoing basis. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results could therefore differ materially from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in Note 2 to our consolidated financial statements, we believe the following accounting policies to be critical to the judgments and estimates used in the preparation of our financial statements.

Revenue Recognition

The Company has one contract with a customer, which is the GSK Collaboration and License Agreement. The GSK Collaboration and License Agreement consists of multiple performance obligations, including the transition of the NY-ESO SPEAR T-cell program to GSK, the development of a second target, PRAME, and the NY-ESO License.

The aggregate transaction price consists of an upfront payment, development milestones achieved, an option exercise fee and an estimate of variable consideration. The Company determines the variable consideration to be included in the transaction price by estimating the most-likely amount that will be received and then applies a constraint to reduce the consideration to the amount which is probable of being received. In estimating the amount of variable consideration to be included in the transaction price, the Company considers the latest project plan and other available information. The determination of whether a milestone is probable includes consideration of the following factors:

Whether achievement of a development milestone is highly susceptible to factors outside the entity’s influence, such as milestones involving the judgment or actions of third parties, including regulatory bodies or the customer;

Whether the uncertainty about the achievement of the milestone is not expected to be resolved for a long period of time;

Whether the Company can reasonably predict that a milestone will be achieved based on previous experience; and

The complexity and inherent uncertainty underlying the achievement of the milestone.

The determination of whether future milestones are probable requires significant judgment and the impact of a change in the determination of whether a milestone is probable is recognized in the period the judgment is revised. This can significantly impact the revenue recognized. In the year ended December 31, 2018, revenue of $10.4 million, was

recognized due to development milestones becoming probable in the period. As the development program progresses and the uncertainties underlying the milestones resolve, further milestones may become probable.

The upfront payment of $42.1 million was allocated between the performance obligations using the Company's best estimate of the relative selling price of each performance obligation. The best estimate of the selling price is determined after considering all reasonably available information, including internal pricing objectives used in negotiating the contract, together with internal data regarding the cost and margin of providing services for each deliverable taking into account the different stage of development of each development program. The variable consideration is allocated to the performance obligation to which it relates.

The amount of the transaction price allocated to the performance obligation is recognized as or when the Company satisfies the performance obligation. The Company satisfies the performance obligations relating to the transition of the NY-ESO SPEAR T-cell program and the development of a second target, PRAME, over time and recognizes revenue based on an estimate of the percentage of completion of the project determined based on the costs incurred on the project as a percentage of the total expected costs. The determination of the percentage of completion

Table of Contents

requires the Company to estimate the costs-to-complete the project. The Company makes a detailed estimate of the costs-to-complete on an annual basis as part of the Company's budgeting process, which is re-assessed every reporting period based on the latest project plan and discussions with project teams, when a change in facts or circumstances occurs, the estimated is adjusted and the revenue is recognized based on the revised estimate. The difference between the cumulative revenue recognized based on the previous estimate and the revenue recognized based on the revised estimate is recognized as an adjustment to revenue in the period in which the change in estimate occurs. In the year ended December 31, 2018, the estimate of the cost to complete for the performance obligation relating to the development and transition of the NY-ESO SPEAR T-cell program was revised, which resulted in a cumulative adjustment of $5.0 million to reduce revenue for the year ended December 31, 2018. Due to the completion of the NY-ESO transition and the PRAME pre-clinical development program in 2018, we do not anticipate any further changes in the cost to complete.

The performance obligation relating to the NY-ESO License was recognized at a point-in-time, upon commencement of the license in September 2018.

Clinical Trial Expenses

Expenses related to clinical trials are recognized as services are received. Nonrefundable advance payments for services are deferred and recognized in the statement of operations as the services are rendered. This determination is based on an estimate of the services received and there may be instances when the payments to vendors exceed the level of services provided resulting in a prepayment of the clinical expense. If the actual timing of the performance of services varies from our estimate, the accrual or prepaid expense is adjusted accordingly.

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. 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.

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. For example, the strategic alliance with MD Anderson involves milestone

payments made in advance of the service being provided. In recognizing the expense, we estimate the cost by patient enrolled and recognize this over the period between initial dosing and estimated cessation of patient monitoring activities. The duration of the clinical trial is estimated based on internal historical data and projections. There is limited data available and our estimate of the duration of the clinical may vary as we obtain further data.

Although we do not expect our estimates of the amounts, status and timing of services performed to be materially different from the actual amounts, status and timing of services performed, if they do vary, 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.

Table of Contents

Clinical materials

Clinical materials for use in research and development with alternative future use are capitalized as either other current assets or other non-current assets, depending on the timing of their expected consumption. The clinical materials with alternative future use consist of Dynabeads® CD3/CD28 technology ("Dynabeads"), which is designed to isolate, activate and expand human T-cells, and is being used in the manufacturing of the Company's affinity enhanced T-cell therapies. The Dynabeads are purchased under a supply agreement, which runs until December 31, 2025. The supply agreement includes minimum purchasing obligations.

As of December 31, 2018, we have $5.0 million of clinical materials, of which we expect to consume $1.0 million within the next 12 months and the remaining amount over the next several years. At each reporting date, we consider whether the Dynabeads on-hand and committed purchase obligations are impaired due to excess quantity over current forecast demand by considering manufacturing forecasts, forecasts of clinical trial enrollments, stability testing results, technological developments and future development programs. As of December 31, 2018, we consider that our current estimate of future demand for Dynabeads exceeds the amount on-hand and the minimum purchase requirements and therefore the clinical materials are not impaired. The assumptions underlying the impairment analysis are based on estimates of forecasts and assumptions surrounding the progress and outcome of clinical trials, which may change as development of our SPEAR T-cells progresses.

U.K. R&D Tax and Expenditure Credits

Research and development expenditure is presented net of reimbursements from the U.K. Small and Medium-sized Entity R&D Tax Credit Scheme and the U.K. Research and Development Expenditure Credit Scheme. Reimbursable tax and expenditure credits are recognized when it is probable that the Company has complied with any attached conditions and will receive the reimbursement. Management is required to develop estimates at each reporting date on the amount of the reimbursable tax and expenditure credits, which includes an estimate of qualifying expenditure. The tax and expenditure credits are claimed from Her Majesty's Revenue and Customs ("HMRC") as part of the annual U.K. tax return. Although, we do not expect our estimates to be materially different from amounts claimed and subsequently reimbursed by HMRC, if our estimates of the qualifying expenditure differ from the amount claimed, we may report amounts that are too high or too low in any particular period. To date, there has been no material differences between our estimates and the amount actually reimbursed.

U.S. Research Tax Credits and Orphan Drug Credit

During the fourth quarter of 2017, the Company initiated a study to identify research and development expenditures incurred in the three years ended December 31, 2017, which are eligible expenses for the Research Tax Credit and the U.S. Orphan Drug Credit. As of December 31, 2017, the Company estimated that it would benefit from Research Tax Credits and Orphan Drug Credits of $0.5 million for the year ended December 31, 2017, of which $0.3 million would offset taxes in the year ended December 31, 2017. In 2018, the R&D tax credit study was completed and we benefited from Research Tax Credits and Orphan Drug Credits of $2.3 million and $1.5 million arising in the years ended December 31, 2017 and 2016, respectively, of which $1.0 million was used to offset taxes arising in the years ended December 31, 2017 and 2016. As of December 31, 2018, the Company estimated that it will benefit from Research Tax Credits and Orphan Drug Credits of $2.0 million for the year ended December 31, 2018, of which $0.7 million will offset taxes in the year ended December 31, 2018. Although we do not expect our estimates to be materially different from amounts claimed, if our estimates of the qualifying expenditure differ from the amount claimed, we may report amounts that are too high or too low in any particular period.

Deferred taxes

Deferred tax is accounted for using the asset and liability method that requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of temporary differences between the financial statement carrying amount and the tax bases of assets and liabilities at the applicable tax rates. As of December 31, 2018, we have deferred tax assets of $42.2 million, offset by deferred tax liabilities of $1.4 million and a valuation allowance of $40.8 million.

Table of Contents

A valuation allowance is provided when it is more-likely-than-not that some portion or all of the deferred tax assets will not be realized. Future realization of the tax benefit of a deferred tax asset depends on the existence of sufficient taxable income of the appropriate character (for example, ordinary income or capital gain) within the carryback or carryforward period available under the tax law. The Company considers the following possible sources of taxable income when assessing whether there is sufficient taxable income to realize a tax benefit for deductible temporary differences and carryforwards:

- future reversals of existing taxable temporary differences;
- future taxable income exclusive of reversing temporary differences and carryforwards;
    - taxable income in prior carryback year(s) if carryback is permitted under the tax law; and
- tax-planning strategies.

The Company considers both positive and negative evidence regarding realization of the deferred tax assets and the subjectivity of this evidence. This assessment includes estimating future taxable income, scheduling reversals of temporary differences, evaluating expectations of future profitability, determining refund potential in the event of net operating loss carrybacks, and evaluating potential tax-planning strategies.

The Company has generated losses in the United Kingdom since inception and is forecasted to generate tax losses for the next several years and therefore the deferred tax assets arising in the United Kingdom are only considered more-likely-than-not of being realized to the extent that reversing temporary taxable differences are available.

The U.S. subsidiary has generated taxable income since the fiscal year ended June 30, 2014 due to a Service Agreement between our U.S. and U.K. operating subsidiaries and is forecast to generate taxable income in future periods. In determining whether the deferred tax asset is more-likely-than-not of being recognized, the Company has taken into account the short history of taxable profits, the forecast of future taxable income, including whether future originating temporary deductible differences are likely to be realized, and the reversal of temporary taxable deductions. Several of the temporary deductible differences reverse over a long time period, such as those relating to share-based compensation expense, which the Company forecasts are likely to reverse predominately in 2020 and 2021. The Company considers that forecasting taxable income beyond the next few years is very subjective due to the nature and extent of the development process subcontracted from the Company in the United Kingdom to the U.S. subsidiary. Less weight has been given to forecasts of taxable income beyond the next few years. The deferred tax asset arising in the United States is only considered more-likely-than-not of being realized to the extent that there are available reversing temporary taxable differences. The Company’s analysis is subject to estimates and judgments particularly relating to the timing of the reversal of temporary deductible differences for stock compensation expense and the availability of future taxable income beyond the next few years, which depend on the nature and extent of the subcontract development work performed by the U.S. subsidiary.

Share-based Compensation

The Company awards certain employees options over the ordinary shares of the parent company. The cost of share-based awards issued to employees is measured at the grant-date fair value of the award and recognized as an expense over the requisite service period, for those awards that are ultimately expected to vest. The fair value of the options is determined using the Black-Scholes option-pricing model. Share options with graded-vesting schedules are recognized on a straight-line basis over the requisite service period for each separately vesting portion of the award.

Valuation of Share Options

The Black-Scholes option pricing model requires the input of assumptions, including share price volatility, the expected term of a share option, the risk free rate and the underlying share valuation. The assumption of the expected

term of share options involves management judgment. We estimate that the expected life of our share options, which is the time from the grant date to the expected exercise date, is five years. The life of the options depends on the option

Table of Contents

expiration date, volatility of the underlying shares and vesting features. We do not have sufficient history to determine the expected life based on internal data and therefore the estimate is based on empirical data.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

We are exposed to market risks in the ordinary course of our business, which are principally limited to interest rate fluctuations, foreign currency exchange rate fluctuations, particularly between pound sterling and U.S. dollar, and credit risk. These risks are managed by maintaining an appropriate mix of cash deposits and securities in various currencies, placed with a variety of financial institutions for varying periods according to expected liquidity requirements.

As of December 31, 2018, we held $136.8 million in marketable securities, with the aim of diversifying our investments and reducing credit risks. We have not entered into investments for trading or speculative purposes.

Interest Rate Risk

Our surplus cash and cash equivalents are invested in interest-bearing savings, money market funds, corporate debt securities and commercial paper from time to time. Our investments in corporate debt securities are subject to fixed interest rates. Our exposure to interest rate sensitivity is impacted by changes in the underlying U.K. and U.S. bank interest rates and the fair market value of our corporate debt securities will fall in value if market interest rates increase. We do not believe an immediate one percentage point change in interest rates would have a material effect on the fair market value of our portfolio, and therefore we do not expect our operating results or cash flows to be significantly affected by changes in market interest rates.

Currency Risk

We are exposed to foreign exchange rate risk because we currently operate in the United Kingdom and the United States. Our revenue from the GSK Collaboration and License Agreement is denominated in pounds sterling and is generated by our U.K.-based subsidiary, which has a pounds sterling functional currency. As a result, these sales are subject to translation into U.S. Dollars when we consolidate our financial statements. Our expenses are generally denominated in the currency in which our operations are located, which are the United Kingdom and the United States. However, our U.K.-based subsidiary incurs significant research and development costs in U.S. dollars and, to a lesser extent, Euros.

The results of operations and cash flows will be subject to fluctuations due to changes in foreign currency exchange rates, which could harm our business in the future. We seek to minimize this exposure by maintaining currency cash balances at levels appropriate to meet foreseeable expenses in U.S. dollars and pounds sterling. To date, we have not used forward exchange contracts or other currency hedging products to manage our exchange rate exposure, although we may do so in the future. The exchange rate as of December 31, 2018, the last business day of the reporting period, was £1.00 to $1.27.

Credit Risk

Our cash and cash equivalents are held with multiple banks and we monitor the credit rating of those banks. Our investments in corporate debt securities and commercial paper are subject to credit risk. Our investment policy limits investments to certain types of instruments, such as money market instruments, corporate debt securities and commercial paper, places restrictions on maturities and concentration by type and issuer and specifies the minimum credit ratings for all investments and the average credit quality of the portfolio.

Trade receivables were $0.2 million and $0.2 million as of December 31, 2018 and 2017, respectively. Trade receivables arise in relation to the GSK Collaboration and License Agreement. We have been transacting with GSK since 2014, during which time no impairment losses have been recognized. There was $0.2 million past due as of December 31, 2018.

Table of Contents

Item 8. Financial Statements and Supplementary Data

The information required by this item may be found beginning on page F 1 of this Annual Report with the exception of the unaudited consolidated quarterly operations data, which is presented below. We have prepared the consolidated quarterly operations data on a consistent basis with the audited consolidated financial statements included elsewhere in this Annual Report. In the opinion of management, the quarterly consolidated operations data reflects all necessary adjustments, consisting only of normal recurring adjustments, necessary for a fair presentation of these data. Historical results are not necessarily indicative of the results to be expected in future periods, and the results for a quarterly period are not necessarily indicative of the operating results for a full year. This information should be read in conjunction with the consolidated financial statements included elsewhere in this Annual Report.

Summarized unaudited quarterly data for 2018 and 2017 are as follows (in thousands, except per share data):

	Three months ended			
	March 31, 2018	June 30, 2018	September 30, 2018	December 31, 2018
Revenue	$ 8,196	$ 9,038	$ 40,792	$ 1,479
Operating (loss) income	(28,400)	(28,877)	7,018	(32,106)
Net (loss) income attributable to ordinary shareholders	(20,738)	(43,845)	5,242	(36,173)
Net (loss) income per ordinary share, basic	(0.04)	(0.08)	0.01	(0.06)
Net (loss) income per ordinary share, diluted	$ (0.04)	$ (0.08)	$ 0.01	$ (0.06)
Weighted average shares outstanding, basic	562,381,995	565,197,217	582,004,954	627,429,277
Weighted average shares outstanding, diluted	562,381,995	565,197,217	621,764,201	627,429,277

	Three months ended			
	March 31, 2017	June 30, 2017	September 30, 2017	December 31, 2017
Revenue	$ 2,857	$ 3,521	$ 27,185	$ 4,270
Operating loss	(22,221)	(23,780)	(4,960)	(29,700)
Net loss attributable to ordinary shareholders	(21,782)	(20,215)	(878)	(27,263)
Net loss per ordinary share, basic and diluted	$ (0.05)	$ (0.04)	$ —	$ (0.05)
Weighted average shares outstanding, basic and diluted	428,961,818	556,776,430	561,239,864	562,119,334

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None

Item 9A. Controls and Procedures

Disclosure Controls and Procedures.

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, has evaluated the effectiveness of our disclosure controls and procedures (as defined in Exchange Act Rules 13a 15(e) and 15d 15(e)) as of the end of the period covered by this Annual Report. Based on such evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that our disclosure controls and procedures were effective to ensure that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms, and is accumulated and communicated to our management, including our Chief Executive and Chief Financial Officer, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure.

Table of Contents

Management's Annual Report on Internal Control over Financial Reporting.

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Securities Exchange Act Rule 13a 15(f). Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Therefore, even those systems determined to be effective can provide only reasonably assurance of achieving their control objectives. Under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting based on the framework in Internal Control—Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on our evaluation under the framework, our management concluded that our internal control over financial reporting was effective as of December 31, 2018.

KPMG, LLP, the independent registered public accounting firm who audited the Company's Consolidated Financial Statements included in this Form 10-K, has issued a report on the Company's internal control over financial reporting, which is included herein.

Changes in Internal Control Over Financial Reporting.

There has been no change in our internal control over financial reporting (as defined in Rule 13a 15(f) under the Exchange Act) that occurred during the fourth quarter of 2018 that has materially affected, or is reasonably likely to materially affect, internal control over financial reporting.

In January 2018, the Company has adopted new guidance on revenue recognition, which has been codified within Accounting Standard Codification Topic 606, Revenue from Contracts with Customers ("ASC 606"). As a consequence of the new guidance, the Company has implemented several new internal controls, including controls to monitor the probability of achievement of contingent milestone payments and the pattern of performance of the performance obligation.

Item 9B. Other Information

None

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information required under this item is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, to be filed with the Commission not later than 120 days after the close of our fiscal year ended December 31, 2018.

Item 11. Executive Compensation

The information required under this item is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, to be filed with the Commission not later than 120 days after the close of our fiscal year ended December 31, 2018.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required under this item is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, to be filed with the Commission not later than 120 days after the close of our fiscal year ended December 31, 2018.

Table of Contents

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information required under this item is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, to be filed with the Commission not later than 120 days after the close of our fiscal year ended December 31, 2018.

Item 14. Principal Accounting Fees and Services

The information required under this item is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, to be filed with the Commission not later than 120 days after the close of our fiscal year ended December 31, 2018.

PART IV

Item 15. Exhibits, Financial Statement Schedules

(a) 1. Financial Statements

As part of this Annual Report on Form 10 K, the consolidated financial statements are listed in the accompanying index to financial statements on page F 1.

2. Financial Statement Schedules

All schedules have been omitted because they are not required, not applicable, not present in amounts sufficient to require submission of the schedule, or the required information is otherwise included.

Table of Contents

3. Exhibit Index

The following is a list of exhibits filed as part of this Annual Report on Form 10 K or are incorporated herein by reference:

Exhibit Number	Description of Exhibit
3.1*	Articles of Association of Adaptimmune Therapeutics plc (incorporated by reference to Exhibit 3.1 to our Form 8 K filed with the SEC on June 16, 2016)
10.1*†	Collaboration Agreement, dated January 5, 2018, between Adaptimmune Limited and Cell Therapy Catapult Limited
10.2*	First Amendment to Employment Agreement, dated January 12, 2018 and effective October 30, 2017, between Adaptimmune LLC and Gwendolyn Binder-Scholl.
10.3*	Lease, dated February 28, 2018, between MEPC Milton Park No. 1 Limited, MEPC Milton Park No. 2 Limited and Adaptimmune Limited relating to 39 Innovation Drive, Milton Park.
10.4*	Rent Security Deposit Deed, dated February 28, 2018, between MEPC Milton Park No. 1 Limited, MEPC Milton Park No. 2 Limited and Adaptimmune Limited relating to 39 Innovation Drive, Milton Park.
14.1*	Code of Business Conduct and Ethics of Adaptimmune Therapeutics plc (incorporated by reference to Exhibit 14.1 to our Form 8 K filed with the SEC on July 20, 2017).
21.1*	List of Subsidiaries (incorporated by reference to Exhibit 21.1 to our Registration Statement on Form F 1 (file no: 333 203267)).
23.1**	Consent of KPMG LLP
31.1**	Certificate of Chief Executive Officer pursuant to 17 CFR 240.13a 14(a).
31.2**	Certificate of Chief Financial Officer pursuant to 17 CFR 240.13a 14(a).
32.1**	Certificate of Chief Executive Officer pursuant to 17 CFR 240.13a 14(b) and 18 U.S.C.1350.
32.2**	Certificate of Chief Financial Officer pursuant to 17 CFR 240.13a 14(b) and 18 U.S.C.1350.
101.INS**	XBRL Instance Document.
101.SCH**	XBRL Taxonomy Extension Schema Document.
101.CAL**	XBRL Taxonomy Extension Calculation Linkbase Document.
101.DEF**	XBRL Taxonomy Extension Definition Linkbase Document.

101.LAB** XBRL Taxonomy Extension Label Linkbase Document.

101.PRE** XBRL Taxonomy Extension Presentation Linkbase Document.

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* Previously filed.

Table of Contents

** Filed herewith.

† Confidential treatment has been granted with respect to portions of this exhibit. A complete copy of this exhibit, including the redacted terms, has been filed separately with the Securities and Exchange Commission.

Item 16. Form 10 K Summary

None.

Table of Contents

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, hereunto duly authorized, in Oxfordshire, England, on February 27, 2019.

ADAPTIMMUNE THERAPEUTICS PLC

By: /s/ James Noble
Name: James Noble
Title: Chief Executive Officer and Director

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints James Noble and Adrian Rawcliffe, and each of them, as his or her true and lawful attorney-in-fact and agent, with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10 K, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or any of them or their or his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed by the following persons on February 27, 2019, in the capacities indicated.

Signature	Title	Date
/s/ James Noble James Noble	Chief Executive Officer and Director (Principal Executive Officer)	February 27, 2019
/s/ Adrian Rawcliffe Adrian Rawcliffe	Chief Financial Officer (Principal Accounting and Financial Officer)	February 27, 2019
/s/ David M. Mott David M. Mott	Chairman of the Board of Directors	February 27, 2019
/s/ Lawrence M. Alleva Lawrence M. Alleva	Director	February 27, 2019
/s/ Ali Behbahani, MD Ali Behbahani, MD	Director	February 27, 2019
/s/ Barbara Duncan Barbara Duncan	Director	February 27, 2019

/s/John Furey John Furey	Director	February 27, 2019
/s/ Giles Kerr Giles Kerr	Director	February 27, 2019
/s/ Elliott Sigal, MD, PhD Elliott Sigal, MD, PhD	Director	February 27, 2019
/s/ Tal Zaks, MD, PhD Tal Zaks, MD, PhD	Director	February 27, 2019

Table of Contents

Index to the Financial Statements:

Reports of Independent Registered Public Accounting Firm	F-2
Consolidated Balance Sheets as of December 31, 2018 and 2017	F-5
Consolidated Statement of Operations for the years ended December 31, 2018, 2017 and 2016	F-6
Consolidated Statements of Comprehensive Loss for the years ended December 31, 2018, 2017 and 2016	F-7
Consolidated Statements of Changes in Equity for the years ended December 31, 2018, 2017 and 2016	F-8
Consolidated Statements of Cash Flows for the years ended December 31, 2018, 2017 and 2016	F-9
Notes to the Consolidated Financial Statements	F-10

Table of Contents

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and Board of Directors Adaptimmune Therapeutics plc:

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Adaptimmune Therapeutics plc and subsidiaries (the Company) as of December 31, 2018 and 2017, the related consolidated statements of operations, comprehensive loss, changes in equity, and cash flows for each of the years in the three year period ended December 31, 2018, and the related notes (collectively, the consolidated financial statements). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2018 and 2017, and the results of its operations and its cash flows for each of the years in the three year period ended December 31, 2018, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2018, based on criteria established in Internal Control – Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission, and our report dated February 27, 2019 expressed an unqualified opinion on the effectiveness of the Company's internal control over financial reporting.

Change in Accounting Principle

As discussed in Note 2(n) to the consolidated financial statements, the Company has changed its method of accounting for revenue recognition in 2018 due to the adoption of Accounting Standard Codification Topic 606, Revenue from Contracts with Customers.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ KPMG LLP

We have served as the Company's auditor since 2010.

KPMG LLP

Reading, United Kingdom
February 27, 2019

F-2

Table of Contents

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and Board of Directors Adaptimmune Therapeutics Plc:

Opinion on Internal Control Over Financial Reporting

We have audited Adaptimmune Therapeutics plc and subsidiaries' (the Company) internal control over financial reporting as of December 31, 2018, based on criteria established in Internal Control – Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission. In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2018, based on criteria established in Internal Control – Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 31, 2018 and 2017, the related consolidated statements of operations, comprehensive loss, changes in equity, and cash flows for each of the years in the three-year period ended December 31, 2018, and the related notes (collectively, the consolidated financial statements), and our report dated February 27, 2019 expressed an unqualified opinion on those consolidated financial statements.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management's Annual Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audit also included performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control Over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have

a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls

Table of Contents

may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ KPMG LLP

Reading, United Kingdom
February 27, 2019

Table of Contents

ADAPTIMMUNE THERAPEUTICS PLC

CONSOLIDATED BALANCE SHEETS

(in thousands, except share data)

	December 31, 2018	December 31, 2017
Assets		
Current assets		
Cash and cash equivalents	$ 68,379	$ 84,043
Marketable securities - available-for-sale debt securities	136,755	124,218
Accounts receivable, net of allowance for doubtful accounts of $0 and $0	192	206
Other current assets and prepaid expenses (including current portion of clinical materials)	25,769	21,716
Total current assets	231,095	230,183
Restricted cash	4,097	4,253
Clinical materials	3,953	4,695
Property, plant and equipment, net	36,118	40,679
Intangibles, net	1,473	1,337
Total assets	276,736	281,147
Liabilities and stockholders’ equity		
Current liabilities		
Accounts payable	4,083	8,378
Accrued expenses and other accrued liabilities	20,354	27,201
Deferred revenue	—	38,735
Total current liabilities	24,437	74,314
Other liabilities, non-current	5,414	3,849
Total liabilities	29,851	78,163
Contingencies and commitments — Note 9		
Stockholders’ equity		
Common stock - Ordinary shares par value £0.001, 701,103,126 authorized and 627,454,270 issued and outstanding (2017: 701,103,126 authorized and 562,119,334 issued and outstanding)	939	854
Additional paid in capital	574,208	455,401
Accumulated other comprehensive loss	(9,763)	(21,641)
Accumulated deficit	(318,499)	(231,630)
Total stockholders' equity	246,885	202,984
Total liabilities and stockholders’ equity	$ 276,736	$ 281,147

See accompanying notes to consolidated financial statements.

Table of Contents

ADAPTIMMUNE THERAPEUTICS PLC

CONSOLIDATED STATEMENTS OF OPERATIONS

(in thousands, except share and per share data)

	Period Ended December 31, 2018	December 31, 2017	December 31, 2016
Development revenue	20,391	37,833	14,198
License revenue	39,114	—	—
Revenue	$ 59,505	$ 37,833	$ 14,198
Operating expenses			
Research and development	(98,269)	(87,388)	(63,789)
General and administrative	(43,601)	(31,106)	(23,208)
Total operating expenses (including purchases from related parties, net of reimbursements of $-, $786, $2,067)	(141,870)	(118,494)	(86,997)
Operating loss	(82,365)	(80,661)	(72,799)
Interest income	2,849	2,230	1,110
Other (expense) income, net	(15,501)	8,744	1,002
Loss before income taxes	(95,017)	(69,687)	(70,687)
Income taxes	(497)	(451)	(892)
Net loss attributable to ordinary shareholders	$ (95,514)	$ (70,138)	$ (71,579)
Net loss per ordinary share - Basic and diluted			
Basic and diluted	$ (0.16)	$ (0.13)	$ (0.17)
Weighted average shares outstanding:			
Basic and diluted	584,338,942	527,637,086	424,713,997

See accompanying notes to consolidated financial statements.

Table of Contents

ADAPTIMMUNE THERAPEUTICS PLC

CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS

(in thousands)

	Year ended December 31, 2018	Year ended December 31, 2017	Year ended December 31, 2016
Net loss	$ (95,514)	$ (70,138)	$ (71,579)
Other comprehensive loss, net of tax			
Foreign currency translation adjustments, net of tax of $0, $0 and $0	8,260	(3,618)	(6,110)
Unrealized gains (losses) on available-for-sale debt securities			
Unrealized holding gains (losses) on available-for-sale debt securities, net of tax of $0, $0 and $0	1,145	(4,420)	—
Reclassification adjustment for losses on available-for-sale debt securities included in net income, net of tax of $0, $0 and $0	2,473	646	—
Total comprehensive loss for the period	$ (83,636)	$ (77,530)	$ (77,689)

See accompanying notes to consolidated financial statements.

Table of Contents

ADAPTIMMUNE THERAPEUTICS PLC

CONSOLIDATED STATEMENTS OF CHANGES IN EQUITY

(in thousands, except share data)

	Common stock	Common stock	Additional paid in capital	Accumulated other income: Accumulated foreign currency translation adjustments	Accumulated other income: Accumulated unrealized gains (losses) on available-for-sale debt securities	Accumulated deficit	Total stockholders' equity
Balance as of January 1, 2016	424,711,900	$ 682	$ 332,363	$ (8,139)	$ —	$ (89,913)	$ 234,993
Issuance of shares upon exercise of stock options	63,192	1	16	—	—	—	17
Other comprehensive loss, net of tax							
Foreign currency translation adjustments	—	—	—	(6,110)	—	—	(6,110)
Net loss	—	—	—	—	—	(71,579)	(71,579)
Share-based compensation expense	—	—	8,821	—	—	—	8,821
Balance as of December 31, 2016	424,775,092	683	341,200	(14,249)	—	(161,492)	166,142
Issuance of shares upon exercise of stock options	1,142,904	1	400	—	—	—	401
Issuance of common stock	136,201,338	170	102,997	—	—	—	103,167
Other comprehensive loss before reclassifications							—
Foreign currency translation adjustments	—	—	—	(3,618)	—	—	(3,618)
	—	—	—	—	(4,420)	—	(4,420)

Unrealized holding losses on available-for-sale debt securities, net of tax of $0							
Reclassification from accumulated other comprehensive income of losses on available-for-sale debt securities included in net income, net of tax of $0	—	—	—	—	646	—	646
Net loss	—	—	—	—	—	(70,138)	(70,138)
Share-based compensation expense	—	—	10,804	—	—	—	10,804
Balance as of December 31, 2017	562,119,334	854	455,401	(17,867)	(3,774)	(231,630)	202,984
Cumulative effect of applying new accounting standards	—	—	—	—	—	8,645	8,645
Balance as of 1 January 2018 (adjusted)	562,119,334	854	455,401	(17,867)	(3,774)	(222,985)	211,629
Issuance of shares upon completion of registered direct offering	60,000,000	78	99,575	—	—	—	99,653
Issuance of shares upon exercise of stock options	5,334,936	7	3,030	—	—	—	3,037
Other comprehensive loss before reclassifications	—	—	—	—	—	—	—
Foreign currency translation adjustments	—	—	—	8,260	—	—	8,260
Unrealized holding losses on available-for-sale debt securities, net of tax of $0	—	—	—	—	1,145	—	1,145
Reclassification from accumulated other comprehensive	—	—	—	—	2,473	—	2,473

income of losses on available-for-sale debt securities included in net income, net of tax of $0, $0, $0 and $0							
Net loss	—	—	—	—	—	(95,514)	(95,514)
Share-based compensation expense	—	—	16,202	—	—	—	16,202
Balance as of December 31, 2018	627,454,270	$ 939	$ 574,208	$ (9,607)	$ (156)	$ (318,499)	$ 246,885

See accompanying notes to consolidated financial statements.

Table of Contents

ADAPTIMMUNE THERAPEUTICS PLC

CONSOLIDATED STATEMENTS OF CASH FLOWS

(in thousands)

	Year ended December 31, 2018	Year ended December 31, 2017	Year ended December 31, 2016
Cash flows from operating activities			
Net loss	$ (95,514)	$ (70,138)	$ (71,579)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation	7,188	5,032	3,126
Amortization	622	391	160
Share-based compensation expense	16,202	10,804	8,821
Realized loss on available-for-sale debt securities	2,473	646	
Unrealized foreign exchange losses (gains)	9,747	(8,599)	(1,314)
Other	237	341	122
Changes in operating assets and liabilities:			
Increase in receivables and other operating assets	(5,162)	(7,346)	(6,533)
Decrease in non-current operating assets	742	2,115	2,221
(Decrease) increase in payables and deferred revenue	(40,923)	12,439	16,808
Net cash used in operating activities	(104,388)	(54,315)	(48,168)
Cash flows from investing activities			
Acquisition of property, plant and equipment	(3,910)	(24,643)	(11,506)
Acquisition of intangibles	(798)	(369)	(1,279)
Proceeds from disposal of property, plant and equipment	—	550	—
Maturity of short-term deposits	—	40,625	73,377
Investment in short-term deposits	—	(18,000)	(42,837)
Maturity or redemption of marketable securities	138,038	29,090	—
Investment in marketable securities	(150,787)	(153,334)	—
Net cash (used in) provided by investing activities	(17,457)	(126,081)	17,755
Cash flows from financing activities			
Proceeds from issuance of common stock, net of issuance costs $347 and $4,774	99,653	103,167	—
Proceeds from exercise of stock options	3,037	401	17
Net cash provided by financing activities	102,690	103,568	17
Effect of currency exchange rate changes on cash, cash equivalents and restricted cash	3,335	2,328	(5,579)
Net decrease in cash and cash equivalents	(15,820)	(74,500)	(35,975)
Cash, cash equivalents and restricted cash at start of period	88,296	162,796	198,771
Cash, cash equivalents and restricted cash at end of period	$ 72,476	$ 88,296	$ 162,796

Supplemental cash flow information			
Interest received	$ 3,114	$ 1,784	$ 1,191
Income taxes paid	258	1,565	34
Allowance for tenant improvements	—	—	2,607

See accompanying notes to consolidated financial statements.

Table of Contents

ADAPTIMMUNE THERAPEUTICS PLC

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

Note 1 — General

Adaptimmune Therapeutics plc is registered in England and Wales. Its registered office is 60 Jubilee Avenue, Milton Park, Abingdon, Oxfordshire, OX14 4RX, United Kingdom. Adaptimmune Therapeutics plc and its subsidiaries (collectively "Adaptimmune" or the "Company") is a clinical-stage biopharmaceutical company focused on providing novel cell therapies to patients, particularly in solid tumors. The Company's comprehensive and proprietary SPEAR (Specific Peptide Enhanced Affinity Receptor) T-cell platform enables it to identify cancer targets, find and genetically engineer T-cell receptors ("TCRs"), and produce therapeutic candidates for administration to patients. Using its affinity engineered TCRs, the Company aims to become a fully integrated cell therapy company and to have the first TCR T-cell approved for a solid tumor indication.

The Company is subject to a number of risks similar to other biopharmaceutical companies in the early stage including, but not limited to, the need to obtain adequate additional funding, possible failure of preclinical programs or clinical programs, the need to obtain marketing approval for its SPEAR T-cells, competitors developing new technological innovations, the need to successfully commercialize and gain market acceptance of the Company's SPEAR T-cells, the need to develop a suitable commercial manufacturing process and protection of proprietary technology. If the Company does not successfully commercialize any of its SPEAR T-cells, it will be unable to generate product revenue or achieve profitability. The Company had an accumulated deficit of $318.5 million as of December 31, 2018

Note 2 — Summary of Significant Accounting Policies

(a) Basis of presentation

The consolidated financial statements of Adaptimmune Therapeutics plc and its subsidiaries and other financial information included in this Annual Report have been prepared in accordance with generally accepted accounting principles in the United States of America ("US GAAP") and are presented in U.S. dollars. All significant intercompany accounts and transactions between the Company and its subsidiaries have been eliminated on consolidation.

(b) Use of estimates in financial statements

The preparation of financial statements, in conformity with U.S. GAAP and SEC regulations, requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, disclosure of contingent assets and liabilities at the date of the consolidated financial statements and reported amounts of revenues and expenses during the reporting period. Estimates and assumptions are primarily made in relation to the valuation of share options, valuation allowances relating to deferred tax assets, revenue recognition, estimating clinical trial expenses and estimating R&D tax and expenditure credits. If actual results differ from the Company's estimates, or to the extent these estimates are adjusted in future periods, the Company's results of operations could either benefit from, or be adversely affected by, any such change in estimate.

(c) Going concern

Management considers that there are no conditions or events, in the aggregate, that raise substantial doubt about the entity's ability to continue as a going concern for a period of at least one year from the date the financial statements are issued. This evaluation is based on relevant conditions and events that are known and reasonably knowable at the date that the financial statements are issued, including:

a. The Company's current financial condition, including its liquidity sources;
b. The Company's conditional and unconditional obligations due or anticipated within one year;

Table of Contents

c. The funds necessary to maintain the Company's operations considering its current financial condition, obligations, and other expected cash flows; and
d. Other conditions and events, when considered in conjunction with the above that may adversely affect the Company's ability to meet its obligations.

(d) Foreign currency

The reporting currency of the Company is the U.S. dollar. The Company has determined the functional currency of the ultimate parent company, Adaptimmune Therapeutics plc, is U.S. dollars because it predominately raises finance and expends cash in U.S. dollars. The functional currency of subsidiary operations is the applicable local currency. Transactions in foreign currencies are translated into the functional currency of the subsidiary in which they occur at the foreign exchange rate in effect on at the date of the transaction. Monetary assets and liabilities denominated in foreign currencies at the balance sheet date are translated into the functional currency of the relevant subsidiary at the foreign exchange rate in effect on the balance sheet date. Foreign exchange differences arising on translation are recognized within other income (expense) in the consolidated statement of operations.

The results of operations for subsidiaries, whose functional currency is not the U.S. dollar, are translated at an average rate for the period where this rate approximates to the foreign exchange rates ruling at the dates of the transactions and the balance sheet are translated at foreign exchange rates ruling at the balance sheet date. Exchange differences arising from this translation of foreign operations are reported as an item of other comprehensive income (loss).

Other income, net includes foreign exchange (losses) gains of $(15,257,000), $8,744,000 $1,002,000 for the years ended December 31, 2018, 2017 and 2016, respectively.

(e) Fair value measurements

The Company is required to disclose information on all assets and liabilities reported at fair value that enables an assessment of the inputs used in determining the reported fair values. The fair value hierarchy prioritizes valuation inputs based on the observable nature of those inputs. The hierarchy defines three levels of valuation inputs:

Level 1 — Quoted prices in active markets for identical assets or liabilities

Level 2 — Inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly

Level 3 — Unobservable inputs that reflect the Company's own assumptions about the assumptions market participants would use in pricing the asset or liability

The carrying amounts of the Company's cash and cash equivalents, short-term deposits, restricted cash, accounts receivable, accounts payable and accrued expenses approximate fair value because of the short-term nature of these instruments. The fair value of marketable securities, which are measured at fair value on a recurring basis is detailed in Note 4, Financial Instruments.

Table of Contents

(f) Accumulated other comprehensive income (loss)

The following amounts were reclassified out of other comprehensive income during the year ended December 31, 2018 (in thousands):

	Amount reclassified			
Component of Accumulated Other Comprehensive Income	Year ended December 31, 2018	Year ended December 31, 2017	Year ended December 31, 2016	Affected line item in the Statement of Operations
Unrealized gains (losses) on available-for-sale securities				
Reclassification adjustment for losses on available-for-sale debt securities	$ 2,473	$ 646	$ —	Other (expense) income, net

(g) Cash, cash equivalents and restricted cash

The Company considers all highly-liquid investments with a maturity at acquisition date of three months or less to be cash equivalents. Cash and cash equivalents comprise cash balances, commercial paper and corporate debt securities with maturities of three months or less at acquisition and short deposits with maturities of three months or less.

The Company’s restricted cash consists of cash providing security for letters of credit in respect of lease agreements.

The following table provides a reconciliation of cash, cash equivalents, and restricted cash reported within the balance sheet that sum to the total of the same such amounts shown in the statement of cash flows (in thousands).

	December 31, 2018	December 31, 2017
Cash and cash equivalents	$ 68,379	$ 84,043
Restricted cash	4,097	4,253
Total cash, cash equivalents, and restricted cash shown in the statement of cash flows	$ 72,476	$ 88,296

(h) Available-for-sale debt securities

As of December 31, 2018, the Company has the following investments in available-for-sale debt securities, which are categorized as cash equivalents or marketable securities – available-for-sale debt securities on the balance sheet depending on their maturity at acquisition (in thousands):

	Maturity	Amortized cost	Gross Unrealized Gains	Gross Unrealized Losses	Aggregate Estimated Fair Value
Marketable securities:					
Corporate debt securities	3 months to 1 year	$ 102,818	$ 5	$ (120)	$ 102,703
Corporate debt securities	1 to 2 years	23,153	—	(43)	23,110
Agency bond	3 months to 1 year	3,963	2	—	3,965
Treasury bills	3 months to 1 year	1,980	—	—	1,980
Certificate of deposit	3 months to 1 year	3,002	—	—	3,002
Commercial paper	3 months to 1 year	1,995	—	—	1,995
		$ 136,911	$ 7	$ (163)	$ 136,755

Table of Contents

As of December 31, 2017, the Company has the following investments in available-for-sale debt securities, which are categorized as cash equivalents or marketable securities — available-for-sale debt securities on the balance sheet depending on their maturity at acquisition (in thousands):

	Maturity	Amortized cost	Gross Unrealized Gains	Gross Unrealized Losses	Foreign currency translation adjustment	Aggregate Estimated Fair Value
Cash equivalents:						
Corporate debt securities	Less than 3 months	$ 1,610	$ —	$ (22)	$ 22	$ 1,610
		$ 1,610	$ —	$ (22)	$ 22	$ 1,610
Marketable securities:						
Corporate debt securities	3 months to 1 year	$ 124,406	$ —	$ (3,723)	$ 3,535	$ 124,218
Commercial paper	3 months to 1 year	—	—	—	—	—
		$ 124,406	$ —	$ (3,723)	$ 3,535	$ 124,218

Management determines the appropriate classification of its investments in available-for-sale debt securities at the time of purchase and reevaluates such designation as of each reporting date. The securities are classified as current or non-current based on the maturity dates and management's intentions.

At December 31, 2018, the Company has classified all of its available-for-sale debt securities, including those with maturities beyond one year, as current assets on the accompanying consolidated balance sheets based on the highly-liquid nature of these investment securities and because these investment securities are considered available for use in current operations.

The investment in available-for-sale debt securities is measured at fair value at each reporting date. Unrealized gains and losses are excluded from earnings and are reported as a component of comprehensive loss. Realized gains and losses, interest income and amortization of premiums and discounts at acquisition are included in other income (expense), net. In the year ended December 31, 2018 and 2017, proceeds from the maturity or redemption of available-for-sale debt securities were $138,038,000 and $29,090,000. There were realized losses of $2,473,000 and $646,000 recognized on the maturity of available-for-sale debt securities during the year ended December 31, 2018 and 2017, respectively, primarily arising due to foreign exchange movements, and, as a result, the Company reclassified this amount out of accumulated other comprehensive loss for the same period.

At each reporting date, the Company assesses whether each individual investment is impaired, which occurs if the fair value is less than the amortized cost, adjusted for amortization of premiums and discounts at acquisition. If the investment is impaired, the impairment is assessed to determine if it is other than temporary. Impairments judged to be other than temporary are included in other income (expense), net when they are identified.

The aggregate fair value (in thousands) and number of securities held by the Company in an unrealized loss position as of December 31, 2018 and 2017 are as follows:

	December 31, 2018			December 31, 2017		
	Fair market value of investments in an unrealized loss position	Number of investments in an unrealized loss position	Unrealized losses	Fair market value of investments in an unrealized loss position	Number of investments in an unrealized loss position	Unrealized losses
Marketable securities:						
Corporate debt securities	$ 117,179	37	$ (163)	$ 125,828	54	$ (3,745)

Table of Contents

As of December 31, 2018 and 2017, these securities are not considered to be other than temporarily impaired because the impairments are not severe, have been for a short duration and are due to normal market and exchange rate fluctuations. No securities have been in an unrealized loss position for more than one year. Furthermore, the Company does not intend to sell the debt securities in an unrealized loss position and it is unlikely that the Company will be required to sell these securities before the recovery of the amortized cost.

The cost of securities sold is based on the specific-identification method. Interest on debt securities is included in interest income.

Our investment in available-for-sale debt securities is subject to credit risk. The Company's investment policy limits investments to certain types of instruments, such as money market instruments and corporate debt securities, places restrictions on maturities and concentration by type and issuer and specifies the minimum credit ratings for all investments and the average credit quality of the portfolio.

(i) Accounts receivable

Accounts receivable are amounts due from customers. As of December 31, 2018 and 2017, the Company had one customer, which was GlaxoSmithKline, or GSK.

Management analyses current and past due accounts and determines if an allowance for uncollectible accounts is required based on collection experience and other relevant information. As of December 31, 2018 and 2017, the allowance for doubtful accounts is $nil. The process of estimating the uncollectible accounts involves assumptions and judgments and the ultimate amounts of uncollectible accounts receivable could be in excess of the amounts provided.

(j) Clinical materials

Clinical materials for use in research and development with alternative future use are capitalized as either other current assets or other non-current assets, depending on the timing of their expected consumption.

(k) Property, plant and equipment

Property, plant and equipment is stated at cost, less any impairment losses, less accumulated depreciation.

Depreciation is computed using the straight-line method over the estimated useful lives of the related assets. The following table provides the range of estimated useful lives used for each asset type:

Computer equipment	3 to 5 years
Laboratory equipment	5 years
Office equipment	5 years
Leasehold improvements	the expected duration of the lease

Assets under construction are not depreciated until the asset is available and ready for its intended use.

The Company assesses property, plant and equipment for impairment whenever events or changes in circumstances indicate that an asset's carrying amount may not be recoverable.

(l) Intangibles

Intangibles includes intellectual property ("IP") rights for licensed technology used in research and development with an alternative future use, which are recorded at cost and amortized over the estimated useful life of the related product.

The weighted-average amortization period for IP rights for licensed technology as of December 31, 2018 is seven years.

Table of Contents

Intangibles also include acquired computer software licenses, which are recorded at cost and amortized over the estimated useful lives of approximately three years.

Intangibles are assessed for impairment whenever events or changes in circumstances indicate that an asset's carrying amount may not be recoverable.

(m) Segmental reporting

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision-maker in making decisions regarding resource allocation and assessing performance. The Company's chief operating decision maker (the "CODM"), its Chief Executive Officer, manages the Company's operations on an integrated basis for the purposes of allocating resources. When evaluating the Company's financial performance, the CODM reviews total revenues, total expenses and expenses by function and the CODM makes decisions using this information on a global basis. Accordingly, the Company has determined that it operates in one operating segment.

(n) Revenue after adoption of ASC 606 on January 1, 2018

On January 1, 2018, the Company adopted new guidance on revenue recognition, which has been codified within ASC 606. The accounting policy applicable from January 1, 2018 is described below and further details on the transition are available in Note 2(x). The comparative financial information for the years ended December 31, 2017 and 2016 and as of December 31, 2017 has not been restated and is prepared in accordance with the accounting policies that are described in Note 2(o).

The Company has one contract with a customer, which is the GSK Collaboration and License Agreement. The GSK Collaboration and License Agreement consists of multiple performance obligations, including the transition of the NY-ESO SPEAR T-cell program to GSK, the development of a second target, PRAME, and an exclusive license (the "NY-ESO License") to research, develop, and commercialize the Company's NY-ESO SPEAR T-cell therapy program.

In September 2017, GSK exercised its option to obtain the NY-ESO License and the first tranche ($26.6 million or £20 million) of the option exercise payment became payable to the Company. In connection with the option exercise, in September 2017, the GSK Agreement was amended to, among other things, include a detailed transition plan identifying the steps needed to complete transition of the IND process with the Food and Drug Administration (FDA) for the NY-ESO SPEAR T-cell program to GSK. On July 23, 2018, the transition activities were substantially completed and the IND for the NY-ESO SPEAR T-cell program transferred to GSK.

GSK nominated a second target program for the PRAME target antigen, which was announced on 9 January 2017. We have since completed all work under this collaboration program. The program led to the development of a final lead candidate SPEAR T-cell directed to a specific peptide from the PRAME antigen. GSK and Adaptimmune agreed that the collaboration should not continue due to the peptide, to which the lead candidate was directed, not reaching GSK criteria.

The aggregate transaction price consists of an upfront payment of $42,123,000 received in June 2014, development milestones achieved of $66,404,000, an option exercise fee of $39,785,000. There was no variable consideration at December 31, 2018.

The Company determines the variable consideration to be included in the transaction price by estimating the most-likely amount that will be received and then applies a constraint to reduce the consideration to the amount which is probable of being received. The determination of whether a milestone is probable includes consideration of the following factors:

Whether achievement of a development milestone is highly susceptible to factors outside the entity's influence, such as milestones involving the judgment or actions of third parties, including regulatory bodies or the customer;

Table of Contents

Whether the uncertainty about the achievement of the milestone is not expected to be resolved for a long period of time;

Whether the Company can reasonably predict that a milestone will be achieved based on previous experience; and.

The complexity and inherent uncertainty underlying the achievement of the milestone.

Under the terms of the GSK Collaboration and License Agreement, the Company may also be entitled to development milestones. The development and regulatory milestones are per product milestones and are dependent on achievement of certain obligations, the nature of the product being developed, stage of development of product, territory in which an obligation is achieved and type of indication or indications in relation to which the product is being developed. In addition, for any program multiple products may be developed to address different HLA-types. These amounts have not been included within the transaction price as of December 31, 2018 because they are not considered probable.

The Company may also receive commercialization milestones upon the first commercial sale of a product based on the indication and the territory and mid-single to low double-digit royalties on worldwide net sales. These amounts have not been included within the transaction price as of December 31, 2018 because they are sales or usage-based royalties promised in exchange for a license of intellectual property, which will be recognized when the subsequent sale or usage occurs.

The payments to the Company under the contract are typically due upon achievement of milestones and within standard payment terms (approximating to 45 days). The contract does not include a significant financing component.

The upfront payment of $42,123,000 was allocated between the performance obligations using the Company's best estimate of the relative selling price. In determining the best estimate, the Company considered internal pricing objectives it used in negotiating the contract, together with internal data regarding the cost and margin of providing services for each deliverable taking into account the different stage of development of each development program included in the contract. The variable consideration is allocated to the performance obligation to which it relates.

The amount of the transaction price allocated to the performance obligation is recognized as or when the Company satisfies the performance obligation. The Company satisfies the performance obligations relating to the transition of the NY-ESO SPEAR T-cell program and the development of a second target, PRAME, over time and recognizes revenue based on an estimate of the percentage of completion of the project determined based on the costs incurred on the project as a percentage of the total expected costs. The Company considers that this depicts the progress of the project, where the significant inputs are internal project resource and third-party clinical and manufacturing costs. The determination of the percentage of completion requires the Company to estimate the costs-to-complete the project. The Company makes a detailed estimate of the costs-to-complete on an annual basis as part of the Company's budgeting process, which is re-assessed every reporting period based on the latest project plan and discussions with project teams. If a change in facts or circumstances occurs, the estimate is adjusted and the revenue is recognized based on the revised estimate. The difference between the cumulative revenue recognized based on the previous estimate and the revenue recognized based on the revised estimate is recognized as an adjustment to revenue in the

period in which the change in estimate occurs.

The Company has determined that the performance obligation relating to the NY-ESO License is recognized at a point-in-time, upon commencement of the license, which occurred in September 2018.

The Company recognizes a contract asset, when the value of satisfied (or part satisfied) performance obligations is in excess of the payment due to the Company, and deferred revenue (contract liability) when the amount of unconditional consideration is in excess of the value of satisfied (or part satisfied) performance obligations. Once a right to receive consideration is unconditional, that amount is presented as a receivable.

Table of Contents

The timing and amount of milestone payments for the development and transition of the NY-ESO SPEAR T-cell program are intended to be commensurate with the cost and effort involved in achieving the milestones and therefore a contract asset would typically arise. The Company received $26,610,000 of the option exercise fee in September 2017, which was included in deferred revenue at January 1, 2018 and this amount was recognized as revenue, along with a further option exercise fee of $13,175,000, in September 2018 upon commencement of the license.

Changes in deferred revenue typically arise due to:

- adjustments arising from a change in the estimate of the cost to complete the project, which results in a cumulative catch-up adjustment to revenue that affects the corresponding contract asset or deferred revenue;

- a change in the estimate of the transaction price due to changes in the assessment of whether variable consideration is constrained because it is not considered probable of being received;

- the recognition of revenue arising from deferred revenue; and

- the reclassification of amounts to receivables when a right to consideration to becomes unconditional.

A change in the estimate of variable consideration constrained (for example, if a development milestone becomes probable of being received) could result in a significant change in the revenue recognized and deferred revenue.

Revenue is recognized when earned and realized or realizable, which is generally when persuasive evidence of an arrangement exists, delivery has occurred or services have been rendered, the seller's price to the buyer is fixed or determinable, and collectability is reasonably assured. Where applicable, all revenues are stated net of value added and similar taxes.

(o) Revenue prior to the adoption of ASC 606 on January 1, 2018

Prior to the adoption of ASC 606, the Company recognized revenue for arrangements with multiple deliverables by identifying the separable deliverables within the arrangement, whereby a deliverable is considered separable if it has value to the customer on a standalone basis. Contingent deliverables, such as the right to nominate further development targets, which represent a substantive option (i.e. the customer is not required or compelled to purchase the optional products or services) and not priced at a significant and incremental discount were not considered to be a deliverable at inception of the arrangement.

When the contract was amended, the amendment was assessed to determine if it should be accounted for as a separate contract or a modification to the existing arrangement. If the amendment was a modification, the modified arrangement was assessed to identify the deliverables at the time of the modification and the non-contingent arrangement consideration was allocated between the separate deliverables using the Company's best estimate of the relative selling price at the time of the modification. The amendments to the GSK Collaboration and License

Agreement in February 2016 and September 2017 were both accounted for as modifications to an existing arrangement.

The non-contingent arrangement consideration was allocated between the separate deliverables using the relative selling price. The relative selling price was determined using vendor-specific objective evidence ("VSOE"), if available, third party evidence if VSOE is not available, or a best estimate of the standalone selling price if neither VSOE nor third party evidence was available. The best estimate of the selling price was estimated after considering all reasonably available information, including market data and conditions, entity-specific factors such as the cost structure of the deliverable, internal profit and pricing objectives and the stage of development, if appropriate. Revenue allocated to each deliverable was recognized as it was delivered. Where delivery occurred over time, revenue was systematically recognized over the period which the Company would be providing services.

Amounts received prior to satisfying the revenue recognition criteria were recorded as deferred revenue in the Company's consolidated balance sheet. Amounts expected to be recognized as revenue within the 12 months following

Table of Contents

the balance sheet date were classified as deferred revenue in current liabilities. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date were classified as deferred revenue, non-current.

Milestone payments which were non-refundable, non-creditable and contingent on achieving clinical milestones are recognized as revenues either on achievement of such milestones if the milestones are considered substantive or over the period the Company has continuing performance obligations, if the milestones were not considered substantive. When determining if a milestone was substantive, the Company considers the following factors:

· The degree of certainty in achieving the milestone,
· The frequency of milestone payments,
· The Company's efforts, which result in achievement of the milestone,
· The amount of the milestone payment relative to the other deliverables and payment terms, and
· Whether the milestone payment is related to future performance or deliverables.

(p) Research and development expenditures

Research and development expenditures are expensed as incurred.

Expenses related to clinical trials are recognized as services are received. Nonrefundable advance payments for services are deferred and recognized in the consolidated statement of operations as the services are rendered. This determination is based on an estimate of the services received and there may be instances when the payments to vendors exceed the level of services provided resulting in a prepayment of the clinical expense. If the actual timing of the performance of services varies from our estimate, the accrual or prepaid expense is adjusted accordingly.

Upfront and milestone payments to third parties for in-licensed products or technology which has not yet received regulatory approval and which does not have alternative future use in R&D projects or otherwise are expensed as incurred. The Company expensed acquired in-process R&D of $210,000, $1,003,000, and $3,000,000 in the years ended December 31, 2018, 2017 and 2016, respectively.

Milestone payments made to third parties either on or subsequent to regulatory approval are capitalized as an intangible asset and amortized over the remaining useful life of the product.

Research and development expenditure is presented net of reimbursements from grants and R&D tax and expenditure credits from the U.K. government, which are recognized over the period necessary to match the reimbursement with the related costs when it is probable that the Company has complied with any conditions attached and will receive the reimbursement. Grant income was $—, $150,000, and $414,000 in the years ended December 31, 2018, 2017 and 2016, respectively. Reimbursable R&D tax and expenditure credits were $17,299,000, $10,576,000, and $6,891,000 in the years ended December 31, 2018, 2017 and 2016, respectively.

(q) Operating leases

Costs in respect of operating leases are charged to the consolidated statement of operations on a straight line basis over the lease term. Rent holidays are recognized on a straight-line basis over the lease term (including any rent holiday period). Lease incentives, including leasehold improvement incentives or allowances, are recorded as deferred rent and amortized as reductions to lease expense over the lease term. Leasehold improvements made by a lessee that are funded by landlord incentives or allowances are recorded as leasehold improvement assets and amortized over the shorter of the useful life of the asset and the non-cancellable lease term.

Table of Contents

In May 2017, the Company entered into an agreement for the lease of a building at Milton Park, Oxfordshire, U.K. The term of the lease expires on October 23, 2041, with termination options exercisable by the Company on the fifth anniversary of the lease commencement date and at approximately five yearly intervals thereafter.

In September 2015, the Company entered into an agreement for a 25-year lease, with early termination options, for a research and development facility in Oxfordshire, U.K. In October 2016, the Company entered into the lease for that facility following the completion of construction.

In July 2015, the Company entered into a 15 year lease agreement, with an early termination option at 123 months, for offices and research facilities in Philadelphia, U.S. The lease commenced upon completion of construction in October 2016.

(r) Share-based compensation

The Company awards certain employees and non-employees options over the ordinary shares of the parent company. The cost of share-based awards issued to employees are measured at the grant-date fair value of the award and recognized as an expense over the requisite service period. The fair value of the options is determined using the Black-Scholes option-pricing model. Share options with graded-vesting schedules are recognized on a straight-line basis over the requisite service period for each separately vesting portion of the award. The Company has elected to account for forfeitures of stock options when they occur by reversing compensation cost previously recognized, in the period the award is forfeited, for an award that is forfeited before completion of the requisite service period.

Prior to January 1, 2018, non-employee share options were measured at the fair value of the goods/services received or the fair value of the equity instrument issued, whichever was more reliably measured, and then remeasured at the then-current fair values at each reporting date until the share options have vested and recognized as an expense over the requisite service period. The Company has adopted new guidance with effect from January 1, 2018, which requires that non-employee share-based payment transactions are measured at the grant-date fair value and are no longer remeasured at the then-current fair values at each reporting date until the share options have vested. Further details on the transition are available in Note 2(x).

(s) Retirement benefits

The Company operates defined contribution pension schemes for its directors and employees. The contributions to this scheme are expensed to the consolidated statement of operations as they fall due. The pension contributions for the years ended December 31, 2018, 2017 and 2016 were $1,847,000, $1,264,000, and $976,000, respectively.

(t) Income taxes

Income taxes for the period comprise current and deferred tax. Income tax is recognized in the consolidated statement of operations except to the extent that it relates to items occurring during the year recognized either in other comprehensive income or directly in equity, in which case it is recognized in other comprehensive income or equity.

Current tax is the expected tax payable or receivable on the taxable income or loss for the current or prior periods using tax rates enacted at the balance sheet date.

Deferred tax is accounted for using the asset and liability method that requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of temporary differences between the financial statement

carrying amount and the tax bases of assets and liabilities at the applicable tax rates and net operating loss and tax credit carryforwards. A valuation allowance is provided when it is more likely than not that some portion or all of the deferred tax assets will not be realized. The Company evaluates the realizability of its deferred tax assets by assessing its valuation allowance and by adjusting the amount of such allowance, if necessary. The factors used to assess the likelihood of realization include the Company's forecast of future taxable income, carryback availability, reversing taxable temporary differences and available tax-planning strategies that could be implemented to realize the deferred tax assets.

Table of Contents

Income tax positions must meet a more-likely-than-not recognition threshold to be recognized. Income tax positions that previously failed to meet the more-likely-than-not threshold are recognized in the first subsequent financial reporting period in which that threshold is met. Previously recognized tax positions that no longer meet the more-likely-than-not threshold are derecognized in the first subsequent financial reporting period in which that threshold is no longer met. Recognized income tax positions are measured at the largest amount that is greater than 50 percent likely of being realized. We recognize potential accrued interest and penalties related to unrecognized tax benefits within the consolidated statement of operations as income tax expense.

In interim periods, the income tax expense (benefit) related to income (loss) from continuing operations before income tax expense (benefit) excluding significant unusual or infrequently occurring items is computed at an estimated annual effective tax rate and the income tax expense (benefit) related to all other items is individually computed and recognized when the items occur.

(u) Loss per share

Basic loss per share is determined by dividing net loss attributable to ordinary shareholders by the weighted average number of ordinary shares outstanding during the period. Diluted loss per share is determined by dividing net loss attributable to ordinary shareholders by the weighted average number of ordinary shares outstanding during the period, adjusted for the dilutive effect of all potential ordinary shares that were outstanding during the period. Potentially dilutive shares are excluded when the effect would be to increase diluted earnings per share or reduce diluted loss per share.

The following table reconciles the numerator and denominator in the basic and diluted loss per share computation (in thousands):

	Year ended December 31, 2018	Year ended December 31, 2017	Year ended December 31, 2016
Numerator for basic and diluted loss per share			
Net loss	$ (95,514)	$ (70,138)	$ (71,579)
Net loss attributable to shareholders used for basic and diluted EPS calculation	$ (95,514)	$ (70,138)	$ (71,579)
Denominator for basic and diluted loss per share			
Weighted average number of shares used to calculate basic and diluted loss per share	584,338,942	527,637,086	424,713,997

The effects of the following potentially dilutive equity instruments have been excluded from the diluted loss per share calculation because they would have an antidilutive effect on the loss per share for the period:

	Year ended December 31, 2018	Year ended December 31, 2017	Six months ended December 31, 2016
Weighted average number of share options(1)	88,553,474	70,374,832	45,882,791

(1)

From January 1, 2019 through to February 28, 2019, the Company granted 10,807,200 options over ordinary shares with an exercise price determined by reference to the market value of an ADS at the date of grant, and 6,498,126 options over ordinary shares with an exercise price equal to the nominal value of the ordinary shares (£0.001 per share).

(w) Related parties

The Company has historically entered into several agreements with Immunocore Limited ("Immunocore"). During the year ended December 31, 2017, Immunocore has invoiced the Company in respect of: (i) services provided

Table of Contents

under a target collaboration agreement (which terminated on March 1, 2017); (ii) costs relating to prosecution of jointly owned patents; and (iii) property rents (effective until June 1, 2017).

During the year ended December 31, 2017, all of the Company's U.K-based research and development and corporate staff moved into the Company's new building at Milton Park, Oxfordshire, which comprises laboratory and office space. Consequently, the Company's lease from Immunocore of premises formerly used for research and development terminated on June 1, 2017 and the Company received $550,000 in relation to leasehold improvements, as provided for under the lease. The lease of the Company's former corporate office premises was assigned to Immunocore effective from July 1, 2017 in a transaction on arms-length terms.

As of the closing of the Company's registered direct offering of its American Depositary Shares on April 10, 2017, Immunocore held less than 5% of the Company's shares. Due to several factors including the decrease in share ownership, the termination of the target collaboration agreement and our lack of common directors, the Company no longer considers Immunocore to be a related party with effect from January 1, 2018.

(x) New accounting pronouncements

Adopted in the year ended December 31, 2018

Revenue from Contracts with Customers

In May 2014, the FASB issued ASU 2014-09 - Revenue from Contracts with Customers ("ASU 2014-09") which requires a new approach to revenue recognition and, in March, April, May and December 2016, the FASB issued additional clarification related to this guidance. This guidance has been codified within ASC 606. The core principle of the guidance is that an entity should recognize revenue to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. To achieve that core principle, an entity should apply the following steps:

Step 1: Identify the contract(s) with a customer.

Step 2: Identify the performance obligations in the contract.

Step 3: Determine the transaction price.

Step 4: Allocate the transaction price to the performance obligations in the contract.

Step 5: Recognize revenue when (or as) the entity satisfies a performance obligation.

The Company has adopted the guidance using the modified retrospective approach, with the cumulative effect of initially applying the guidance recognized as an adjustment to the opening balance of equity at January 1, 2018. Therefore, the comparative information has not been adjusted and continues to be reported under previous guidance.

The quantitative impacts of the changes on the statement of operations for the year ended December 31, 2018 are set out below (in thousands):

	Under previous revenue guidance $'000	Adjustment $'000	As reported $'000
Revenue	67,802	$ (8,297)	$ 59,505
Operating loss	(74,068)	(8,297)	(82,365)
Loss before income taxes	(86,720)	(8,297)	(95,017)
Net loss attributable to ordinary shareholders	(87,217)	(8,297)	(95,514)
Net loss per ordinary share - Basic and diluted	(0.15)		(0.16)

Table of Contents

The quantitative impacts of the changes on the balance sheet as of December 31, 2018 are set out below (in thousands):

	Under previous revenue guidance $'000	Adjustment $'000	As reported $'000
Accumulated other comprehensive loss	(9,415)	(348)	(9,763)
Accumulated deficit	(318,847)	348	(318,499)
Total stockholders' equity	246,885	—	246,885

The quantitative impacts of the changes on the statement of cash flows for the year ended December 31, 2018 are set out below (in thousands):

	Under previous revenue guidance $'000	Adjustment $'000	As reported $'000
Net loss	(87,217)	(8,297)	(95,514)
Decrease in payables and deferred revenue	(49,220)	8,297	(40,923)

The cumulative effect of adopting the guidance on our financial statements at January 1, 2018 is a credit to opening accumulated losses and corresponding decrease in deferred revenue of $8,645,000. The tax impact of the credit to opening accumulated losses is to reduce deferred tax assets by $1,469,000, which is fully offset by a reduction in the deferred tax valuation allowance.

The adoption of ASC 606 has had a material impact on the Company's financial statements due to the following:

Under the GSK Collaboration and License Agreement, the Company will receive non-substantive milestone payments in the future upon achievement of specified development milestones. Non-substantive milestones are currently included within the transaction price upon achievement of the milestone and recognized over the period during which the Company is delivering services to GSK. ASC 606 requires an entity to estimate the amount of consideration to which the entity will be entitled in exchange for transferring the promised goods or services to a customer. This includes an estimate of variable consideration to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is subsequently resolved. This results in certain milestone payments being recognized earlier under ASC 606 than under

existing guidance, if it is considered probable that the milestone will be achieved.

Upfront payments and non-refundable milestone payments were previously recognized in revenue using the proportional performance model ratably over the period that services are rendered, unless another attribution method more closely approximates the delivery of the goods or services to the customer. ASC 606 requires an entity to recognize revenue using a measure of progress that depicts the transfer of control of the goods or services to the customer. The Company considers that an input measure, such as costs incurred, relative to the total expected inputs is the appropriate measure to depict the transfer of control of the services under the GSK Collaboration and License Agreement, which impacts the timing of its revenue from the GSK Collaboration and License Agreement.

The Company has applied the practical expedient for contracts that were modified before the adoption of ASU 2014-09, which permits entities to not retrospectively restate the contract for those contract modifications. Instead, the aggregate effect of all modifications that occurred before the adoption date has been reflected when:

a. Identifying the satisfied and unsatisfied performance obligations

b. Determining the transaction price

Table of Contents

c. Allocating the transaction price to the satisfied and unsatisfied performance obligations.

ASC 606 requires an entity to provide financial statement users with sufficient information to understand the nature, amount, timing and uncertainty of revenue and cash flows arising from contracts with customers. To help achieve this objective, ASC 606 requires certain quantitative and qualitative disclosures included within Note 2(d) and Note 3, which are more extensive than the previously required revenue disclosures.

Recognition and Measurement of Financial Assets and Financial Liabilities

The Company has adopted ASU 2016-01 - Financial Instruments - Overall: Recognition and Measurement of Financial Assets and Financial Liabilities, which amended the guidance on the recognition and measurement of financial assets and financial liabilities. The new guidance requires that equity investments (except those accounted for under the equity method of accounting, or those that result in consolidation of the investee) are measured at fair value with changes in fair value recognized in net income. The guidance also requires the use of an exit price when measuring the fair value of financial instruments for disclosure purposes, eliminates the requirement to disclose the methods and significant assumptions used to estimate the fair value that is required to be disclosed for financial instruments measured at amortized cost and requires separate presentation of financial assets and financial liabilities by measurement category and form of financial asset. The guidance did not have a material impact on the Company’s consolidated financial statements.

Improvements to Nonemployee Share-Based Payment Accounting

The Company has adopted ASU 2018-07 — Compensation — Stock Compensation — Improvements to Nonemployee Share-Based Payment Accounting, which simplifies the accounting for nonemployee share-based payment transactions by expanding the scope of existing guidance on employee share-based payment transactions to include nonemployee transactions. Under the simplified guidance, nonemployee share-based payment transactions are measured at the grant-date fair value and are no longer remeasured at the then-current fair values at each reporting date until the share options have vested. The guidance has been adopted using a modified-retrospective approach, which requires that unsettled equity-classified awards for which a measurement date has not been established are measured at the adoption date fair value. The guidance did not have a material impact on the Company’s consolidated financial statements.

To be adopted in future periods

Accounting for Leases

In February 2016, the FASB issued ASU 2016-02 - Leases. The guidance requires that lessees recognize a lease liability, which is a lessee's obligation to make lease payments arising from a lease, measured on a discounted basis; and a right-of-use asset, which is an asset that represents the lessee's right to use, or control the use of, a specified asset for the lease term at the commencement date. The guidance also makes targeted improvements to align lessor accounting with the lessee accounting model and guidance on revenue from contracts with customers. The guidance is effective for the fiscal year beginning January 1, 2019, including interim periods within that fiscal year. Early application is permitted.

The guidance must be adopted on a modified retrospective transition approach for leases existing, or entered into after, the beginning of the earliest comparative period presented in the financial statements. The FASB has issued ASU 2018-11 - Leases, which, in addition to the existing requirements to transition, permits an entity to transition to the new guidance by recognizing a cumulative-effect adjustment to the opening balance of retained earnings in the period of adoption without restating prior periods and the Company intends to adopt the guidance in this manner. The Company's assessment of the impact of the guidance on its consolidated financial statements is ongoing. We anticipate that the adoption of the guidance will have a material impact on the Company's consolidated balance sheet due to the recognition of a lease liability and corresponding right-of-use asset. We have not finalized the assessment of the amount of the lease liability and right-of-use asset, but we anticipate that it will result in the recording of lease assets of approximately $21 million and a corresponding lease liability of approximately $26 million.

Table of Contents

Measurement of Credit Losses on Financial Instruments

In June 2016, the FASB issued ASU 2016-13 — Financial Instruments — Credit losses, which replaces the incurred loss impairment methodology for financial instruments in current GAAP with a methodology that reflects expected credit losses and requires consideration of a broader range of reasonable and supportable information to inform credit loss estimates. The guidance is effective for the fiscal year beginning January 1, 2020, including interim periods within that fiscal year. Early application is permitted for the fiscal year beginning January 1, 2019, including interim periods within that fiscal year. The guidance must be adopted using a modified-retrospective approach and a prospective transition approach is required for debt securities for which an other-than-temporary impairment had been recognized before the effective date. The Company is currently evaluating the impact of the guidance on its consolidated financial statements.

Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That Is a Service Contract

In August 2018, the FASB issued ASU 2018-15 — Intangibles — Goodwill and Other — Internal-Use Software (Subtopic 350-40) Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That Is a Service Contract, which aligns the requirements for capitalizing implementation costs incurred in a hosting arrangement that is a service contract with the requirements for capitalizing implementation costs incurred to develop or obtain internal-use software (and hosting arrangements that include an internal use software license). The guidance is effective for the fiscal year beginning January 1, 2020, including interim periods within that fiscal year. Early application is permitted for the fiscal year beginning January 1, 2019, including interim periods within that fiscal year. The guidance may be applied either retrospectively or prospectively to all implementation costs incurred after the date of adoption. The Company is currently evaluating the impact of the guidance on its consolidated financial statements.

Changes to the Disclosure Requirements for Fair Value Measurement

In August 2018, the FASB issued ASU 2018-13 — Fair Value Measurement (Topic 820) - Disclosure Framework— Changes to the Disclosure Requirements for Fair Value Measurement, which modifies the disclosure requirements on fair value measurements in Topic 820, Fair Value Measurement. The guidance is effective for the fiscal year beginning January 1, 2020, including interim periods within that fiscal year. Early application is permitted. Certain amendments apply prospectively with the all other amendments applied retrospectively to all periods presented upon their effective date. The Company is currently evaluating the impact of the guidance on its consolidated financial statements.

Note 3 — Revenue

After the adoption of ASC 606

Revenue from contracts with customers arises from one customer, which is GSK, in one geographic location, which is the United Kingdom.

Revenue comprises the following categories (in thousands):

	Year ended December 31, 2018
Development	$ 20,391
Licenses	39,114
	$ 59,505

The deferred revenue balance as of January 1, 2018 and December 31, 2018 is as follows (in thousands):

Table of Contents

	December 31, 2018	January 1, 2018
Deferred revenue	$ —	$ 30,090

Deferred revenue has decreased from $30,090,000 at January 1, 2018 to $0 at December 31, 2018 primarily due to the recognition of license revenue of $39,114,000 for the NY-ESO License which commenced in September 2018, of which $27,001,000 was included in the opening balance of deferred revenue. A further $3,089,000 of the deferred revenue at January 1, 2018 was recognized in the year ended December 31, 2018.

The impact of changes in variable consideration in the year ended December 31, 2018 was a reduction in deferred revenue of $10,396,000, respectively, and the impact of changes in the percentage of completion in the year ended December 31, 2018 was to increase deferred revenue by $5,027,000.

At December 31, 2018, there were no unsatisfied (or partially satisfied) performance obligations. The NY-ESO program transferred to GSK on July 23, 2018 which resulted in the revenue allocated to the NY-ESO License and the transition activities being recognized in year ended December 31, 2018. The revenue allocated to the PRAME pre-clinical development program was recognized over the development period, which was completed as at December 31, 2018.

Note 4 — Financial instruments

The Company’s financial instruments consist primarily of cash and cash equivalents, marketable securities, restricted cash, accounts receivable, accounts payable and accrued expenses.

Assets and liabilities measured at fair value on a recurring basis based on Level 1, Level 2, and Level 3 fair value measurement criteria as of December 31, 2018 are as follows (in thousands):

		Fair value measurements using		
	December 31, 2018	Level 1	Level 2	Level 3
Assets:				
Marketable securities:				
Corporate debt securities	$ 125,813	$ 125,813	$ —	$ —
Agency bond	3,965	—	3,965	—
Treasury bills	1,980	—	1,980	—
Certificate of deposit	3,002	—	3,002	—
Commercial paper	1,995	—	1,995	—
	$ 136,755	$ 125,813	$ 10,942	$ —

Assets and liabilities measured at fair value on a recurring basis based on Level 1, Level 2, and Level 3 fair value measurement criteria as of December 31, 2017 are as follows (in thousands):

		Fair Value Measurements Using		
	December 31, 2017	Level 1	Level 2	Level 3
Assets:				
Marketable securities:				
Corporate debt securities	$ 124,218	$ 124,218	$ —	$ —

The Company estimates the fair value of available-for-sale debt securities with the aid of a third party valuation service, which uses actual trade and indicative prices sourced from third-party providers on a daily basis to estimate the fair value. If observed market prices are not available (for example securities with short maturities and infrequent

Table of Contents

secondary market trades), the securities are priced using a valuation model maximizing observable inputs, including market interest rates.

Significant concentration of credit risk

The Company held cash and cash equivalents of $68,379,000, marketable securities of $136,755,000 and restricted cash of $4,097,000 as of December 31, 2018. The cash and cash equivalents and restricted cash are held with multiple banks and the Company monitors the credit rating of those banks. The Company maintains cash balances in excess of amounts insured by the Federal Deposit Insurance Corporation in the United States and the U.K. Government Financial Services Compensation Scheme in the United Kingdom.

The Company has one customer as a result of the GSK Collaboration and License Agreement. Trade receivables were $192,000 and $206,000 as of December 31, 2018 and December 31, 2017. Trade receivables arise in relation to the GSK Collaboration and License Agreement. The Company has been transacting with GSK since June 2014, during which time no impairment losses have been recognized. As of December 31, 2018, there was $192,000 of accounts receivable which was overdue.

Foreign exchange risk

The Company is exposed to foreign exchange rate risk because it currently operates in the United Kingdom and the United States. The Company's revenue from the GSK Collaboration and License Agreement is denominated in pounds sterling and is generated by our U.K.-based subsidiary, which has a pounds sterling functional currency. As a result, these sales are subject to translation into U.S. Dollars when the financial statements are consolidated. Expenses are generally denominated in the currency in which the Company's operations are located, which are the United Kingdom and the United States. However, the U.K.-based subsidiary incurs significant research and development costs in U.S. dollars and, to a lesser extent, Euros.

The results of operations and cash flows will be subject to fluctuations due to changes in foreign currency exchange rates, which could harm the Company's business in the future. Management seeks to minimize this exposure by maintaining currency cash balances at levels appropriate to meet foreseeable expenses in U.S. dollars and pounds sterling. To date, the Company has not used forward exchange contracts or other currency hedging products to manage exchange rate exposure, although it may do so in the future. The exchange rate as of December 31, 2018, the last business day of the reporting period, was £1.00 to $1.27.

Interest Rate Risk

Surplus cash and cash equivalents are invested in interest-bearing savings, money market funds, corporate debt securities and commercial paper from time to time. Investments in corporate debt securities are subject to fixed interest rates. The Company's exposure to interest rate sensitivity is impacted by changes in the underlying U.K. and U.S. bank interest rates and the fair market value of its corporate debt securities will fall in value if market interest rates increase. Management believes that an immediate one percentage point change in interest rates would not have a material effect on the fair market value of our portfolio, and therefore does not expect the operating results or cash flows to be significantly affected by changes in market interest rates.

Table of Contents

Note 5 — Other current assets

Other current assets consisted of the following (in thousands):

	December 31, 2018	December 31, 2017
Corporate tax receivable	$ 16,459	$ 11,454
Prepayments	6,279	6,120
Clinical materials	1,087	3,760
VAT receivable	1,505	—
Other current assets	439	382
	$ 25,769	$ 21,716

Note 6 — Property, plant and equipment, net

Property and equipment, net consisted of the following (in thousands):

	December 31, 2018	December 31, 2017
Computer equipment	$ 2,916	$ 2,706
Laboratory equipment	21,280	18,745
Office equipment	847	858
Leasehold improvements	26,873	27,441
Assets under construction	126	393
	52,042	50,143
Less accumulated depreciation	(15,924)	(9,464)
	$ 36,118	$ 40,679

Depreciation expense was $7,188,000, $5,032,000 and $3,126,000 for the years ended December 31, 2018 2017, and 2016, respectively.

The Company has disposed of leasehold improvements resulting in a loss on disposal of $7,000, $194,000 and $122,000 in the years ended December 31, 2018 and 2017, respectively, which is included within general and administrative expenses in the statement of operations.

Note 7 — Intangible assets, net

Intangible assets, net consisted of the following (in thousands):

	December 31,	December 31,

	2018	2017
Acquired software licenses	$ 2,494	$ 1,789
Licensed IP rights – completed technology used in R&D	197	200
	2,691	1,989
Less accumulated amortization	(1,218)	(652)
	$ 1,473	$ 1,337

Amortization expense was $622,000, $391,000 and $160,000 for the years ended December 31, 2018, 2017 and 2016, respectively. The estimated aggregate amortization expense in respect of these assets for each of the five years ended 2023 is $659,000, $360,000, $137,000, $23,000 and $13,000, respectively.

Table of Contents

Note 8 — Accrued expenses and other current liabilities

Accrued expenses and other current liabilities consisted of the following (in thousands):

	December 31, 2018	December 31, 2017
Accrued clinical & development expenditure	$ 9,637	$ 10,065
Accrued employee expenses	7,553	6,592
Accrued rent and property expenses	426	1,856
VAT	—	5,741
Other accrued expenditure	2,422	2,590
Other	316	357
	$ 20,354	$ 27,201

Note 9 — Contingencies and commitments

Leases

Future minimum lease payments under operating leases as of December 31, 2018 are presented below (in thousands):

	December 31, 2018
2019	$ 3,682
2020	3,695
2021	3,728
2022	3,772
2023	3,309
Thereafter	13,772
	$ 31,958

The Company leases property under operating leases expiring through 2027. Lease expenses amounted to $3,399,000, $3,617,000, $2,255,000 for the years ended December 31, 2018, 2017 and 2016, respectively, which is included within research and development and general and administrative expenses in the Company's consolidated statements of operations.

In February 2018, the Company entered into the lease of a building at Milton Park, Oxfordshire, U.K. The term of the lease expires on October 23, 2041, with termination options exercisable by the Company on the fifth anniversary of the lease commencement date and at approximately five yearly intervals thereafter. The related lease commitments are included in the table above.

Capital commitments

As of December 31, 2018, the Company had commitments for capital expenditure totaling $963,000, which the Company expects to incur within one year.

Commitments for clinical materials, clinical trials and contract manufacturing

As of December 31, 2018, the Company had non-cancellable commitments for purchase of clinical materials, contract manufacturing and committed funding under the MD Anderson strategic alliance of up to $25,849,000, of which the Company expects to pay $13,213,000 within one year and $12,636,000 in one to three years. The amount and timing of these payments vary depending on the rate of progress of development. Future clinical trial expenses have not been included within the purchase commitments because they are contingent on enrollment in clinical trials and the activities required to be performed by the clinical sites. The Company's subcontracted costs for clinical trials and contract

Table of Contents

manufacturing were $41,580,000 $41,505,000, $23,565,000 for the years ended December 31, 2018, 2017 and 2016, respectively.

Bellicum Pharmaceuticals Inc., Co-Development and Co-Commercialization Agreement

On December 16, 2016, the Company entered into a Co-Development and Co-Commercialization Agreement with Bellicum Pharmaceuticals, Inc. ("Bellicum") in order to facilitate a staged collaboration to evaluate, develop and commercialize next generation T-cell therapies.

Under the agreement, the Company will evaluate Bellicum's GoTCR technology (inducible MyD88/CD40 co-stimulation, or iMC) with the Company's SPEAR T-cells for the potential to create enhanced T-cell therapeutics. Depending on results of the initial preclinical proof-of-concept phase, the agreement may progress to a two-target co-development and co-commercialization phase. To the extent necessary, and in furtherance of the parties' proof-of-concept and co-development efforts, the parties granted each other a royalty-free, non-transferable, non-exclusive license covering their respective technologies for purposes of facilitating such proof-of-concept and co-development efforts. In addition, as to covered therapies developed under the agreement, the parties granted each other a reciprocal exclusive license for the commercialization of such therapies. During the proof of concept phase, each party bears its own costs and there are no payments made between the Company and Bellicum. Any research and development costs incurred by the Company with third parties have been accounted for in accordance with the Company's accounting policy for research and development expenses.

With respect to any joint commercialization of a covered therapy, the parties agreed to negotiate in good faith the commercially reasonable terms of a co-commercialization agreement. The parties also agreed that any such agreement shall provide for, among other things, equal sharing of the costs of any such joint commercialization and the calculation of profit shares as set forth in the agreement.

The agreement will expire on a country-by-country basis once the parties cease commercialization of the T-cell therapies covered by the agreement, unless earlier terminated by either party for material breach, non-performance or cessation of development, bankruptcy/insolvency, or failure to progress to co-development phase.

MD Anderson Strategic Alliance

On September 26, 2016, the Company announced that it had entered into a multi-year strategic alliance with The University of Texas MD Anderson Cancer Center ("MD Anderson") designed to expedite the development of T-cell therapies for multiple types of cancer. The Company and MD Anderson are collaborating on a number of studies including clinical and preclinical development of the Company's SPEAR T-cell therapies targeting NY-ESO, MAGE-A10 and MAGE-A4 and will collaborate on future clinical stage first and second generation SPEAR T-cell therapies across a number of cancers.

Under the terms of the agreement, the Company has committed at least $19,644,000 to fund studies. Payment of this funding is contingent on mutual agreement to study orders in order for any study to be included under the alliance and the performance of set milestones by MD Anderson. The Company made an upfront payment of $3,412,000 to MD Anderson in the year ended December 31, 2017 and milestone payments of $2,325,000 in the year ended December 31, 2018. The Company is obligated to make further payments to MD Anderson as certain milestones are achieved. These costs are expensed to research and development as MD Anderson renders the services under the strategic alliance.

The agreement may be terminated by either party for material breach by the other party. Individual studies may be terminated for, amongst other things, material breach, health and safety concerns or where the institutional review

board, the review board at the clinical site with oversight of the clinical study, requests termination of any study. Where any legal or regulatory authorization is finally withdrawn or terminated, the relevant study will also terminate automatically.

Table of Contents

Universal Cells Research, Collaboration and License Agreement

On November 25, 2015, the Company entered into a Research, Collaboration and License Agreement relating to gene editing and Human Leukocyte Antigen ("HLA") engineering technology with Universal Cells, Inc. ("Universal Cells"). The Company paid an upfront license and start-up fee of $2.5 million to Universal Cells in November 2015, a milestone payment of $3.0 million in February 2016 and further milestone payments of $0.2 million and $0.9 million in the year ended December 31, 2018 and 2017, respectively. Further milestone payments of up to $43.5 million are payable if certain development and product milestones are achieved. Universal Cells would also receive a profit-share payment for the first product, and royalties on sales of other products utilizing its technology. The upfront license and start-up fee and milestone payments were expensed to research and development when incurred.

ThermoFisher License Agreement

In 2012, the Company entered into a series of license and sub-license agreements with Life Technologies Corporation, part of ThermoFisher Scientific, Inc. ("ThermoFisher") that provide the Company with a field-based exclusive license under certain intellectual property rights owned or controlled by ThermoFisher. The Company paid upfront license fees of $1.0 million relating to the license and sublicense agreements and has an obligation to pay minimum annual royalties (in the 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 and a low single-digit running royalty payable on the net selling price of each licensed product. The upfront payment made in 2012 was expensed to research and development when incurred. Subsequent milestone payments have been recognized as an intangible asset due to the technology having alternative future use in research and development projects at the time of the payment. The minimum annual royalties have been expensed as incurred.

On June 16, 2016, the Company entered into a supply agreement with ThermoFisher for the supply of the Dynabeads® CD3/CD28 technology. The Dynabeads® CD3/CD28 technology is designed to isolate, activate and expand human T-cells, and is being used in the manufacturing of the Company's affinity enhanced T-cell therapies. The supply agreement runs until December 31, 2025. Under the supply agreement the Company is required to purchase its requirements for CD3/CD28 magnetic bead product exclusively from ThermoFisher for a period of 5 years and there are also minimum purchasing obligations, which are included within 'Purchase commitments for clinical materials, clinical trials and contract manufacturing' set forth above. ThermoFisher has the right to terminate the supply agreement for material breach or insolvency.

Note 10 — Stockholders' equity

Ordinary shares

Each holder of ordinary shares is entitled to one vote, on a show of hands and one vote per share on a poll, at general meetings of the Company. On the winding up of the Company, the assets of the Company available for distribution to holders remaining after payment of all other debts and liabilities of the Company shall be paid to the shareholders in proportion to the number of shares held by each of them. The payment of dividends by Adaptimmune Therapeutics plc is governed by English law

Effective from June 21, 2017, the Directors have the authority to allot new ordinary shares or to grant rights to subscribe for or to convert any security into ordinary shares in the Company up to a maximum aggregate nominal amount of £140,000.This authority runs for five years and will expire on June 20, 2022. Effective from June 21, 2017, the Directors also have the authority to allot ordinary shares for cash or to grant rights to subscribe for or to convert any security into ordinary shares in the Company without first offering them to existing shareholders in proportion to their existing holdings up to an aggregate maximum nominal amount of £140,000. This power will expire at the end of

the Annual General Meeting of the Company to be held in 2019.

Table of Contents

2018 Registered direct offering

On September 7, 2018, the Company completed a registered direct offering of its American Depositary Shares ("ADSs") following its entry into a definitive agreement with Matrix Capital Management Company, LP, New Enterprise Associates 16, L.P., New Enterprise Associates 14, L.P. and Syncona Portfolio Limited. The Company sold 10,000,000 ADSs (representing 60,000,000 ordinary shares) at a price of $10.00 per ADS. The net proceeds were $99,653,000 after deducting offering expenses of $347,000.

Underwritten public offering

On March 27, 2017, the Company completed an underwritten public offering of the Company's American Depositary Shares. The Company sold 15,700,223 ADSs (representing 94,201,338 ordinary shares) at a price to the public of $4.20 per ADS. The net proceeds were $61,397,000 after deducting offering expenses of $4,544,000.

2017 Registered direct offering

On April 10, 2017, the Company completed a registered direct offering of the Company's ADSs following its entry into a definitive agreement with Matrix Capital Management Company, LP. The Company sold 7,000,000 ADSs (representing to 42,000,000 ordinary shares) at a price of $6.00 per ADS. The net proceeds were $41,770,000 after deducting offering expenses of $230,000.

Note 11 — Share-based compensation

The Company grants options over ordinary shares in Adaptimmune Therapeutics plc under the following option plans: (i) the Adaptimmune Therapeutics plc Employee Share Option Scheme (adopted on January 14, 2016), (ii) the Adaptimmune Therapeutics plc 2015 Share Option Scheme and (adopted March 16, 2015) (ii) the Adaptimmune Therapeutics plc Company Share Option Plan (adopted March 16, 2015).

The Adaptimmune Therapeutics plc Company Share Option Plan 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 ("CSOP") options. Grants may not exceed the maximum value of £30,000 per participant for the shares under the option, which is a CSOP compliance requirement.

Generally, the vesting dates for the options granted under these plans up to December 31, 2018 are 25% on the first anniversary of the grant date and 75% in monthly installments over the following three years. However, the options granted to non-executive directors under the Adaptimmune Therapeutics plc 2015 Share Option Scheme vest and become exercisable as follows:

Options granted to non-executive directors on May 11, 2015:	Immediately on grant date
Options granted to a non-executive director on June 23, 2016:	25% on the first anniversary of the grant date and 75% in monthly installments over the following two years
Options granted to non-executive directors on August 11, 2016:	100% on the first anniversary of the grant date
Options granted to non-executive directors on November 28, 2016:	25% on the first anniversary of the grant date and 75% in monthly installments over the following two years

Options granted to non-executive directors on July 3, 2017	100% on the first anniversary of the grant date
Options granted to non-executive directors on June 22, 2018:	100% on the first anniversary of the grant date
Options granted to a non-executive director on July 5, 2018:	25% on the first anniversary of the grant date and 75% in monthly instalments over the following two years

Table of Contents

Effective from January 2018, the Company has also granted restricted stock unit style options ("RSU-style"). The RSU-style options over ordinary shares in Adaptimmune Therapeutics plc are granted under the Adaptimmune Therapeutics plc Employee Share Option Scheme (adopted on January 14, 2016). These options have an exercise price equal to the nominal value of an ordinary share, of £0.001, and generally vest over four years, with 25% on the first, and each subsequent, anniversary of the grant date.

Options granted under these plans are not subject to performance conditions. The contractual term of options granted under these plans is ten years.

The maximum aggregate number of options which may be granted under these plans and any incentive plans adopted by the Company cannot exceed a scheme limit that equates to 8% of the initial fully diluted share capital of the Company immediately following its 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 the Board, or an appropriate committee of the Board, may determine). The automatic increase is effective from July 1, 2016.

Prior to December 31, 2014, the Company granted options to purchase ordinary shares in Adaptimmune Limited under three option schemes:

(i) The Adaptimmune Limited Share Option Scheme was adopted on May 30, 2008. Under this scheme Enterprise Management Incentive ("EMI") options (which are potentially tax-advantaged in the United Kingdom) have been granted (subject to the relevant conditions being met) to its employees who are eligible to receive EMI options under applicable U.K. tax law and unapproved options (which do not attract tax advantages) have been granted to its employees who are not eligible to receive EMI options, and to its Directors and consultants. In May 2014, the Company no longer qualified for EMI status and since that date, no further EMI options were granted under this scheme; however, unapproved options have been under granted under this scheme since that date.

(ii) The Adaptimmune Limited 2014 Share Option Scheme was adopted on April 11, 2014. EMI options were granted (subject to the relevant conditions being met) under this scheme to our employees who are eligible to receive EMI options under applicable U.K. tax law. Unapproved options were granted to its employees who are not eligible to receive EMI options and to directors. In May 2014, the Company no longer qualified for EMI status and since that date, no further EMI options were granted under this scheme; however, unapproved options have been under granted under this scheme since that date.

(iii) The Adaptimmune Limited Company Share Option Plan was adopted on December 16, 2014. This scheme allowed the grant of options to our eligible employees prior to the Company's corporate reorganization in 2015. This scheme is a tax efficient option scheme and options were granted on December 19, 2014 and on December 31, 2014 to our part-time and full-time employees.

As part of the 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. The Company does not intend to grant any further options under these schemes.

Generally, the vesting dates for the Replacement Options under the Adaptimmune Limited 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

The contractual life of options granted under these schemes is ten years.

Table of Contents

In August 2016, the Company accelerated the vesting of 361,222 share options held by two non-executive directors, such that those options became vested and exercisable on December 30, 2016 when the non-executive directors stepped down from the Board, and the options expired on December 31, 2018.

The following table shows the total share-based compensation expense included in the consolidated statement of operations (thousands):

	Year ended December 31,		
	2018	2017	2016
Research and development	$ 8,340	5,268	$ 4,185
General and administrative	7,862	5,536	4,636
	$ 16,202	10,804	$ 8,821

As of December 31, 2018, there was $13,686,000 of total unrecognized compensation cost related to stock options granted but not vested under the plans. That cost will be recognized over an expected remaining weighted-average period of 2.9 years.

There were 20,771,970, 29,924,787 and 19,404,373 options granted in the years ended December 31, 2018, 2017 and 2016, respectively, of which 8,603,676 had a nominal exercise price (similar to a restricted stock unit (RSU). The weighted average fair value of stock options with an exercise price equating to the fair market value on the date of grant granted in the years ended December 31, 2018, 2017 and 2016 were $0.87, $0.35 and $0.74, respectively. The weighted average fair value of RSU-style stock options granted in the year ended December 31, 2018 was $1.37.

The following table summarizes all stock option activity for the year ended December 31, 2018:

	Options	Weighted average exercise price per option	Average remaining contractual term (years)	Aggregate intrinsic value (thousands)
Outstanding at January 1, 2018	74,943,667	£ 0.58		
Changes during the period:				
Granted	20,771,970	£ 0.63		
Exercised	(5,334,936)	£ 0.42		
Forfeited	(2,815,982)	£ 0.80		
Outstanding at December 31, 2018	87,564,719	£ 0.60	7.6	$ 25,905
Exercisable at December 31, 2018	47,678,481	£ 0.55	6.7	$ 15,207

The following table summarizes information about stock options outstanding as of December 31, 2018:

Outstanding				Exercisable	
	Total share	Weighted-average remaining	Weighted-average	Total share	Weighted-average

Exercise price	options	contractual life	exercise price	options	exercise price
£ 0	8,099,412	9.2	£ 0.00	—	£ —
0.01 - 0.25	7,268,412	4.9	0.12	7,268,412	0.12
0.26 - 0.50	16,714,988	6.1	0.43	16,156,497	0.42
0.51 - 0.75	28,617,051	8.2	0.61	13,465,614	0.61
0.76 - 1.00	22,317,845	8.0	0.93	9,323,729	0.90
1.01 - 1.50	2,751,818	8.5	1.18	934,295	1.04
1.51 - 2.00	1,795,243	8.6	1.71	529,934	1.82
Total	87,564,769	7.6	£ 0.60	47,678,481	£ 0.55

Table of Contents

There were 5,334,936, 1,142,904 and 63,192 share options exercised in the years ended December 31, 2018, 2017 and 2016, respectively. In the years ended December 31, 2018, 2017 and 2016 the total intrinsic value of stock options exercised was $6,727,000, $1,522,000 and $40,000, respectively and the cash received from exercise of stock options was $3,037,000, $401,000 and $17,000, respectively. The Company recognizes tax benefits arising on the exercise of stock options regardless of whether the benefit reduces current taxes. The tax benefit arising on the exercise of stock options was $1,325,000, $73,000 and $8,000 for the year ended December 31, 2018, 2017 and 2016, respectively. The Company satisfies the exercise of stock options through newly issued shares.

The fair value of the stock options granted during the period was calculated using the Black-Scholes option-pricing model using the following assumptions:

	Year ended December 31, 2018	Year ended December 31, 2017	Year ended December 31, 2016
Expected term (years)	5 years	5 years	5 years
Expected volatility	66 - 69%	66 - 71%	68 - 73%
Risk free rate	0.90 - 1.15%	0.40 - 0.76%	0.17 - 1.07%
Expected dividend yield	0%	0%	0%

The expected term of the option is based on management judgment. Due to the Company's lack of sufficient history as a publicly traded company, management's estimate of expected volatility for grants prior to May 2017 are based on the average volatilities of seven public companies with similar attributes to the Company. For grants subsequent to May 2017, there is over two years of historical data upon which to determine the volatility of the Company's share price, which management consider is sufficient to estimate the volatility based on the Company's historical share price. The risk free rate is based on the Bank of England's estimates of gilt yield curve as of the respective grant dates.

Note 12 — Income taxes

Loss before income taxes is as follows (in thousands):

	Year ended December 31, 2018	Year ended December 31, 2017	Year ended December 31, 2016
U.S.	$ (1,650)	$ (3,121)	$ (3,373)
U.K.	(93,367)	(66,566)	(67,314)
Loss before income taxes	$ (95,017)	$ (69,687)	$ (70,687)

Table of Contents

The components of income tax expense are as follows (in thousands):

	Year ended December 31, 2018	Year ended December 31, 2017	Year ended December 31, 2016
United States:			
Federal	$ 400	$ 459	$ 752
State and local	97	(8)	140
U.K.	—	—	—
Total current tax expense	497	451	892
United States:			
Federal	—	—	—
State and local	—	—	—
U.K.	—	—	—
Total deferred tax expense	—	—	—
Total income tax expense	$ 497	$ 451	$ 892

As of December 31, 2018 and 2017 the tax effects of temporary differences and carryforwards that give rise to deferred tax assets and liabilities were as follows (in thousands):

	December 31, 2018	December 31, 2017
Deferred tax liabilities		
Property, plant and equipment:	$ (1,415)	$ (2,159)
Accruals	—	(3)
Total	(1,415)	(2,162)
Deferred tax assets		
Share-based compensation expense	8,020	5,603
Intangibles	575	381
Other	286	254
Net operating loss and expenditure credit carryforwards	33,310	23,357
Total	42,191	29,595
Valuation allowance	(40,776)	(27,433)
	1,415	2,162
Net deferred tax asset (liability)	$ —	$ —

The valuation allowances are primarily related to deferred tax assets for operating loss and tax credit carry-forwards and temporary differences relating to share-based compensation expense. Deferred tax assets have been recognized without a valuation allowance to the extent supported by reversing taxable temporary differences. A valuation allowance has been provided over the remaining deferred tax assets, which management considered are not more likely than not of being realized after weighing all available positive and negative evidence including cumulative losses in recent years and projections of future taxable losses.

Table of Contents

The movements in the deferred tax valuation allowance for the year ended December 31, 2018 and 2017 is as follows (thousands):

	2018	2017
Valuation allowance at January 1,	$ 27,433	$ 17,613
Impact of adopting ASC 606	(1,469)	—
Valuation allowance at January 1, restated	25,964	17,613
Increase in valuation allowance	16,659	8,098
Foreign exchange translation adjustments	(1,847)	1,722
	$ 40,776	$ 27,433

Reconciliation of the U.K. statutory income tax rate to the Company's effective tax rate is as follows (in percentages):

	Year ended December 31, 2018		Year ended December 31, 2017		Year ended December 31, 2016	
U.K. tax rate	19.0	%	19.3	%	20.0	%
Reimbursable tax credits	3.5	%	2.6	%	1.6	%
Surrender of R&D expenditures for R&D tax credit refund	(10.0)	%	(8.4)	%	(5.9)	%
Change in valuation allowances	(17.5)	%	(13.5)	%	(14.7)	%
Difference in tax rates	(1.3)	%	(1.4)	%	(2.6)	%
R&D tax credits generated	5.1	%	0.7	%	—	%
Other	0.8	%	0.1	%	0.3	%
Effective income tax rate	(0.5)	%	(0.6)	%	(1.3)	%

The Company is headquartered in the United Kingdom and has subsidiaries in the United Kingdom and the United States. The Company incurs tax losses in the United Kingdom. The weighted-average U.K. corporate tax rate for the years ended December 31, 2018, 2017 and 2016 was 19%, 19.25% and 20%, respectively. The Company’s subsidiary in the United States has generated taxable profits due to a service agreement between the Company’s subsidiaries in the United States and the United Kingdom. The U.S. federal corporate tax rate was 21%, 34% and 34% for the years ended December 31, 2018, 2017 and 2016, respectively.

The United Kingdom’s 2016 Finance Bill, which was enacted on September 15, 2016, contained reductions in corporation tax to 19% from April 1, 2017 and 17% from April 1, 2020. The Company used a 17% tax rate as of December 31, 2018 in respect of the measurement of deferred taxes arising in the United Kingdom, which reflects the currently enacted tax rate and the anticipated timing of the unwinding of the deferred tax balances. In respect of the measurement of deferred taxes arising in the U.S, the Company has adopted a 21% tax rate as of December 31, 2018.

As of December 31, 2018, we do not have unremitted earnings in our U.S. subsidiary.

As of December 31, 2018, we had U.K. net operating loss of approximately $175.6 million, expenditure credit carryforwards of $0.6 million and U.S. tax credit carryforwards of $4.2 million. Unsurrendered U.K. tax losses and tax credit carryforwards can be carried forward indefinitely to be offset against future taxable profits, however this is restricted to an annual £5 million allowance in each standalone company or group and above this allowance, there will be a 50% restriction in the profits that can be covered by losses brought forward. U.S. tax credit carryforwards can be carried forward for 20 years. The tax credit carryforwards begin expiring in 2036.

Our tax returns are under routine examination in the U.K. and U.S. tax jurisdictions. The scope of these examinations includes, but is not limited to, the review of our taxable presence in a jurisdiction, our deduction of certain items, our claims for research and development credits, our compliance with transfer pricing rules and regulations and the inclusion or exclusion of amounts from our tax returns as filed. The Company is no longer subject to examinations by tax authorities for the tax years 2011 and prior in the United Kingdom. However, U.K. net operating losses from the tax years 2011 and prior would be subject to examination if and when used in a future tax return to offset taxable income. Our U.K. income tax returns have been accepted by Her Majesty's Revenue and Customs through the period

Table of Contents

ended December 31, 2016. The Company is subject to examinations by tax authorities in the United States for all tax years 2013 through 2017. Our U.S. federal income tax return for the year ended June 30, 2014 was audited by the U.S. Internal Revenue Service and resulted in no changes and our U.S. federal income tax return for the year ended December 31, 2016 is being audited by the U.S. Internal Revenue Service. We are also subject to audits by U.S. state taxing authorities where we have operations.

Unrecognized tax benefits arise when the estimated benefit recorded in the financial statements differs from the amounts taken or expected to be taken in a tax return because of the uncertainties described above. As of December 31, 2018 and December 31, 2017, the Company had no unrecognized tax benefits.

Note 13 — Geographic information

Operations by geographic area

Revenue represents recognized income from the GSK Collaboration and License Agreement. All revenue was derived in the United Kingdom.

Long-lived assets (excluding intangibles and financial instruments) were located as follows (in thousands):

	December 31, 2018	December 31, 2017
U.K.	$ 18,828	$ 22,786
U.S.	17,290	17,893
Total long-lived assets(1)	$ 36,118	$ 40,679

(1) Clinical materials of $3,953,000 and 4,695,000, included within non-current assets as of December 31, 2018 and 2017, respectively, are not included within the table above because they can easily be transferred between geographic locations.

Major customers:

During the years ended December 31, 2018, 2017 and 2016 100% of revenues were generated from one customer, which was GSK.