
**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549**

FORM 10-Q

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

For the quarterly period ended June 30, 2018

OR

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

Commission File Number 001-37368

ADAPT IMMUNE THERAPEUTICS PLC

(Exact name of Registrant as specified in its charter)

England and Wales

(State or other jurisdiction of incorporation or organization)

Not Applicable

(I.R.S. Employer Identification No.)

**60 Jubilee Avenue, Milton Park
Abingdon, Oxfordshire OX14 4RX
United Kingdom
(44) 1235 430000**

(Address of principal executive offices)

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

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

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

Large accelerated filer
Non-accelerated filer

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 standard provided pursuant to Section 13(a) of the Exchange Act.

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

As of July 31, 2018 the number of outstanding ordinary shares par value £0.001 per share of the Registrant is 566,496,400.

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General information

In this Quarterly Report on Form 10-Q (“Quarterly Report”), “Adaptimmune,” the “Group,” the “Company,” “we,” “us” and “our” refer to Adaptimmune Therapeutics plc and its consolidated subsidiaries, except where the context otherwise requires.

Information Regarding Forward-Looking Statements

This Quarterly 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 Quarterly 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 MAGE-A10, MAGE-A4 and AFP SPEAR T-cells 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 GlaxoSmithKline (“GSK”) including nomination of further targets by GSK under the collaboration;
- 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 SPEAR T-cells;
- government regulation and approval, including, but not limited to, the expected regulatory approval timelines for SPEAR T-cells and the level of pricing and reimbursement for SPEAR T-cells, if approved for marketing;
- the existence of any third party patents preventing further development of any SPEAR T-cells, including, any inability to obtain appropriate third party licenses, or enforcement of patents against us or our collaborators;
- our ability to obtain granted patents covering any 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;
- increased competition from other companies in the biotechnology and pharmaceutical industries including where such competition impacts ability to recruit patients in to clinical trials;
- claims for personal injury or death arising from the use of SPEAR T-cell candidates;

- our ability to attract and retain qualified personnel;
- a change in our status as an emerging growth company under the Jumpstart Our Business Start-ups Act of 2012, or JOBS Act; 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 II, Item 1A in this Quarterly 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 Quarterly 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 Quarterly 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.

PART I — FINANCIAL INFORMATION**Item 1. Financial Statements.**

ADAPTIMMUNE THERAPEUTICS PLC
UNAUDITED CONDENSED CONSOLIDATED BALANCE SHEETS
(In thousands, except share data)

	June 30, 2018	December 31, 2017
Assets		
Current assets		
Cash and cash equivalents	\$ 42,312	\$ 84,043
Marketable securities - available-for-sale debt securities	86,716	124,218
Accounts receivable, net of allowance for doubtful accounts of \$- and \$-	—	206
Other current assets and prepaid expenses (including current portion of clinical materials)	32,626	21,716
Total current assets	161,654	230,183
Restricted cash	4,195	4,253
Clinical materials	4,782	4,695
Property, plant and equipment, net	39,472	40,679
Intangibles, net	1,196	1,337
Total assets	211,299	281,147
Liabilities and stockholders' equity		
Current liabilities		
Accounts payable	4,131	8,378
Accrued expenses and other accrued liabilities	21,457	27,201
Deferred revenue	16,722	38,735
Total current liabilities	42,310	74,314
Other liabilities, non-current	3,887	3,849
Total liabilities	46,197	78,163
Stockholders' equity		
Common stock - Ordinary shares par value £0.001, 701,103,126 authorized and 566,496,400 issued and outstanding (2017: 701,103,126 authorized and 562,119,334 issued and outstanding)	860	854
Additional paid in capital	466,229	455,401
Accumulated other comprehensive loss	(14,419)	(21,641)
Accumulated deficit	(287,568)	(231,630)
Total stockholders' equity	165,102	202,984
Total liabilities and stockholders' equity	\$ 211,299	\$ 281,147

See accompanying notes to unaudited condensed consolidated financial statements.

ADAPTIMMUNE THERAPEUTICS PLC
UNAUDITED CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS
(In thousands, except share and per share data)

	Three months ended June 30,		Six months ended June 30,	
	2018	2017	2018	2017
Revenue	\$ 9,038	\$ 3,521	\$ 17,234	\$ 6,378
Operating expenses				
Research and development	(26,624)	(19,591)	(52,016)	(38,206)
General and administrative	(11,291)	(7,710)	(22,495)	(14,173)
Total operating expenses	(37,915)	(27,301)	(74,511)	(52,379)
Operating loss	(28,877)	(23,780)	(57,277)	(46,001)
Interest income	540	506	1,199	746
Other (expense) income, net	(15,406)	3,224	(8,276)	3,654
Loss before income taxes	(43,743)	(20,050)	(64,354)	(41,601)
Income taxes	(102)	(165)	(229)	(396)
Net loss attributable to ordinary shareholders	\$ (43,845)	\$ (20,215)	\$ (64,583)	\$ (41,997)
Net loss per ordinary share				
Basic and diluted	\$ (0.08)	\$ (0.04)	\$ (0.11)	\$ (0.09)
Weighted average shares outstanding:				
Basic and diluted	565,197,217	556,776,430	563,804,832	493,392,465

See accompanying notes to unaudited condensed consolidated financial statements.

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ADAPTIMMUNE THERAPEUTICS PLC
UNAUDITED CONDENSED CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS
(In thousands)

	Three months ended June 30,		Six months ended June 30,	
	2018	2017	2018	2017
Net loss	\$ (43,845)	\$ (20,215)	\$ (64,583)	\$ (41,997)
Other comprehensive loss, net of tax				
Foreign currency translation adjustments, net of tax of \$-, \$-, \$- and \$-	6,107	(1,192)	3,582	(1,309)
Unrealized holding gains (losses) on available-for-sale debt securities, net of tax of \$-, \$-, \$- and \$-	5,223	(1,296)	1,167	(1,296)
Reclassification adjustment for losses on available-for-sale debt securities included in net loss, net of tax of \$-, \$-, \$- and \$-	1,310	—	2,473	—
Total comprehensive loss for the period	\$ (31,205)	\$ (22,703)	\$ (57,361)	\$ (44,602)

See accompanying notes to unaudited condensed consolidated financial statements.

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ADAPTIMMUNE THERAPEUTICS PLC
UNAUDITED CONDENSED CONSOLIDATED STATEMENT OF CHANGE IN EQUITY
(In thousands, except share data)

	Common stock	Common stock	Additional paid in capital	Accumulated other comprehensive loss		Accumulated deficit	Total stockholders' equity
				Accumulated foreign currency translation adjustments	Accumulated unrealized gains (losses) on available-for- sale debt securities		
Balance as of 1 January 2018 (under previous guidance)	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)		854	455,401	(17,867)	(3,774)	(222,985)	211,629
Net loss						(64,583)	(64,583)
Issuance of shares upon exercise of stock options	4,377,066	6	2,417	—	—	—	2,423
Other comprehensive loss before reclassifications							
Foreign currency translation adjustments	—	—	—	3,582	—	—	3,582
Unrealized holding gains on available-for-sale debt securities, net of tax of \$-	—	—	—	—	1,167	—	1,167

Reclassification from accumulated other comprehensive loss of losses on available-for-sale debt securities included in net loss, net of tax of \$-	—	—	—	—	2,473	—	2,473
Share-based compensation expense	—	—	8,411	—	—	—	8,411
Balance as of June 30, 2018	566,496,400	\$ 860	\$ 466,229	\$ (14,285)	\$ (134)	\$ (287,568)	\$ 165,102

See accompanying notes to unaudited condensed consolidated financial statements.

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ADAPT IMMUNE THERAPEUTICS PLC
UNAUDITED CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

	Six months ended June 30,	
	2018	2017
Cash flows from operating activities		
Net loss	\$ (64,583)	\$ (41,997)
<i>Adjustments to reconcile net loss to net cash used in operating activities:</i>		
Depreciation	3,499	2,023
Amortization	304	159
Share-based compensation expense	8,411	4,757
Realized loss on available-for-sale debt securities	2,473	—
Unrealized foreign exchange losses (gains)	2,915	(3,206)
Other	16	194
<i>Changes in operating assets and liabilities:</i>		
(Increase) decrease in receivables and other operating assets	(11,602)	2,301
Decrease (increase) in non-current operating assets	87	(554)
Decrease in payables and deferred revenue	(24,162)	(10,125)
Net cash used in operating activities	(82,642)	(46,448)
Cash flows from investing activities		
Acquisition of property, plant and equipment	(3,139)	(21,188)
Acquisition of intangibles	(10)	(266)
Proceeds from disposal of property, plant and equipment	—	550
Maturity of short-term deposits	—	22,857
Investment in short-term deposits	—	(18,000)
Maturity or redemption of marketable securities	70,717	—
Investment in marketable securities	(33,556)	(79,774)
Net cash provided by (used in) investing activities	34,012	(95,821)
Cash flows from financing activities		
Proceeds from issuance of common stock, net of issuance costs \$4,774	—	103,167
Proceeds from exercise of stock options	2,424	31
Net cash provided by financing activities	2,424	103,198
Effect of currency exchange rate changes on cash, cash equivalents and restricted cash	4,417	2,429
Net decrease in cash, cash equivalents and restricted cash	(41,789)	(36,642)
Cash, cash equivalents and restricted cash at start of period	88,296	162,796
Cash, cash equivalents and restricted cash at end of period	\$ 46,507	\$ 126,154

See accompanying notes to unaudited condensed consolidated financial statements.

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ADAPT IMMUNE THERAPEUTICS PLC
NOTES TO UNAUDITED CONDENSED 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.

The Company is subject to a number of risks similar to other biopharmaceutical companies in the early stage of clinical development 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 \$287.6 million as of June 30, 2018.

Note 2 - Summary of Significant Accounting Policies

(a) Basis of presentation

The condensed consolidated interim financial statements of Adaptimmune Therapeutics plc and its subsidiaries and other financial information included in this Quarterly Report are unaudited and have been prepared in accordance with generally accepted accounting principles in the United States of America (“U.S. 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.

The unaudited condensed interim financial statements presented in this Quarterly Report should be read in conjunction with the consolidated financial statements and accompanying notes included in the Company’s Annual Report on Form 10-K filed with the SEC on March 15, 2018 (the “Annual Report”). The balance sheet as of December 31, 2017 was derived from audited consolidated financial statements included in the Company’s Annual Report but does not include all disclosures required by U.S. GAAP. The Company’s significant accounting policies are described in Note 2 to those consolidated financial statements.

Certain information and footnote disclosures normally included in financial statements prepared in accordance with U.S. GAAP have been condensed or omitted from these interim financial statements. However, these interim financial statements include all adjustments, consisting only of normal recurring adjustments, which are, in the opinion of management, necessary to fairly state the results of the interim period. The interim results are not necessarily indicative of results to be expected for the full year.

On January 1, 2018, the Company adopted new 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 three and six months ended June 30, 2017 and as of December 31, 2017 has not been restated.

(b) Use of estimates in interim financial statements

The preparation of interim 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 reimbursements from 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.

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(c) 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, 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 6, *Fair value measurements*.

(d) Revenue from contracts with customers

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(f). The comparative financial information for the three and six months ended June 30, 2017 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 to the consolidated financial statements included in the Annual Report.

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 to research, develop, and commercialize the Company’s NY-ESO SPEAR T-cell therapy program.

The aggregate transaction price consists of an upfront payment of \$42,123,000 received in June 2014, development milestones achieved of \$53,691,000, an option exercise fee of \$26,610,000, which was received in September 2017, and an estimate of variable consideration of \$25,544,000. The variable consideration relates to further milestone payments and the remaining option exercise fee of approximately \$13,198,000, which are expected to be received following transition of the NY-ESO program to GSK in July 2018 (see Note 3 for further details).

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;
- 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 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.

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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 exclusive license to research, develop, and commercialize the Company's NY-ESO SPEAR T-cell therapy program is recognized at a point-in-time, upon commencement of the license, which occurs once transition of the NY-ESO program is completed and all amounts due under the agreement are paid.

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.

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. However, the Company received \$26,610,000 of the option exercise fee in September 2017, which will not be recognized as revenue until the commencement of the licenses, with the remaining amount of approximately \$13,198,000 payable following transition of the program to GSK in July 2018. The associated revenue will be recognized upon commencement of the license, which occurs later resulting in deferred revenue.

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.

(e) Share-based compensation

The Company has awarded share options to nonemployees for consultancy services. Prior to January 1, 2018, these 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 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. Further details on the transition are available in Note 2(f).

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(f) New accounting pronouncements

Adopted in the period

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 three months ended June 30, 2018 are set out below (in thousands):

	Under previous revenue guidance	Adjustment	As reported
Revenue	\$ 3,267	\$ 5,771	\$ 9,038
Operating loss	(34,648)	5,771	(28,877)
Loss before income taxes	(49,514)	5,771	(43,743)
Net loss attributable to ordinary shareholders	(49,616)	5,771	(43,845)
Net loss per ordinary share - Basic and diluted	(0.09)		(0.08)

The quantitative impacts of the changes on the statement of operations for the six months ended June 30, 2018 are set out below (in thousands):

	Under previous revenue guidance	Adjustment	As reported
Revenue	\$ 12,263	\$ 4,971	\$ 17,234
Operating loss	(62,248)	4,971	(57,277)
Loss before income taxes	(69,325)	4,971	(64,354)
Net loss attributable to ordinary shareholders	(69,554)	4,971	(64,583)
Net loss per ordinary share - Basic and diluted	(0.12)		(0.11)

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The quantitative impacts of the changes on the balance sheet as of June 30, 2018 are set out below (in thousands):

	Under previous revenue guidance	Adjustment	As reported
Deferred revenue	\$ 30,338	\$ (13,616)	\$ 16,722
Total current liabilities	55,926	(13,616)	42,310
Total liabilities	59,813	(13,616)	46,197
Accumulated deficit	(301,184)	13,616	(287,568)
Total stockholders' equity	151,486	13,616	165,102

The quantitative impacts of the changes on the statement of cash flows for the six months ended June 30, 2018 are set out below (in thousands):

	Under previous revenue guidance	Adjustment	As reported
Net loss	\$ (69,554)	\$ 4,971	\$ (64,583)
Decrease in payables and deferred revenue	(19,191)	(4,971)	(24,162)

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 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:

- Identifying the satisfied and unsatisfied performance obligations
- Determining the transaction price
- Allocating the transaction price to the satisfied and unsatisfied performance obligations.

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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 also proposed another transition method, which is anticipated to be issued in an ASU shortly, 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. 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 \$25 million and a corresponding lease liability of approximately \$25 million.

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.

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(g) Related parties

In the three and six months ended June 30, 2017, research and development expenses includes purchases of \$178,000 and \$780,000 from Immunocore Ltd ("Immunocore"). As described in Note 2(w) to the consolidated financial statements included in the Annual Report, the Company no longer considered Immunocore to be a related party with effect from January 1, 2018.

Note 3 — Revenue

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):

	Three months ended June 30, 2018	Six months ended June 30, 2018
Development	\$ 9,038	\$ 17,234
Licenses	—	—
	<u>\$ 9,038</u>	<u>\$ 17,234</u>

The following table shows movements in deferred revenue for the six months ended June 30, 2018 (in thousands):

	Deferred revenue
Deferred revenue at January 1, 2018 under previous guidance	\$ 38,735
Cumulative effect of adopting ASC 606	(8,645)
Deferred revenue at January 1, 2018	30,090
Revenue recognized included in the opening deferred revenue	(11,910)
Change in variable consideration	(10,396)
Change in percentage of completion	5,072
Revenue in the period	(17,234)
Amounts invoiced in the period	4,210
Foreign exchange arising on consolidation	(344)

The aggregate amount of the transaction price, excluding variable consideration which is constrained to reduce the consideration to the amount which is probable of being received, allocated to the performance obligations that are unsatisfied (or partially satisfied) as of the end of the reporting period was \$42,653,000 at June 30, 2018. This amount comprises \$946,000 of revenue allocated to partially satisfied performance obligations for the NY-ESO program, \$39,593,000 of revenue allocated to the exclusive license to research, develop, and commercialize the Company's NY-ESO SPEAR T-cell therapy program and a further \$2,114,000 of revenue allocated to the remaining performance obligations for the PRAME program.

The IND for the NY-ESO program and the responsibility for the NY-ESO program transferred to GSK on July 23, 2018. Therefore, management anticipates that the revenue allocated to NY-ESO program and the exclusive license to research, develop, and commercialize the Company's NY-ESO SPEAR T-cell therapy program will be recognized in the third quarter of 2018.

The revenue allocated to the PRAME program will be recognized over the next twelve months as the development of the second target, PRAME, progresses.

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Note 4 — Other income (expense), net

Other income (expense), net consisted of the following (in thousands):

	Three months ended June 30,		Six months ended June 30,	
	2018	2017	2018	2017
Foreign exchange (losses) gains	\$ (14,022)	\$ 3,289	\$ (5,605)	\$ 3,718
Losses on redemption or maturity of available-for-sale debt securities	(1,310)	—	(2,473)	—
Other	(74)	(65)	(198)	(64)
	<u>\$ (15,406)</u>	<u>\$ 3,224</u>	<u>\$ (8,276)</u>	<u>\$ 3,654</u>

Note 5 — Loss per share

The dilutive effect of 87,434,329 and 67,082,914 stock options outstanding as of June 30, 2018 and 2017, respectively, 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.

Note 6 — Fair value measurements

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 June 30, 2018 are as follows (in thousands):

	June 30, 2018	Fair value measurements using		
		Level 1	Level 2	Level 3
Assets:				
Marketable securities:				
Corporate debt securities	\$ 77,688	\$ 77,688	\$ —	\$ —
Government bonds	6,028	6,028	—	—
Commercial paper	3,000	—	3,000	—
	<u>\$ 86,716</u>	<u>\$ 83,716</u>	<u>\$ 3,000</u>	<u>\$ —</u>

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

Note 7 — Available-for-sale debt securities

As of June 30, 2018, the Company has the following investments in available-for-sale debt securities (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	\$ 77,820	\$ —	\$ (132)	\$ 77,688
Government bonds	3 months to 1 year	6,030	—	(2)	6,028
Commercial paper	3 months to 1 year	3,000	—	—	3,000
		<u>\$ 86,850</u>	<u>\$ —</u>	<u>\$ (134)</u>	<u>\$ 86,716</u>

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In the three and six months ended June 30, 2018, realized losses recognized on the maturity of available-for-sale debt securities of \$1,310,000 and \$2,473,000, respectively, primarily arising due to foreign exchange movements, were reclassified out of accumulated other comprehensive loss.

As of June 30, 2018 and December 31, 2017, the aggregate fair value of securities held by the Company in an unrealized loss position was \$81,714,000 and \$125,828,000, respectively, which consisted of 33 and 54 securities, respectively. One security, with a fair value of \$1,400,000 with an unrealized loss of \$2,000 has been in an unrealized loss position for more than one year. As of June 30, 2018, the securities in an unrealized loss position 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 fluctuations. 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.

Note 8 — Other current assets

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

	June 30, 2018	December 31, 2017
Corporate tax receivable	\$ 18,605	\$ 11,454
Prepayments	9,059	6,120
Clinical materials	2,993	3,760
Other current assets	1,969	382
	<u>\$ 32,626</u>	<u>\$ 21,716</u>

Note 9 — Accrued expenses and other current liabilities

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

	June 30, 2018	December 31, 2017
Accrued clinical and development expenditure	\$ 11,357	\$ 10,065
Accrued employee expenses	5,419	6,592
VAT	—	5,741
Other accrued expenditure	4,238	4,446
Other liabilities	443	357
	<u>\$ 21,457</u>	<u>\$ 27,201</u>

The Company typically has a receivable for VAT. As of December 31, 2017, there was a VAT payable due to VAT arising on the milestone payments invoiced to GSK in 2017.

Note 10 — Share-based compensation

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

	Three months ended June 30,		Six months ended June 30,	
	2018	2017	2018	2017
Research and development	\$ 2,071	\$ 871	\$ 4,285	\$ 2,229
General and administrative	2,008	1,201	4,126	2,528
	<u>\$ 4,079</u>	<u>\$ 2,072</u>	<u>\$ 8,411</u>	<u>\$ 4,757</u>

There were 1,435,685 and 1,252,176 options over ordinary shares granted in the three months ended June 30, 2018 and 11,430,341 and 20,203,152 options over ordinary shares granted in the six months ended June 30, 2018 and 2017, respectively, with a weighted average fair value of \$1.18, \$0.42, \$0.80 and \$0.35, respectively. Additionally, in the three and six months ended June 30, 2018, 151,056 and 6,703,692 options were granted, which have a nominal exercise price (similar to a restricted stock unit (RSU)), with a weighted average fair value of \$1.88 and \$1.35, respectively.

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The RSU-style options over ordinary shares in Adaptimmune Therapeutics plc were 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. The RSU-style options are not subject to performance conditions and the contractual term is ten years.

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

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

The following discussion should be read in conjunction with the unaudited consolidated financial statements and accompanying notes included elsewhere in this Quarterly Report and our consolidated financial statements and accompanying notes included within our Annual Report.

We are a clinical-stage biopharmaceutical company focused on novel cancer immunotherapy products based on our proprietary SPEAR T-cell platform. We have developed a comprehensive proprietary platform that enables us to identify cancer targets, find and genetically engineer TCRs, and produce TCR therapeutic candidates for administration to patients. We engineer TCRs to increase their affinity to cancer specific peptides in order to destroy cancer cells in patients.

Update on Clinical Pipeline Progress

Wholly owned SPEAR T-cells

We have Phase 1/2 clinical trials ongoing with our wholly owned MAGE-A10, MAGE-A4 and AFP SPEAR T-cells in a total of ten solid tumor types including non-small cell lung cancer (“NSCLC”), head and neck cancer, ovarian, urothelial, melanoma, hepatocellular, esophageal, gastric, synovial sarcoma and myxoid round cell liposarcoma (“MRCLS”) cancers.

MAGE-A10 SPEAR T-cell

Phase 1 clinical trials are ongoing with our MAGE-A10 SPEAR T-cell 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 in up to 28 patients with escalating doses of 100 million (Cohort 1), 1 billion (Cohort 2), and 1.2-6 billion (Cohort 3) transduced SPEAR T-cells to evaluate safety, including dose limiting toxicities (DLTs) followed by a possible expansion phase with doses of up to 10 billion SPEAR T-cells.

The MAGE-A10 SPEAR T-cell has continued to show a favorable safety profile and on July 18, 2018 it was announced that the Safety Review Committee endorsed escalation to the third dose cohort (1.2-6 billion transduced SPEAR T-cells) in both the NSCLC and the triple tumor study (urothelial, melanoma and head and neck cancers).

As of July 18, 2018, eight patients have received 100 million transduced MAGE-A10 SPEAR T-cells in the first dose cohorts across both studies, and three patients have received one billion cells in the second cohort of the NSCLC study. No evidence of toxicity related to off-target binding or alloreactivity has been reported. Most adverse events were consistent with those typically experienced by cancer patients undergoing cytotoxic chemotherapy or other cancer immunotherapies. Additional safety data from the two ongoing MAGE A-10 SPEAR T-cell studies was presented at the American Society of Clinical Oncology (ASCO) annual meeting in June 2018.

Further preliminary data from the MAGE-A10 trials are anticipated during the second half of 2018.

MAGE-A4 SPEAR T-cell

A Phase 1 clinical trial is ongoing in nine tumor indications namely urothelial, melanoma, head and neck, ovarian, NSCLC, esophageal and gastric cancers, synovial sarcoma and MRCLS. The addition of the synovial sarcoma and MRCLS indications was announced on June 4, 2018.

The primary objective of the study is to evaluate the safety and tolerability of MAGE-A4 SPEAR T-cell therapy. Additional objectives include anti-tumor activity, persistence of genetically modified cells in the body and evaluation of the phenotype and functionality of genetically modified cells isolated from peripheral blood or tumor post infusion. Multiple sites in the United States are now active and recruiting.

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Patients were initially treated with a target dose of 100 million T-cells (safety dose). On June 4, 2018, it was announced that the Safety Review Committee had endorsed dose escalation to treatment with 1 billion MAGE A-4 SPEAR T-cells and treatment of patients at this dose is now ongoing.

Preliminary data is anticipated during 2018.

AFP SPEAR T-cell

We are dosing in a Phase 1, open label, dose escalation study designed to evaluate the safety and anti-tumor activity of our alpha fetoprotein (“AFP”) therapeutic candidate in hepatocellular carcinoma (“HCC”). The trial is open in the United States, United Kingdom and Spain. The Phase 1 clinical trial will include a dose escalation to evaluate safety, including dose limiting toxicities (DLTs), followed by expansion of a tolerable dose to further explore safety and initial evidence of anti-tumor activity.

The NY-ESO SPEAR T-cell Program (now transitioned to GSK)

Transition of Program to GSK

The NY-ESO SPEAR T-cell program transitioned to GSK as of July 23, 2018. As a result of the transition, GSK has assumed full responsibility for future research, development, and potential commercialization of the NY-ESO SPEAR T-cell (referred to as GSK3377794 or GSK ‘794 by GSK). Certain transition completion activities remain ongoing and are subject to a further amendment to the GSK Collaboration and License Agreement. Successful continuation of development and subsequent commercialization of GSK ‘794 by GSK will trigger additional payments for development milestones, tiered sales milestones, and mid-single to low double-digit royalties on worldwide net sales.

Background to the NY-ESO SPEAR T-cell program

99 patients were enrolled and treated with the NY-ESO SPEAR T-cell across multiple indications, namely synovial sarcoma, MRCLS, NSCLC, melanoma, multiple myeloma (including in combination with Pembrolizumab) and ovarian cancer prior to transition of the program to GSK.

Synovial Sarcoma and MRCLS:

Enrollment in both the synovial sarcoma and MRCLS trials was completed as of the date of transition of the program to GSK. As of June 2018, data in the synovial sarcoma and MRCLS studies continued to suggest a favorable benefit:risk profile for the NY-ESO SPEAR T-cells. Initial anti-tumor activity was observed across all cohorts, including synovial sarcoma patients with low NY-ESO expression levels. NY-ESO SPEAR T-cells continue to be well-tolerated with myelosuppression and cytokine release syndrome being common adverse events. In both studies, the preliminary data suggests that SPEAR T-cell expansion and persistence correlates with response.

MRCLS

As of transition to GSK, the MRCLS trial was fully enrolled.

Initial data for the MRCLS trial was presented at ASCO in June 2018. As of June 2, 2018 and with eight patients treated, best overall responses as assessed by investigator included three confirmed partial responses, one unconfirmed partial response, three stable disease and one patient awaiting assessment. An overall trend in tumor burden decrease was observed in a majority of patients with the tumor burden decrease across target lesions ranging from 16.9% to 50%. There was one event of cytokine release syndrome (CRS) \geq Grade 3, which was characterized by fever, hypotension, rash, headache, and supraventricular tachycardia. The CRS resolved six days post-infusion of SPEAR T-cells. There were four serious adverse events reported for three patients including the CRS, two further grade 2 CRS events (both of which resolved) and a grade 2 pleural effusion.

Synovial Sarcoma

As of transition to GSK, all synovial sarcoma cohorts were fully enrolled.

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An update on all cohorts from the pilot study of NY-ESO SPEAR T-cells in synovial sarcoma was presented during an oral presentation session at CTOS in November 2017. At that time, of the twelve patients treated in Cohort 1, five were alive with a median predicted overall survival of 120 weeks (~28 months). Confirmed responses were observed across all cohorts as follows:

- Cohort 1 (follow-up only; High Flu/Cy, High NY-ESO): 6 /12 (50%) patients

- Cohort 2 (ongoing; High Flu/Cy, Low NY-ESO): 3/10 (33%) patients
- Cohort 3 (follow-up only; Cy alone, High NY-ESO): 1/5 (20%) patients
- Cohort 4 (ongoing; Lower Flu/Cy, High NY-ESO): 4/11 (36%) patients; overall survival was not assessed at the time of this update as the data were not mature enough; progression free survival was 23 weeks at the time

Further data from cohort 1 of the synovial sarcoma trials was presented in Cancer Discovery, an American Association of Cancer Research publication, and announced in June 2018. The paper reported data from cohort 1 of the synovial sarcoma study including a median duration of response of 30.9 weeks (range 13 — 72 weeks), an overall response rate of 50% (6/12 patients) and 60% among the ten patients who received the target dose of at least 1 billion transduced cells. As previously reported there was one confirmed response and five confirmed partial responses seen with the first infusion of SPEAR T-cells. Median progression-free survival (PFS) was 15 weeks (range 8 — 38 weeks) and the estimate of median overall survival was reported to be approximately 120 weeks among the patients in cohort 1.

In addition, at ASCO initial results seen with recent second infusions of SPEAR T-cells in patients were reported. It was reported that of these five recent patients, one patient had a confirmed complete response.

Multiple Myeloma program:

NY-ESO SPEAR T-cells have also been evaluated in multiple myeloma in the context of autologous stem cell transplant (ASCT), and an update in all 25 patients treated in this study was presented during an oral presentation at ASH in December 2017. The NY-ESO SPEAR T-cell therapy demonstrated promising efficacy and acceptable safety in patients. The overall response rate (ORR) at 100 days and one year were 76% and 44% respectively, using International Myeloma Working Group criteria. Three patients remain disease-progression free at 3, 4.5, and 5 years post-treatment. Five of eighteen patients tested were minimal residual disease negative at day 100, and the median duration of response was greater than 12 months. Of the twenty-five patients treated in this study, eleven were alive at data cut-off; the median predicted overall survival was reported as approximately three years.

Enrollment of patients is ongoing in a multiple myeloma combination study with Merck's anti-programmed death-1 ("PD-1") inhibitor, KEYTRUDA® (pembrolizumab). GSK will assume responsibility for the continuation of this combination study.

NSCLC program:

In the NSCLC study enrollment has now completed and dosing is ongoing. GSK will assume responsibility for any further development for this indication.

Significant Events in the Three Months Ended June 30, 2018

- On April 12, 2018, it was announced that in a planned transition, John Furey would be appointed as an independent Non-Executive Director, and Peter Thompson, M.D., Ph.D., would be stepping down from the Board. Both changes were effective from July 5, 2018.
- Updated clinical data were also announced and are covered in the Update on the Clinical Pipeline Progress.

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"). The comparative financial information for the three and six months ended June 30, 2017 and as of December 31, 2017 has not been restated and is prepared in accordance with the previous accounting guidance.

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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 development of a second target, PRAME, and an exclusive license to research, develop, and commercialize the Company's NY-ESO SPEAR T-cell therapy program.

The aggregate transaction price consists of an upfront payment of \$42.1 million in June 2014, development milestones achieved of \$53.7 million, an option exercise fee of \$26.6 million, which was received in September 2017 and an estimate of variable consideration of \$25.6 million. The contract includes a significant amount of variable consideration due to the milestone payments, which the Company is entitled to upon achievement of development milestones and the remaining option exercise fee of approximately \$13.2 million which will be received following successful transition of the NY-ESO program to GSK, which are expected to be received following transition of the NY-ESO program to GSK in July 2018.

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.

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.

Research and development expenditures are expensed as incurred.

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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 II — Item 1A Risk Factors — Risks Related to the Development of our SPEAR T-cells of our Quarterly 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;
- professional fees for auditors, lawyers and other consulting expenses;
- costs of facilities, communication, and office expenses;
- information technology expenses;

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- amortization and depreciation of property, plant and equipment and intangible assets not related to research and development activities; and
- share-based compensation expenses.

Other (Expense) Income, net

Other (expense) income, 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 holds our investment in marketable securities, 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, is included in other comprehensive income.

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.

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. 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. The Company also benefits from the U.S. Research Tax Credit and Orphan Drug Credit.

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.

Critical Accounting Policies and Significant Judgments and Estimates

The preparation of our unaudited condensed consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities, disclosure of contingent assets and liabilities, and the revenues and expenses incurred during the reported periods. We base our estimates on historical experience and on various other factors that we believe are relevant under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. The accounting policies considered to be critical to the judgments and estimates used in the preparation of our financial statements are disclosed in the Management's Discussion and Analysis of Financial Condition and Results of Operations included in our Annual Report. There has been no change in the accounting policies considered to be critical accounting judgments and estimates other than the accounting judgments and estimates relating to revenue recognition, which have been changed from January 1, 2018 due to the adoption of ASC 606.

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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, post-transition activities to finalize the transfer of the NY-ESO SPEAR T-cell program to GSK, the development of a second target, PRAME, and an exclusive license to research, develop, and commercialize the Company's NY-ESO SPEAR T-cell therapy program.

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 three and six months ended June 30, 2018, revenue of \$7.1 million and \$10.3 million, respectively, was recognized due to development milestones becoming probable in the period. As the development program progresses and the uncertainties underlying the milestones resolve, it is likely that further milestones will 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 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 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. In the three and six months ended June 30, 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 to reduce revenue of \$2.1 million and \$5.1 million for the three and six months ended June 30, 2018. Due to the inherent difficulties in determining the cost of completion for development programs, small changes in the cost to complete are likely to occur.

The Company has determined that the performance obligation relating to the exclusive license to research, develop, and commercialize the Company's NY-ESO SPEAR T-cell therapy program is recognized at a point-in-time, upon commencement of the license, which occurs once transition of the NY-ESO program is completed and all amounts due under the agreement in relation to the NY-ESO program transition are paid.

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Results of Operations

Comparison of Three Months Ended June 30, 2018 and 2017

The following table summarizes the results of our operations for the three months ended June 30, 2018 and 2017, together with the changes to those items (in thousands).

	Three months ended June 30,		Increase/decrease	
	2018	2017		
Revenue	\$ 9,038	\$ 3,521	\$ 5,517	157 %
Research and development expenses	(26,624)	(19,591)	(7,033)	36 %
General and administrative expenses	(11,291)	(7,710)	(3,581)	46 %
Total operating expenses	(37,915)	(27,301)	(10,614)	39 %
Operating loss	(28,877)	(23,780)	(5,097)	21 %
Interest income	540	506	34	7 %
Other income (expense), net	(15,406)	3,224	(18,630)	(578) %
Loss before income taxes	(43,743)	(20,050)	(23,693)	118 %
Income taxes	(102)	(165)	63	(38) %
Loss for the period	\$ (43,845)	\$ (20,215)	\$ (23,630)	117 %

Revenue

Revenue increased by \$5.5 million to \$9.0 million in the three months ended June 30, 2018 compared to \$3.5 million for the three months ended June 30, 2017. Revenue in the three months ended June 30, 2018 was recognized due to the continued performance under the NY-ESO transition program and the PRAME development plan. The revenue benefited from a change in the estimate of variable consideration of \$7.1 million due to additional development milestones being considered probable, which was partially offset by \$2.1 million arising due to a change in percentage of completion.

Revenue for the three months ended June 30, 2018 has been recognized under new accounting guidance which is effective January 1, 2018. Revenue in the comparative period of 2017 has been recognized under the previous guidance. Revenue in the three months ended June 30, 2018 under the previous guidance would be \$3.3 million, compared to \$3.5 million for the same period of 2017.

Future revenues will fluctuate depending on the progress of the transition and development program for NY-ESO and development program for the second target, PRAME, which is difficult to predict. However, the Investigational New Drug Application ("IND") for the NY-ESO program and the responsibility for the NY-ESO program transferred to GSK on July 23, 2018. Therefore, we anticipate that \$0.9 million of revenue allocated to NY-ESO program and \$39.6 million of revenue allocated to the exclusive license to research, develop, and commercialize the Company's NY-ESO SPEAR T-cell therapy program will be recognized in the third quarter of 2018. A further \$2.1 million will be recognized over the next twelve months as the development of the second target, PRAME, progresses.

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Research and Development Expenses

Research and development expenses increased by 36% to \$26.6 million for the three months ended June 30, 2018 from \$19.6 million for the three months ended June 30, 2017. Our research and development expenses comprise the following (in thousands):

	Three months ended June 30,		Increase/decrease	
	2018	2017		
Salaries, materials, equipment, depreciation of property, plant and equipment and other employee-related costs(1)	\$ 15,467	\$ 11,234	\$ 4,233	38 %
Subcontracted expenditure	12,755	9,590	3,165	33 %
Share-based compensation expense	2,071	871	1,200	138 %
Reimbursements for research and development tax and expenditure credits	(3,669)	(2,104)	(1,565)	74 %
	\$ 26,624	\$ 19,591	\$ 7,033	36 %

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

The net increase in our research and development expenses of \$7.0 million for the three months ended June 30, 2018 compared to the same period in 2017 was primarily due to the following:

- an increase of \$4.2 million in salaries, materials, equipment, depreciation of property, plant and equipment and other employee-related costs. The driver for these is the increase in the average number of employees engaged in research and development from 247 to 317;
- an increase of \$3.2 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 MAGE-A4, MAGE-A10 and AFP, and an increase in process development relating to manufacturing; and
- an increase in share-based compensation expense of \$1.2 million;

offset by:

an increase in reimbursements for research and development tax and expenditure credits of \$1.6 million.

Our subcontracted costs for the three months ended June 30, 2018 were \$12.8 million, compared to \$9.6 million in the same period of 2017. This includes \$8.1 million of costs associated with manufacturing for both the NY-ESO SPEAR T-cells and our internal pipeline, including our MAGE-A10 and MAGE-A4 and AFP SPEAR T-cells and \$4.7 million of costs associated with clinical trials, including \$1.4 million for the NY-ESO SPEAR T-cells.

Our research and development expenses are highly dependent on the phases and progression of our research projects and therefore fluctuate from period to period. We anticipate that our research and development expenses will be higher in the year ended December 31, 2018 compared to the year ended December 31, 2017. The increase in research and development is due to an increase in expenditure on clinical trials as enrollment in our clinical trials progress and we also expect to increase the number of staff employed in our research and development departments in order to invest in our future pipeline of SPEAR T-cells, develop our platform and manage clinical trials and further developing our manufacturing capabilities at our U.S. facility. This will significantly increase the related salaries and share-based compensation expenses, as well as require higher expenditures on facilities, materials and equipment.

General and Administrative Expenses

General and administrative expenses increased by 46% to \$11.3 million for the three months ended June 30, 2018 from \$7.7 million in the same period in 2017.

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The net increase of \$3.6 million was primarily due to an increase in personnel costs and share-based compensation expense, due to the addition of key management and other professionals, an increase in costs associated with developing our IT infrastructure, and an increase in other costs to support our growth.

We expect that our general and administrative expenses will continue to increase as we continue to expand our operations.

Other Income (Expense), Net

Other income (expense), net was an expense of \$15.4 million for the three months ended June 30, 2018 compared to an income of \$3.2 million for the three months ended June 30, 2017. Other income (expense), net primarily relates to unrealized foreign exchange gains and losses on cash, cash equivalents and intercompany loans held in U.S. dollars by our U.K. subsidiary. Unrealized foreign exchange losses have increased primarily due to a decrease in our cash balances arising as a consequence of our investment of cash and cash equivalents into marketable securities. The unrealized foreign exchange gains (losses) arising on marketable securities are recognized within Other Comprehensive Income.

Income taxes

Income taxes decreased by 38% to \$102,000 for the three months ended June 30, 2018 from \$165,000 for the three months ended June 30, 2017 due to the impact of US R&D tax credits. Income taxes arise in the United States and we incur losses in the United Kingdom.

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Comparison of Six Months Ended June 30, 2018 and 2017

The following table summarizes the results of our operations for the six months ended June 30, 2018 and 2017, together with the changes to those items (in thousands).

	Six months ended June 30,		Increase/decrease	
	2018	2017		
Revenue	\$ 17,234	\$ 6,378	\$ 10,856	170 %
Research and development expenses	(52,016)	(38,206)	(13,810)	36 %
General and administrative expenses	(22,495)	(14,173)	(8,322)	59 %
Total operating expenses	(74,511)	(52,379)	(22,132)	42 %
Operating loss	(57,277)	(46,001)	(11,276)	25 %
Interest income	1,199	746	453	61 %
Other income, net	(8,276)	3,654	(11,930)	(326)%
Loss before income taxes	(64,354)	(41,601)	(22,753)	55 %
Income taxes	(229)	(396)	167	(42)%
Loss for the period	\$ (64,583)	\$ (41,997)	\$ (22,586)	54 %

Revenue

Revenue increased by \$10.8 million to \$17.2 million in the six months ended June 30, 2018 compared to \$6.4 million for the six months ended June 30, 2017. Revenue in the six months ended June 30, 2018 was recognized due to the continued performance under the NY-ESO transition program and the PRAME development plan. The revenue benefited from a change in the estimate of variable consideration of \$10.4 million due to additional development milestones being considered probable, which was partially offset by \$5.1 million arising due to a change in percentage of completion.

Revenue for the six months ended June 30, 2018 has been recognized under new accounting guidance which is effective January 1, 2018. Revenue in the comparative period of 2017 has been recognized under the previous guidance. Revenue in the six months ended June 30, 2018 under the previous guidance would be \$12.3 million, compared to \$6.4 million for the same period of 2017. The significant increase in revenue compared to the same period of 2017 has arisen due to a reduction in the period over which we are recognizing revenue following GSK's exercise of the option over the NY-ESO program in September 2017 and additional milestones achieved in the second half of 2017 and the first quarter of 2018 of \$14.4 million, which are recognized over the period we are providing services to GSK.

Future revenues will fluctuate depending on the progress of the transition and development program for NY-ESO and development program for the second target, PRAME, which is difficult to predict. However, the Investigational New Drug Application ("IND") for the NY-ESO program and the responsibility for the NY-ESO program transferred to GSK on July 23, 2018. Therefore, we anticipate that \$0.9 million of revenue allocated to NY-ESO program and \$39.6 million of revenue allocated to the exclusive license to research, develop, and commercialize the Company's NY-ESO SPEAR T-cell therapy program will be recognized in the third quarter of 2018. A further \$2.1 million will be recognized over the next twelve months as the development of the second target, PRAME, progresses.

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[Table of Contents](#)**Research and Development Expenses**

Research and development expenses increased by 36% to \$52.0 million for the six months ended June 30, 2018 from \$38.2 million for the six months ended June 30, 2017. Our research and development expenses comprise the following (in thousands):

	Six months ended June 30,		Increase/decrease	
	2018	2017		
Salaries, materials, equipment, depreciation of property, plant and equipment and other employee-related costs(1)	\$ 30,596	\$ 22,485	\$ 8,111	36 %
Subcontracted expenditure	25,019	17,295	7,724	45 %
Share-based compensation expense	4,285	2,230	2,055	92 %
Payments for in-process research and development	—	501	(501)	(100)%
Reimbursements for research and development tax and expenditure credits and government grants	(7,884)	(4,305)	(3,579)	83 %
	<u>\$ 52,016</u>	<u>\$ 38,206</u>	<u>\$ 13,810</u>	<u>36 %</u>

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

The net increase in our research and development expenses of \$13.8 million for the six months ended June 30, 2018 compared to the same period in 2017 was primarily due to the following:

- an increase of \$8.1 million in salaries, materials, equipment, depreciation of property, plant and equipment and other employee-related costs. The driver for these is the increase in the average number of employees engaged in research and development from 244 to 309;
- an increase of \$7.7 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 MAGE-A4, MAGE-A10 and AFP, and an increase in process development relating to manufacturing; and
- an increase in share-based compensation expense of \$2.1 million;

offset by:

- a decrease of \$0.5 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 of \$3.6 million.

Our subcontracted costs for the six months ended June 30, 2018 were \$25.0 million, compared to \$17.3 million in the same period of 2017. This includes \$14.8 million of costs associated with manufacturing for both the NY-ESO SPEAR T-cells and our internal pipeline, including our MAGE-A10 and MAGE-A4 and AFP SPEAR T-cells and \$10.2 million of costs associated with clinical trials, including \$2.7 million for the NY-ESO SPEAR T-cells.

Our research and development expenses are highly dependent on the phases and progression of our research projects and therefore fluctuate from period to period. We anticipate that our research and development expenses will be higher in the year ended December 31, 2018 compared to the year ended December 31, 2017. The increase in research and development is due to an increase in expenditure on clinical trials as enrollment in our clinical trials progress and we also expect to increase the number of staff employed in our research and development departments in order to invest in our future pipeline of SPEAR T-cells, develop our platform and manage clinical trials and further developing our manufacturing capabilities at our U.S. facility. This will significantly increase the related salaries and share-based compensation expenses, as well as require higher expenditures on facilities, materials and equipment.

General and Administrative Expenses

General and administrative expenses increased by 59% to \$22.5 million for the six months ended June 30, 2018 from \$14.2 million in the same period in 2017.

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The net increase of \$8.3 million was primarily due to an increase in personnel costs and share-based compensation expense, due to the addition of key management and other professionals, an increase in costs associated with developing our IT infrastructure, and an increase in other costs to support our growth.

We expect that our general and administrative expenses will continue to increase as we continue to expand our operations.

Other Income (Expense), Net

Other income (expense), net was an expense of \$8.3 million for the six months ended June 30, 2018 compared to an income of \$3.7 million for the six months ended June 30, 2017. Other income (expense), net primarily relates to unrealized foreign exchange gains and losses on cash, cash equivalents and intercompany loans held in U.S. dollars by our U.K. subsidiary. Unrealized foreign exchange losses have increased primarily due to a decrease in our cash balances arising as a consequence of our investment of cash and cash equivalents into marketable securities. The unrealized foreign exchange gains (losses) arising on marketable securities are recognized within Other Comprehensive Income.

Income taxes

Income taxes decreased by 42% to \$229,000 for the six months ended June 30, 2018 from \$396,000 for the six months ended June 30, 2017 due to the impact of US R&D tax credits. Income taxes arise in the United States and we incur 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 Agreement, government grants and research and development tax and expenditure credits. From inception through to June 30, 2018, we have raised:

- \$413.3 million, net of issue costs, through the issuance of shares, including \$176.0 million raised through our initial public offering in May 2015, \$61.4 million raised through a follow-on public offering in March 2017 and \$41.8 million raised through a registered direct offering in April 2017;
- \$122.4 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
- \$13.7 million in the form of reimbursable 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 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 June 30, 2018, we had cash and cash equivalents of \$42.3 million and Total Liquidity of \$129.0 million. We believe that our Total Liquidity and income from GSK upon transition of the NY-ESO program will be sufficient to fund our operations, based upon our currently anticipated research and development activities and planned capital spending, through to early 2020.

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Cash Flows

The following table summarizes the results of our cash flows for the six months ended June 30, 2018 and 2017 (in thousands).

	Six months ended June 30,	
	2018	2017
Net cash used in operating activities	\$ (82,642)	\$ (46,448)
Net cash provided by (used in) investing activities	34,012	(95,821)
Net cash provided by financing activities	2,424	103,198
Cash, cash equivalents and restricted cash	46,507	126,154

Operating Activities

Net cash used in operating activities increased by \$36.2 million to \$82.6 million for the six months ended June 30, 2018 from \$46.4 million for the six months ended June 30, 2017. The increase in cash used in operations was primarily the result of the 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 due to the expansion of our operations.

Net cash used in operating activities of \$82.6 million for the six months ended June 30, 2018 comprised a net loss of \$64.6 million and a net cash outflow of \$35.7 million from changes in operating assets and liabilities, offset by noncash items of \$17.7 million. The noncash items consisted primarily of depreciation expense on plant and equipment of \$3.5 million, share-based compensation expense of \$8.4 million, a realized loss on sale of marketable securities of \$2.5 million and unrealized foreign exchange losses of \$2.9 million.

Investing Activities

Net cash used in investing activities of \$34.0 million for the six months ended June 30, 2018 and net cash provided by investing activities of \$95.8 million for the six months ended June 30, 2017, consisted of:

- purchases of property and equipment of \$3.1 million and \$21.2 million for the six months ended June 30, 2018 and 2017, respectively;
- cash outflows from investment in marketable securities of \$33.6 million and \$79.8 million for the six months ended June 30, 2018 and 2017, respectively, and cash inflows from maturity or redemption of marketable securities of \$70.7 million for the six months ended June 30, 2018; and
- investment in short-term cash deposits with maturities greater than three months but less than 12 months of \$22.8 million and cash inflows from maturity of short-term deposits of \$18.0 for the six months ended June 30, 2017.

Financing Activities

Net cash from financing activities of \$2.4 million in the six months ended June 30, 2018, consisted of proceeds from share option exercises, and net cash from financing activities for the six months ended June 30, 2017 of \$103.2 million consisted of proceeds from a follow-on public offering of ADSs of \$61.4 million in March 2017 and proceeds of \$41.8 million from a registered direct offering in April 2017.

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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 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):

	June 30, 2018	December 31, 2017
Cash and cash equivalents	\$ 42,312	\$ 84,043

Marketable securities		86,716	124,218
Total Liquidity		\$ 129,028	\$ 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 investments, which are highly-liquid and available to use in our current operations, such as marketable securities.

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.

Contractual Obligations

For a discussion of our contractual obligations, see “Part II, Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations” in our 2017 Annual Report on Form 10-K. There have not been any material changes to our contractual obligations in the six months ended June 30, 2018.

Safe Harbor

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

Item 3. Quantitative and Qualitative Disclosures about Market Risk.

For a discussion of our quantitative and qualitative disclosures about market risk, see “Part II, Item 7A. Quantitative and Qualitative Disclosures about Market Risk” in our 2017 Annual Report on Form 10-K. There have been no material changes in the six months ended June 30, 2018.

Item 4. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, has evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e)) under the Securities and Exchange Act of 1934, as amended (“Exchange Act”) as of June 30, 2018. Based on such evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that, as of June 30, 2018, 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.

Changes in Internal Control over Financial Reporting

In January 2018, the Company 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 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 in the quarter ended March 31, 2018.

No changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the quarter ended June 30, 2018 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

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PART II - OTHER INFORMATION

Item 1. Legal Proceedings.

As of June 30, 2018, we were not a party to any material legal proceedings.

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 Quarterly Report, including our condensed 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.

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 the NY-ESO SPEAR T-cell), 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, 2017 and 2016 and six months ended December 31, 2015 and the year ended June 30, 2015, we incurred net losses of \$70.1 million, \$71.6 million, \$23.0 million and \$22.1 million, respectively. As of June 30, 2018, we had accumulated losses of \$287.6 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, the PRAME program and any future SPEAR T-cell programs under the collaboration and license agreement with GSK) and achieving a level of revenues adequate to support our cost structure. We may never achieve profitability, and unless and until we do, we will continue to need to raise additional cash.

We have never generated any revenue from sales of our 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 (including the NY-ESO SPEAR T-cell), 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:

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- 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 and the NY-ESO SPEAR T-cell 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 and the NY-ESO SPEAR T-cell for which we or our collaborator complete clinical trials;
- progressing our clinical trials within predicted timeframes and without any substantial delays, for example as may be caused by delays in patient recruitment, regulatory requirements to hold or suspend any clinical trials or delays in obtaining approvals required to conduct clinical trials;
- developing sustainable and scalable manufacturing and supply processes for our 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 the SPEAR T-cells is approved for commercial sale whether by us or by a collaborator, 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 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.

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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 June 30, 2018, we had \$42.3 million of cash and cash equivalents and \$86.7 million of marketable securities. We expect to use these funds to advance and accelerate the clinical development of our MAGE-A10, MAGE-A4 and AFP SPEAR T-cells, 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 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 (for example, completion of post-transition NY-ESO program activities and nomination of any further targets under the collaboration), may cause us to increase our spending significantly faster than we currently anticipate. We may require additional capital for the further development and commercialization of our 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 the NY-ESO SPEAR T-cell and our existing SPEAR T-cell candidates including the MAGE-A10SPEAR T-cell, MAGE-A4 SPEAR T-cell and AFP SPEAR T-cell, 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 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 or in other investigator-initiated clinical programs utilizing the NY-ESO therapeutic candidate 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.

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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 our 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 our 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 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 in the process of expanding our clinical trial foot print to Europe. This requires gaining the approval of country specific review bodies for GMO application and CTA. As this is not a harmonized process, the requirements can vary considerably and delays can be incurred at a country level.

In the USA, 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.

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 any 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 or our collaborator's 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.

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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 our or our collaborator's ability or inability to achieve regulatory approval or commercialization of SPEAR T-cells.

Use of any 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 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 SPEAR T-cells, the end users and medical personnel require a substantial amount of education and training in their administration of 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, for example CAR-T products, or in clinical trials conducted by our collaborators may impact on the further advancement of our clinical trials. Based on the data currently available to us in relation to our clinical trials there is no evidence that the type and severity of neurotoxic events observed with CD19-directed CAR-T cell treatments, in particular the fatal events observed in the NCT02535364 trial, occur with our SPEAR TCRs (including the NY-ESO SPEAR T-cell). 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.

Results seen in clinical trials using products that are used in our combination clinical trials, may impact on the further advancement of our clinical trials. For example, the FDA placed a clinical hold on three combination studies using KEYTRUDA (pembrolizumab), an anti-PD-1 therapy used to treat multiple myeloma. There is no guarantee that further reviews of safety data with KEYTRUDA or other anti-PD-1 therapies will not result in delays or holds to our clinical trials or the requirement to amend the protocol for such clinical trials.

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 SPEAR T-cell is not completely understood, which means that we cannot predict the long-term effects of treatment with SPEAR T-cells (whether by us or a collaborator). 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 (including the NY-ESO SPEAR T-cell) 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 or our collaborator's ability to conduct clinical trials, to obtain regulatory approvals, if at all, and to successfully commercialize any SPEAR T-cell.

Clinical trials and the investigator-initiated clinical trials using the NY-ESO TCR therapeutic are still in the early stages, and it is difficult to predict the results that will be obtained by our collaborator in ongoing clinical trials or the next phase or phases of any clinical program. Our SPEAR T-cells have not previously been tested in combination clinical trials, for example use in combination with Merck's PD-1 inhibitor, KEYTRUDA® (pembrolizumab) in patients with multiple myeloma. It is difficult to predict the way in which SPEAR T-cells will interact with third-party products used in combination clinical trials. Data seen in other combination trials with KEYTRUDA has resulted in certain combination trials with KEYTRUDA being placed on clinical hold by the FDA. We do not, as yet know, whether similar negative side effects will be seen

using KEYTRUDA in combination with the NY-ESO T-cell therapy. 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 the 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 any 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. Serious adverse events seen with other immunotherapy products, such as the severe neurotoxic events observed with CD19-directed CAR-T cell treatments, may also occur at any stage of the clinical program. Further, following infusion of any 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. 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.

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Common and more severe adverse events as of September 5, 2017 considered by investigators to be at least possibly related to administration of our SPEAR T-cells (including the NY-ESO SPEAR T-cell) include: fever, fatigue, chest pain, nausea, diarrhea, enterocolitis, anemia, leukopenia, neutropenia, febrile neutropenia, lymphopenia, thrombocytopenia, bone marrow failure, dehydration, hyponatremia, ALT increased, rhabdomyolysis, rash, acute inflammatory demyelinating polyradiculoneuropathy, dyspnea, hypoxia, pneumonitis, respiratory failure, pericardial effusion, supraventricular tachycardia, hypotension, embolism, CRS (including grade 3 and 4 events which resolved with treatment), and graft versus host disease (GVHD). There has been one report of fatal (grade 5) bone marrow failure, which was considered related to the study treatment regimen (preconditioning plus SPEAR T-cell). Internal investigations have not identified a mechanism by which NY-ESO SPEAR T-cells may have caused bone marrow failure. To date, GVHD, impacting the skin and gastrointestinal tract, has only been reported in our myeloma study involving autologous stem cell transplants (ASCT). Although GVHD is a known complication of ASCT, symptoms such as rash, enterocolitis and diarrhea have been reported in other SPEAR T-cell studies.

In addition to our Company sponsored clinical programs, the NY-ESO TCR therapeutic has also been used in an investigator-initiated clinical program funded by the European Union, referred to as the ATTACK 2 program. The therapy, which was produced under a different manufacturing process than Adaptimmune's NY-ESO TCR therapy, was being evaluated for the treatment of patients with advanced gastro-esophageal cancer. Two patients have been treated under this protocol, one of whom passed away 46 days after initial treatment. Said patient experienced enterocolitis and bone marrow failure followed by fatal gangrenous gastrointestinal necrosis and hemorrhage. The investigator determined there was a reasonable possibility that these events were caused by study treatment.

Enrollment in the trial was temporarily paused pending investigation of the patient fatality, but an independent data monitoring committee recommended that recruitment could resume following a protocol amendment. Despite this, the study is expected to terminate and is not currently recruiting.

Because administration 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. This risk may be increased where SPEAR T-cells are used in clinical programs that we do not control or sponsor and, should an error be made in the administration of our SPEAR T-cells in such clinical programs, this could affect the steps required in our own clinical programs and manufacturing process requiring the addition of further tracking mechanisms to ensure fail-safe tracking. 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.

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

Our SPEAR T-cells (including the NY-ESO SPEAR T-cell) and their potential associated risks are still under investigation. For example, there is a potential risk that, given that the TCR chains are produced separately and then assembled within patient T cells into full TCRs, the TCR chains from both transduced and naturally occurring T cells could be assembled into an unintended end TCR due to mis-pairing of TCR chains, which could create unknown recognition and cross-reactivity problems within patients. Although this phenomenon has not been reported in humans, it remains a theoretical risk for our 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 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 or our collaborators 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 MAGE-A10 SPEAR T-cell 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 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 MAGE-A10, presentation of the peptide antigen is seen in a lower number of patients than anticipated and with our AFP SPEAR T-cells recruitment of patients remains difficult due to the nature of the patient population targeted for the trial. This has delayed recruitment of patients into trials 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.

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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. For example, the standard of care in melanoma has changed since the start of our clinical trials in melanoma with the NY-ESO SPEAR T-cell and as a result the clinical trial has been halted due to anticipated unavailability of patients. 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.

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 and our collaborator's ability to advance the development of our SPEAR T-cells.

Comparability studies related to the manufacturing of any 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 such SPEAR T-cells. For example, comparability studies are ongoing in relation to changes made to the process for manufacture of the NY-ESO SPEAR T-cells. The results from these comparability studies may impact the start date for any registration 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 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.

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Manufacturing and administering SPEAR T-cells is complex and we and our collaborators may encounter difficulties in production, particularly with respect to process development or scaling up of manufacturing capabilities. If we or our collaborators encounter such difficulties, our or our collaborators' 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 SPEAR T-cells is complex and highly regulated. The manufacture of SPEAR T-cells involves complex processes, including manufacture of a lentiviral delivery vector containing the gene for our affinity-enhanced engineered TCR. Administration of 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 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 at 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, failure in any step of the manufacturing process, failure to maintain a GMP environment, 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 can not 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, 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 MAGE-A10 and MAGE-A4 SPEAR T-cells at our Navy Yard manufacturing facility. Should there be a contamination event at the facility resulting in the close-down of that facility it may not be possible to find alternative manufacturing capability for the MAGE-A10 and MAGE-A4 SPEAR T-cells 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

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- 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 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 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-aphere 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.

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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 both our Navy Yard facility and at our third party contract manufacturing facilities. 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 own manufacturing facility. 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 the facility is operated. This may result in a delay in our ability to manufacture SPEAR T-cells at our own facility. In addition, now our manufacturing facility is operating there is no guarantee that any SPEAR T-cells produced in such facility 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 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 clinical trials may fail to demonstrate adequately the safety and efficacy of any SPEAR T-cells which would prevent or delay regulatory approval and commercialization.

There is a risk in any clinical trial (whether sponsored by us, a collaborator, or investigator-initiated) that side effects from SPEAR T-cells will require a hold on, or termination of, clinical programs or further adjustments to clinical programs in order to progress any SPEAR T-cell. The SPEAR T-cells are novel and unproven and regulators will therefore require evidence that the SPEAR T-cells are safe before permitting clinical trials to commence and evidence that the SPEAR T-cells are safe 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 are safe, pure and 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 the SPEAR T-cells will not be sufficient to obtain regulatory approval unless we or our collaborators 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. For example, safety concerns have been reported in combination trials with KEYTRUDA which resulted in clinical holds to those combination trials. The clinical holds to such trials have not, as yet, impacted our own combination study with KEYTRUDA in multiple myeloma but there is no guarantee that the FDA or other regulatory authorities will not issue a similar hold in relation to our combination trials as data continues to emerge. Any such hold will require addressing by the us and our collaborators and will inevitably delay progression of the clinical trials concerned, if such clinical trials progress at all.

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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 predictive of later clinical trials. In addition, the results of trials in one set of patients or line of treatment may not be predictive of those obtained in another and protocols may need to be revised based on unexpected early results. For example, in our ovarian cancer trial with 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. This level of cytokine release syndrome had not been seen in previous patients from trials using the NY-ESO SPEAR T-cell. As another example, in both the European investigator-initiated clinical program in gastro-esophageal cancer and in our own sponsored synovial sarcoma trial 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 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 assessed. For example, the trial design for our MAGE-A4, MAGE-A10 and AFP trials includes dose escalation and therefore efficacy data may not be obtained from initial patients treated 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 or our collaborators do. Accordingly, more trials may be required before we can submit any 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 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.

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 states that are more limited than desirable. This could result in the failure of any products reaching the market or a reduction in the patient population for which any SPEAR T-cell can be used.

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Common and more severe adverse events as of September 5, 2017 considered by investigators to be at least possibly related to administration of SPEAR T-cells (including the NY-ESO SPEAR T-cell) include: fever, fatigue, chest pain, nausea, diarrhea, enterocolitis, anemia, leukopenia, neutropenia, febrile neutropenia, lymphopenia, thrombocytopenia, bone marrow failure, dehydration, hyponatremia, ALT increased, rhabdomyolysis, rash, acute inflammatory demyelinating polyradiculoneuropathy, dyspnea, hypoxia, pneumonitis, respiratory failure, pericardial effusion, supraventricular tachycardia, hypotension, embolism, CRS (including grade 3 and 4 events which resolved with treatment), and graft versus host disease (GVHD). There has been one report of fatal (grade 5) bone marrow failure, which was considered related to the study treatment regimen (preconditioning plus SPEAR T-cell). Internal investigations have not identified a mechanism by which NY-ESO SPEAR T-cells may have caused bone marrow failure. To date, GVHD, impacting the skin and gastrointestinal tract, has only been reported in our myeloma study involving autologous stem cell transplants (ASCT). Although GVHD is a known complication of ASCT, symptoms such as rash, enterocolitis and diarrhea have been reported in other SPEAR T-cell studies.

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 Adaptimmune 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. In addition to our Company sponsored clinical programs, the NY-ESO TCR therapeutic has also been used in an investigator-initiated clinical program funded by the European Union, referred to as the ATTACK 2 program. The therapy, which was produced under a different manufacturing process than Adaptimmune's NY-ESO TCR therapy, was being evaluated for the treatment of patients with advanced gastro-esophageal cancer for the first time. To date, two patients have been treated under this protocol, one of whom passed away 46 days after initial treatment. Said patient experienced enterocolitis and bone marrow failure followed by fatal gangrenous gastrointestinal necrosis and hemorrhage. The investigator determined there was a reasonable possibility that these events were caused by study treatment. Enrollment in the trial was temporarily paused pending investigation of the patient fatality. The investigator determined there was a reasonable possibility that these events were caused by study treatment. Enrollment in the trial was temporarily paused pending investigation of the patient fatality but an independent data monitoring committee has since recommended that recruitment can resume following a protocol amendment. Despite this, the study is expected to terminate and is not currently recruiting.

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-cells 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 use in combination with Merck'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. SPEAR T-cells have not previously been used in any combination clinical trials. 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. Adverse events seen in other clinical trials using the same combination product, for example other clinical combination trials using Merck's PD-1 inhibitor, KEYTRUDA® (pembrolizumab), may affect our ability to progress our own combination trial, resulting in pausing or holding of recruitment or require changes to be made to the protocol to the clinical trial. Merck has recently announced that the FDA has determined that the data available at the present time indicate that the risks of KEYTRUDA plus pomalidomide or lenalidomide outweigh any potential benefit for patients with multiple myeloma. All patients enrolled in KEYNOTE-183 and KEYNOTE-185 combination studies and those in the KEYTRUDA/lenalidomide/dexamethasone cohort in KEYNOTE-023 will discontinue investigational treatment with KEYTRUDA. This clinical hold does not currently apply to other studies with KEYTRUDA.

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

Clinical trials, depending on the stage, can be costly as well as difficult to implement and define, particularly with technologies that are not tried and tested, such as our 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.

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In particular, eligible patients must be screened for the target peptide and HLA type, which may reduce the number of patients who can be recruited for any clinical program. For example, low target peptide expression levels in the NY-ESO SPEAR T-cell and MAGE-A10 SPEAR T-cell programs affected speed of patient recruitment. The ability to administer 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 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. For example, in our Phase 1/2 melanoma trial with the NY-ESO SPEAR T-cell, there was a delay in enrollment as a result of competition from other emerging therapies. Identifying and qualifying patients, including testing of patients for appropriate target peptides 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
- ability to monitor patients adequately during and after treatment, for example where patients decide not to attend follow-up appointments.

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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 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 competition sooner than anticipated. Additionally, this period of regulatory exclusivity does not apply to companies pursuing regulatory approval via their own traditional BLA, rather than via the abbreviated pathway. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

Foreign countries also have abbreviated regulatory pathways for biosimilars and hence even where the FDA does not approve a biosimilar biologic, a biosimilar could be approved using an abbreviated regulatory pathway in other markets where our 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 the 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 the NY-ESO SPEAR T-cells or from us for other SPEAR T-cells.

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, the sponsor of an investigator-initiated trial, 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.

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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 obtained breakthrough therapy status for the 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. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. The FDA and foreign regulatory authorities also have substantial discretion in the drug and biologics approval process. The number and types of preclinical programs and clinical trials that will be required for regulatory approval varies depending on the SPEAR T-cell, the disease or condition that the SPEAR T-cell is designed to address, 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 or our collaborators' clinical trials;
- we or our collaborators 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 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;

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- our manufacturing processes or facilities or those of the third-party manufacturers we use 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 no 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 or our collaborators 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 or our collaborators intend to charge for SPEAR T-cells is also subject to approval.

We or our collaborators may also submit marketing 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 I; 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.

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

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

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- untitled or warning letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenue;
- suspension or withdrawal of regulatory approvals;
- refusal to permit the import or export of our products;
- product seizure;
- injunctions;
- imposition of civil penalties; or
- criminal prosecution.

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

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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.

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.

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A drug is clinically superior if it is safer, more effective or makes a major contribution to patient care. Orphan drug marketing exclusivity rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition. There can be no assurance that any 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 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.

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.

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

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

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 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

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- 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 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.

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Risks Related to the Commercialization of Our SPEAR T-cells

The market opportunities for 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.

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 SPEAR T-cells is based on published information. This information may not be accurate in relation to 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 the 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. 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 we or our collaborators 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.

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If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our 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;
- 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 or our collaborators 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 SPEAR T-cells are accepted in the market, including:

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

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- 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 SPEAR T-cells as well as competitive products;
- the cost of treatment in relation to alternative treatments;
- the availability of coverage, adequate reimbursement and pricing by third-party payors and government authorities;
- the willingness of patients to pay for SPEAR T-cells on an out-of-pocket basis in the absence of coverage by third-party payors and government authorities;
- relative convenience and ease of administration as compared to alternative treatments and competitive therapies; and
- the effectiveness of our sales and marketing efforts.

In addition, although we are not utilizing embryonic stem cells or replication competent vectors, adverse publicity due to the ethical and social controversies surrounding the therapeutic use of such technologies, and reported side effects from any clinical trials using these technologies or the failure of such trials to demonstrate that these therapies are safe and effective may limit market acceptance of 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 SPEAR T-cells achieve market acceptance, we or our collaborators may not be able to maintain that market acceptance over time if new products or technologies are introduced that are more favorably received than the SPEAR T-cells, are more cost effective or render the SPEAR T-cells obsolete.

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

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

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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, 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 SPEAR T-cells unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of the 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 SPEAR T-cells will depend significantly on the availability of coverage and adequate reimbursement from third-party payors for the 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 SPEAR T-cells, if we or our collaborators obtain regulatory approval;
- our or our collaborators' ability to set a price that is fair for our SPEAR T-cells;
- our or our collaborators' ability to generate revenue and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

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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 both in relation to the collaboration and license agreement and associated payments and also progression of the NY-ESO SPEAR T-cell therapy through to commercialization.

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.

On September 7, 2017, we announced that GSK exercised its option under the GSK Collaboration and License Agreement signed in 2014 to exclusively license the right to research, develop, and commercialize our NY-ESO SPEAR T-cell program. The NY-ESO program transitioned to GSK on July 23, 2018 (and was announced on July 24, 2018). The amount of time and level of resources required to complete all activities for the transition the program to GSK may impact on our ability to progress other wholly owned programs and divert resources required to further develop our SPEAR T-cells or the manufacturing process for our SPEAR T-cells. Additional work may also be required in order to successfully complete transition of the NY-ESO SPEAR T-cell program to GSK that is not currently planned or resourced.

The current development plans or any future development plan agreed upon between GSK and us, including those relating to the PRAME SPEAR T-cell and NY-ESO SPEAR T-cell, may be unsuccessful or fail to result in candidate therapies that are feasible for further development or commercialization. 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, the development plans agreed upon with GSK (whether relating to transition of the NY-ESO SPEAR T-cell or to the PRAME SPEAR T-cell) and any future development plans will be subject to change as a result of risks inherent with the development of any pharmaceutical, biological or gene therapy product. Changes 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 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.

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GSK and Novartis have publicly announced that Novartis has opt-in rights over GSK's current and future oncology research and development pipeline. As part of that announced transaction, GSK has sold the rights to GSK's marketed oncology portfolio, related R&D activities and the AKT Inhibitors currently in development. GSK has also agreed to grant Novartis preferred partner rights for co-development and commercialization of GSK's current and future oncology pipeline products for a period of 12.5 years from completion of the applicable transactions between GSK and Novartis. The 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 future 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.

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.

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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 partly 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 at each stage of the manufacturing process, 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.
- 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.

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

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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. As of December 31, 2017, Immunocore owns less than 5% of our ordinary shares. Certain of our shareholders also hold shares in Immunocore. Our scientific founder and advisor, Bent Jakobsen, is also an employee of Immunocore.

Due to several factors including the decrease in Immunocore's share ownership in 2017, the termination of the target collaboration agreement that terminated March 1, 2017 and our lack of common directors, the Company no longer considers Immunocore to be a related party, 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. The contents of this target database are highly confidential and if disclosed to a third party, either as a result of a breach of the confidentiality terms between us and Immunocore or through a change of control in Immunocore, our business could be adversely impacted.

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.

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.

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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.

In addition to our Company sponsored clinical programs, the NY-ESO TCR therapeutic has also been used in an investigator-initiated clinical program funded by the European Union, referred to as the ATTACK 2 program. The therapy, which was produced under a different manufacturing process than Adaptimmune's NY-ESO TCR therapy and was administered under a different protocol, was being evaluated for the treatment of patients with advanced gastro-esophageal cancer for the first time. To date, two patients have been treated under this protocol, one of whom passed away 46 days after initial treatment. Said patient experienced enterocolitis and bone marrow failure followed by fatal gangrenous gastrointestinal necrosis and hemorrhage. The investigator determined there was a reasonable possibility that these events were caused by study treatment. Enrollment in the trial was temporarily paused pending investigation of the patient fatality but an independent data monitoring committee has since recommended that recruitment can resume. Despite this, the study is expected to terminate and is not currently recruiting.

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 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

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 any SPEAR T-cells we have developed 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 SPEAR T-cells and the extent of commercialization possible in relation to such SPEAR T-cells.

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

We may be forced to litigate to enforce or defend our intellectual property rights against infringement and unauthorized use by competitors, and to protect our trade secrets. In so doing, we may place our intellectual property at risk of being invalidated, held unenforceable, narrowed in scope or otherwise limited. Further, an adverse result in any litigation or defense proceedings may increase the risk of non-issuance of pending applications. In addition, if any licensor fails to enforce or defend its intellectual property rights, this may adversely affect our ability to develop and commercialize our 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 enforcement of patents and other intellectual property rights, particularly those relating to pharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business.

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

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.

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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.

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.

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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 have also identified a family of third party patents under which a license may be required in relation to a structural component of our lentiviral vector (cPPT). Such license may be required prior to any commercialization of the NY-ESO SPEAR T-cell and depending on the timelines associated with such commercialization. The requirement for such a license and the scope of such license will depend on progression of the NY-ESO SPEAR T-cell through clinical programs. The NY-ESO program has now transitioned to GSK and GSK will determine any requirement for any license. We believe such licenses are available and can be negotiated.

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.

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 collaborators 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.

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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 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 & Development, Dr. Gwendolyn Binder, our Chief Technology Officer, 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.

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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' notice periods in the case of senior managers and mutual one and two 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, Dr. Binder, Mr. Bertrand and Mr. Rawcliffe must provide 60 days' written notice for termination without cause. This means that any of our employees in the United States, except for Dr. Amado, Dr. Binder, Mr. Bertrand and Mr. Rawcliffe, could leave our employment at any time, with or without notice. Our success also depends on our ability to continue to attract, retain and motivate highly skilled junior, mid-level and senior managers as well as junior, mid-level and senior scientific and medical personnel.

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

As of June 30, 2018, we had 398 full-time equivalent employees. As our development and commercialization plans and strategies develop, we must add a significant number of additional managerial, operational, sales, marketing, financial, and other personnel. Future growth will impose significant added responsibilities on members of management, including:

- 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;

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- 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 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 expect any competition to increase further as SPEAR T-cells and CAR-T technologies progress further.

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Within the TCR T-cell area, TCR T-cells are being developed by competitors that are directed towards a multitude of targets including: HPV-16 E6, KRAS, MAGE-A1, MAGE-A3, MAGE A3/A6, NRAS, NY-ESO-1, PRAME, TGFβRII frameshift antigen and WT1. 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 other competitors include, but are not limited to: 3T, Adaptive Biotechnologies, Baylor College, Bellicum, BioNTech, bluebird bio, Cell Medica Ltd, Fred Hutchinson Cancer Research Center, Immatics, Immunocellular Therapeutics, Immunocore, Intellia Therapeutics, Inc (with Ospedale SDan Raffaele), Juno Therapeutics, Kite Pharma (Gilead), Lion TCR LTD, MD Anderson Cancer Center, MediGene AG, NCI, Parker Institute, Roswell Park Cancer Institute, Takara Bio Inc, Takeda (T-CIRA), TCR x immunotherapies, T-Knife, Tmunity, Zelluna (with Oslo University Hospital) and Ziopharm Oncology.

From other immunotherapies we expect to see competition from the following technologies and third parties:

- 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). A number of companies and academic institutions are developing CAR-T cell products including but not limited to Allogene Therapeutics, Autolus, Baylor College of Medicine, Bellicum Inc, bluebird bio, Celyad, CARMA Therapeutics, Collectis, CRISPR Therapeutics, Mustang Bio, Novartis, Janssen (JNJ with Nanjing Legend), Juno Therapeutics, Kite Pharma (Gilead), 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, IL13 α 2, Lewis Y, L1-CAM, Mesothelin, MUC16, PSCA, PSMA and ROR1. Competitors include but are not limited to: Allogene Therapeutics, Amgen, Aurora Biopharma, Avid Biotics / Xyphos, Baylor College of Medicine, Cell Medica, Bellicum, BioNTech, Carisma Therapeutics (formerly CARMA Therapeutics), Carsgen, Collectis 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, Morphosys Tactiva Therapeutics, Xencor 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) 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, CytomX, Celgene, Fate Therapeutics, Fortress Biotech, Gadeta (with Kite Pharma), Gamma Delta Therapeutics (with Takeda), Gamida cell, Glycostem Therapeutics, iCell Gene Therapeutics, Immatics, Iovance Biotherapeutics (formerly Lion Bio), Multimmune, NantKwest, Sorrento Therapeutics, TapImmune/Marker Therapeutics, Tessa Therapeutics, TC Biopharm (with bluebird bio) WindMIL Therapeutics and Ziopharm Oncology.

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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.

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.

On June 23, 2016, a majority of voters in the United Kingdom elected to withdraw from the European Union in a national referendum. Intention to withdraw from the European Union was provided to the European Council on March 29, 2017. This notification has triggered a negotiation period for the terms of withdrawal from the European Union that may last for at least two years. The decision to withdraw from the European Union has created significant uncertainty about the future relationship between the United Kingdom and the European Union, including with respect to the laws and regulations that will apply as the United Kingdom determines which European Union laws to replace or replicate in the event of a withdrawal. It is not known at this time how Brexit will impact the relationship between the United Kingdom and the European Union. Any negotiated relationship could negatively impact the free movement of goods and individuals between the United Kingdom and the European Union or required additional presence (directly or indirectly) to be established within the European Union in order to support clinical trials within the European Union. The decision to withdraw and ongoing Brexit negotiations have also caused significant market volatility and currency exchange rate fluctuations. These developments, or the perception that any of them could occur, may have a material adverse effect on global economic conditions and the stability of global financial markets, and may significantly reduce global market liquidity and restrict the ability of key market participants to operate in certain financial markets. Any of these factors could depress economic activity and restrict our access to capital, which could have a material adverse effect on our business, financial condition and results of operations and reduce the price of our securities. In addition, currency exchange rates in the pounds sterling and the euro with respect to each other and the U.S. dollar have already been adversely affected by these developments. Should this foreign exchange volatility continue, it could cause volatility in our quarterly financial results which may affect the market price of our ADSs.

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.

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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, 2017. 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;
- 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 SPEAR T-cells;

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- 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 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 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.

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 June 30, 2018, an aggregate of 43,014,310 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.

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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 will apply to us when we cease to be an emerging growth company. 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. 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.

In the future, we may not be exempt from various reporting requirements that apply to us as an emerging growth company. For example, while the Sarbanes-Oxley Act currently requires us, among other things, to assess the effectiveness of our internal control over financial reporting annually and to assess the effectiveness of our disclosure controls and procedures quarterly, once we cease to be an emerging growth company our independent registered public accounting firm will be required to attest to and report on the effectiveness of our internal control over financial reporting which will require us to incur substantial accounting expenses and expand significant management time on compliance related issues.

For as long as we are an emerging growth company, the reduced disclosure requirements applicable to emerging growth companies may make our ADSs less attractive to investors.

We are an “emerging growth company,” as defined in the Jumpstart Our Business Start-ups Act of 2012, or the JOBS Act, and have elected to take advantage of the following provisions of the JOBS Act: the exemption from the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act; not providing all of the compensation disclosure that may be required of non-emerging growth public companies under the U.S. Dodd-Frank Wall Street Reform and Consumer Protection Act; not disclosing certain executive compensation-related items such as the correlation between executive compensation and performance and comparisons of the Chief Executive Officer’s compensation to employee compensation; not complying with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor’s report providing additional information about the audit and the financial statements (auditor discussion and analysis and an extended transition period to comply with new or revised accounting standards applicable to public companies). In addition we have elected to take advantage of (1) reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements; and (2) exemptions from the requirements of holding a non-binding advisory vote on executive compensation including golden parachute compensation. As a result of these elections, our future financial statements may not be comparable to companies that comply with these obligations and our investors may not have access to certain information they may deem important.

Our independent registered public accounting firm will not be required to provide an attestation report on the effectiveness of our internal control over financial reporting as long as we qualify as an “emerging growth company,” which may increase the risk that weaknesses or deficiencies in our internal control over financial reporting go undetected and may make it more difficult for investors and securities analysts to evaluate our company. We may take advantage of these reporting exemptions until we are no longer an emerging growth company. We will remain an emerging growth company until the earliest of (i) December 31, 2020, (ii) the last day of the fiscal year (a) in which we have total annual gross revenue of at least \$1.07 billion or (b) in which we are deemed to be a large accelerated filer, which requires the market value of our ordinary shares that are held by non-affiliates to exceed \$700.0 million as of the prior June 30th, and (iii) the date on which we have issued more than \$1.0 billion in non-convertible debt during the prior three-year period. We cannot predict if investors will find our ADSs less attractive because we may rely on these exemptions. If some investors find our ADSs less attractive, there may be a less active trading market for our ADSs, and the price of our ADSs may be more volatile and may decline. We currently expect that, as of December 31, 2018, we will no longer be an emerging growth company.

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

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

The presence of material weaknesses could result in financial statement errors which, in turn, could lead to errors in our financial reports, delays in our financial reporting, could require us to restate our operating results or our auditors may be required to issue a qualified audit report. We might not identify one or more material weaknesses in our internal controls in connection with evaluating our compliance with Section 404(a) of the Sarbanes-Oxley Act. In order to maintain and improve the effectiveness of our disclosure controls and procedures and internal controls over financial reporting, we will need to expend significant resources and provide significant management oversight. Implementing any appropriate changes to our internal controls may require specific compliance training of our directors and employees, entail

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

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

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

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

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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 that may have anti-takeover effects do not apply to us.

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 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.

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

None.

Item 3. Defaults Upon Senior Securities.

None.

Item 4. Mine Safety Disclosures.

Not applicable.

Item 5. Other Information.

None.

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Item 6. Exhibits.

The following exhibits are either provided with this Quarterly Report on Form 10-Q or are incorporated herein by reference:

<u>Exhibit Number</u>	<u>Description of Exhibit</u>
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†**	Amendment Agreement No. 6, dated July 20, 2018 between Adaptimmune Limited and GlaxoSmithKline Intellectual Property Development Ltd.
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.

* Previously filed.

** Filed herewith.

† Confidential treatment to be requested as to portions of the exhibit. Confidential materials omitted and filed separately with the Securities and Exchange Commission.

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SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

ADAPTIMMUNE THERAPEUTICS PLC

August 2, 2018

/s/ James Noble
James Noble
Chief Executive Officer

August 2, 2018

/s/ Adrian Rawcliffe
Adrian Rawcliffe
Chief Financial Officer

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EXECUTION COPY

CONFIDENTIAL INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY [***], HAS BEEN OMITTED AND FILED SEPARATELY WITH THE SECURITIES AND EXCHANGE COMMISSION PURSUANT TO RULE 24B-2 UNDER THE SECURITIES EXCHANGE ACT OF 1934, AS AMENDED. AMENDMENT AGREEMENT NO. 6

DATED: 20th July 2018 (“Amendment Effective Date”)

PARTIES

- (1) **ADAPT IMMUNE LIMITED** a company incorporated in the United Kingdom under number 06456741 whose registered office is at 91 Milton Park, Abingdon, Oxon OX14 4RY, United Kingdom (“**Adaptimmune**”); and
- (2) **GLAXOSMITHKLINE INTELLECTUAL PROPERTY DEVELOPMENT LTD** whose registered office is at 980 Great West Road, Middlesex, TS8 9GS, United Kingdom (“**GSK**”).

BACKGROUND

- (A) GSK and Adaptimmune entered into a Collaboration and Licence Agreement with effective date of May 30, 2014, which was amended by Amendment Agreement No 1 (with Amendment Effective date of 08 May 2015) and Amendment Agreement No. 2 (with Amendment Effective date of 02 February 2016), Amendment Agreement No. 3 (with Amendment Effective date of 29 September 2016), Amendment Agreement No. 4 dated 11 November 2016 and Amendment Agreement No. 5 (with Amendment Effective date of 7 September 2017) (the “**Collaboration Agreement**”).
- (B) GSK and Adaptimmune now want to amend the Collaboration Agreement in accordance with Section 16.8 of the Collaboration Agreement, as set out in this sixth Amendment Agreement.

1. DEFINITIONS

- 1.1 In this Amendment Agreement words and expressions shall have the same meaning as set out in the Collaboration Agreement save as explicitly provided otherwise in this section 1.1 or elsewhere in this Amendment Agreement:

Amendment Agreement	Shall mean this amendment agreement.
Amendment Effective Date	Shall mean the date set out above.

- 1.2 In this Amendment Agreement:

- 1.2.1 References to sections and clauses are to sections and clauses of this Amendment Agreement unless otherwise provided;
- 1.2.2 Headings are used for convenience only and do not affect interpretation of the terms;
- 1.2.3 (a) the word “including” shall be deemed to be followed by the phrase “without limitation” or like expression; (b) the singular shall include the plural and vice versa; and (c) masculine, feminine and neuter pronouns and expressions shall be interchangeable; and
- 1.2.4 References to a statutory provision include references to the statutory provision as modified or re-enacted or both from time to time and to any subordinate legislation made under the statutory provision.

2. EFFECT OF AMENDMENTS

- 2.1 The amendments set out in section 3 below shall come into effect on the Amendment Effective Date and shall amend the Collaboration Agreement as from the Amendment Effective Date.
- 2.2 Save as explicitly amended by this Amendment Agreement, the Collaboration Agreement will continue in full force and effect in accordance with the terms set forth therein. In the event of a conflict of terms between this Amendment Agreement and the Collaboration Agreement, the terms of this Amendment Agreement shall control.

3. AMENDMENTS

- 3.1 The definition of the Anticipated Transition Date shall be deleted and replaced with the following definition:
 ““**Anticipated Transition Date**” shall mean 20 July 2018.”
- 3.2 The Transition Plan will be amended as set out in Exhibit 1 to this Agreement.
- 3.3 Schedule 2 to the Collaboration Agreement will be amended and further clarified as set out in Exhibit 2 to this Agreement.
- 3.4 In addition to any communication of information required under the Collaboration Agreement, GSK agrees to provide the following information to Adaptimmune on the terms set forth below.

- 3.4.1 The following items would be provided as soon as possible after GSK becomes aware of such items and in any event within 48 hours of awareness:
- (a) [***];
- (b) [***]; and

(c) [***].

In relation to communications provided under clause 3.4.1 above, Adaptimmune anticipates a potential need to make a press release or other announcement in accordance with applicable laws including stock exchange rules and regulations. Adaptimmune will assess such requirement on provision of the information (and in any case within 24 hours after receipt) and if determined by legal counsel that a press release or announcement is required due to the materiality of the information provided, Adaptimmune will work with GSK to agree the form and contents of such release. [***]. Depending on the materiality of the information, the press release may need to be reviewed and agreed very quickly and the Parties agree to work together to enable such release to occur within required timelines. GSK will have final approval on the form and content of the data in the release.

3.4.2 Except as provided below in this clause 3.4.2, the following items would only be communicated at GSK’s discretion:

- (a) [***];
- (b) [***]
- (c) [***]; and
- (d) [***],

Provided that where any of the foregoing items in Section 3.4.2(a) — (d) are going to be publicly disclosed by GSK either directly through a press release or the like, or indirectly by complying with applicable laws and regulations (e.g. an update to clinicaltrials.gov), GSK will use reasonable efforts to inform Adaptimmune at least 48 hours prior to any such public disclosure. All such communications under this clause 3.4.2 shall be provided to Adaptimmune for information purposes only and Adaptimmune will hold such information as Confidential Information of GSK; provided, that in the event that Adaptimmune believes it is required under applicable laws to disclose any of the items in Section 3.4.2(a) — (d), then the principles set forth above in Section 3.4.1 regarding such releases shall apply *mutatis mutandis* to disclosures

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under this Section 3.4.2.

4. GENERAL

4.1 This Amendment Agreement is governed by and shall be construed in accordance with English law.

4.2 This Amendment Agreement together with the Collaboration Agreement (incorporating all schedules and exhibits) constitutes the entire agreement between the parties relating to its subject matter. Each party acknowledges that it has not entered into this Amendment Agreement on the basis of any warranty, representation, statement, agreement or undertaking except those expressly set out in this Amendment Agreement or the Collaboration Agreement (as amended). Each party waives any claim for breach of this Amendment Agreement, or any right to rescind this Amendment Agreement in respect of, any representation which is not an express provision of this Amendment Agreement together with the Collaboration Agreement (as amended). Nothing in this clause excludes any liability which either party may have to the other (or any right which either party may have to rescind this Amendment Agreement) in respect of any fraudulent misrepresentation or fraudulent concealment prior to the execution of this Amendment Agreement.

The parties agree to enter into, and be bound by, this Amendment Agreement by their duly authorised representatives as of the Amendment Effective Date.

SIGNED for and on behalf of **ADAPT IMMUNE LIMITED**:

 /s/ H.K. Tayton-Martin (signature)

 Chief Business Officer (position)

 H.K. Tayton-Martin (name)

SIGNED for and on behalf of **GLAXOSMITHKLINE INTELLECTUAL PROPERTY DEVELOPMENT LIMITED**:

_____ (signature)	_____ (signature)
Authorised Signatory For and on behalf of Edinburgh Pharmaceutical Industries Limited The Corporate Director (position)	Authorised Signatory For and on behalf of Glaxo Group Limited The Corporate Director (position)
_____ (name)	_____ (name)

Exhibit 1 — Amendments to Transition Plan

The following amendments will be made to the Transition Plan:

Provision or term being amended	Amendment
Multiple provisions	To the extent not already completed as at the Amendment Effective Date, all actions or deliverables required for delivery by [***] will be required by Anticipated Transition Date unless another date is set out in this Amendment Agreement or the parties mutually agree otherwise.
Paragraph 3.1.2. of the Transition Plan ([***], patient numbers)	An additional bullet point will be added to paragraph 3.1.2 as follows: “[***].”
Paragraph 3.1.2 of the Transition Plan ([***], amendment 1)	[***]. An additional bullet point will be added to paragraph 3.1.2 as follows: “[***].”
Paragraph 3.1.3 of the Transition Plan ([***], patient numbers)	[***] patients have been enrolled in to the MRCLS study. The second bullet point will be amended to read as follows: “Adaptimmune will continue to manage and conduct study up to Transition Date including enrolment of [***] patients. [***].”
Paragraph 3.1.7 of the Transition Plan ([***])	[***]
Paragraph 3.1.9 of the Transition Plan (ADP-0000-002 LTFU protocol)	[***]. GSK will manage and conduct the LTFU Protocol at these sites from the Transition Date and [***].
Paragraph 3.1.5 of the Transition Plan ([***] ADP-0011-008, Multiple myeloma combination study)	An additional bullet point will be added as follows: “[***].”
Paragraph 3.1.5 of the Transition Plan (ADP-	As of the Amendment Effective Date, there is

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Amendment Agreement No. 6 Exhibit 1

0011-008, Multiple myeloma combination study)	[***].
Paragraph 3.1.10 of the Transition Plan ([***])	Transfer of Study conduct for each site that participates in an ongoing NY-ESO study will require site contracts to be fully negotiated as of Anticipated Transition Date rather than [***] as currently provided. [***].
Paragraph 3.1.11 of Transition Plan ([***])	An additional bullet will be added as follows: “[***].”
Paragraph 5.3 of Transition Plan (CSRs)	For clarity, GSK will also be responsible for reporting obligations for ADP-01411 protocol in relation to long term follow-up of patients. For clarity, the [***].
Paragraph 8.4 of the Transition Plan ([***])	The following will be added to provisions relating to [***].
Paragraph 9.4 of Transition Plan ([***])	The following shall be added to the transfer activity relating to CDISC datasets and shall amend previous provisions where applicable: “[***].”
Paragraph 8 of Transition Plan (Database transfer)	The following additional paragraph shall be added: “[***].”
Paragraph 10 of the Transition Plan (Transfer of HBS Samples)	A new paragraph 10.1.5 shall be added as follows and paragraph 10.2 shall be amended accordingly: [***]
Paragraph 11 of the Transition Plan (publications)	The following additional publications will be added to paragraph 11.1 and GSK and Adaptimmune will work together to agree and progress the publications being submitted or published after the Transition Date. [***] In order for Adaptimmune to support publication of certain of the above publications after

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Amendment Agreement No. 6 Exhibit 1

	Transition Date, the parties shall work together to ensure provision of required datasets. Exhibit 1B sets out a process for agreeing provision of any additional datasets, should such be required to support the publications. [***]
Paragraph 12.2 of Transition Plan ([***])	[***]
Paragraph 12.3 ([***])	[***]
Paragraph 13.1.1 of Transition Plan ([***])	Paragraph 13.1.1 shall be amended to reflect the following: [***]

Paragraph 13.1.4 of the Transition Plan ([***)	[***)
Paragraph 13 of the Transition Plan ([***)	A new paragraph 13.1.5 will be added as follows: “[***)”
Exhibit A1 (Biomarkers, PGx)	[***)
Exhibit A1 (BRs)	[***)
New Provision ([***)	[***)
New Provision ([***)	[***)
New Provision ([***)	[***)
New Provision ([***)	[***)
New Provision ([***)	[***)
New Provision ([***)	[***)
New Provision ([***)	An additional paragraph will be added to the Transition Plan as follows: “[***)”
New Provision ([***)	[***)
New Provision ([***)	In anticipation of the Transition Date, [***)
Preclinical data transfer	[***)

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Amendment Agreement No. 6 Exhibit 1

File Transfer	[***)
New Provision (sharing of safety information)	Following the Transition Date, the sharing of safety data between ADP and GSK will be governed by the separate Letter of Understanding executed between the parties prior to the Transition Date.

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Amendment Agreement No. 6 Exhibit 1

Exhibit 1A — Inventory of Manufactured Patient Product

Amendment Agreement No. 6 Exhibit 2

THIS PAGE HAS BEEN OMITTED AND FILED SEPARATELY WITH THE SECURITIES AND EXCHANGE COMMISSION PURSUANT TO A REQUEST FOR CONFIDENTIAL TREATMENT

[***)

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Amendment Agreement No. 6 Exhibit 2

Exhibit 1B — Required datasets

THIS PAGE HAS BEEN OMITTED AND FILED SEPARATELY WITH THE SECURITIES AND EXCHANGE COMMISSION PURSUANT TO A REQUEST FOR CONFIDENTIAL TREATMENT

[***)

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Amendment Agreement No. 6 Exhibit 2

EXHIBIT 2 — SCHEDULE 2 clarifications

Schedule 2 shall be amended and clarified as follows. Save as provided explicitly below existing milestones and payments under Schedule 2 shall remain as previously provided.

In addition to the milestones set out currently in Schedule 2 or by way of further clarification to certain of those milestones (such modifications or clarification italicised below):

- As of the Transition Date, GSK will pay to Adaptimmune a milestone equivalent to [***]
- As of the Transition Date, GSK will pay to Adaptimmune a milestone equivalent to [***].
- As of the Transition Date, GSK will pay to Adaptimmune the amount of [***]
- *As of the Transition Date, GSK will pay an amount of [***].*
- Any further planned [***] activities would be set out in the Transition Plan. Further or additional activities, if any, at [***] would be agreed by the JSC. [***]
- *In accordance with the [***].*
- *To the extent that Adaptimmune is [***].*

- Where [***].

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Amendment Agreement No. 6 Exhibit 2

Form of Certification Required by Rule 13a-14(a) or 15d-14(a) under the Securities Exchange Act of 1934 as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

I, James Noble, certify that:

1. I have reviewed this quarterly report on Form 10-Q of Adaptimmune Therapeutics plc;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)), for the registrant and have:
 - a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
 - c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter that has materially affected or is reasonably likely to materially affect the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: August 2, 2018

/s/ James Noble
James Noble
Chief Executive Officer

Form of Certification Required by Rule 13a-14(a) or 15d-14(a) under the Securities Exchange Act of 1934 as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

I, Adrian Rawcliffe, certify that:

1. I have reviewed this quarterly report on Form 10-Q of Adaptimmune Therapeutics plc;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)), for the registrant and have:
 - a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
 - c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter that has materially affected or is reasonably likely to materially affect the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: August 2, 2018

/s/ Adrian Rawcliffe
Adrian Rawcliffe
Chief Financial Officer

Section 906 Certificate

Certification Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 (subsections (a) and (b) of Section 1350, Chapter 63 of Title 18, United States Code), I, James Noble, Chief Executive Officer of Adaptimmune Therapeutics plc, a public limited company incorporated under English law (the "Company"), hereby certify, to my knowledge, that:

1. The Company's Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2018, to which this Certification is attached as Exhibit 32.1 (the "Quarterly Report") fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
2. The information contained in the Quarterly Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: August 2, 2018

/s/ James Noble
James Noble
Chief Executive Officer

Section 906 Certificate

Certification Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 (subsections (a) and (b) of Section 1350, Chapter 63 of Title 18, United States Code), I, Adrian Rawcliffe, Chief Financial Officer of Adaptimmune Therapeutics plc, a public limited company incorporated under English law (the "Company"), hereby certify, to my knowledge, that:

1. The Company's Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2018, to which this Certification is attached as Exhibit 32.2 (the "Quarterly Report") fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
2. The information contained in the Quarterly Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: August 2, 2018

/s/ Adrian Rawcliffe
Adrian Rawcliffe
Chief Financial Officer
