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, 2019

OR

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

Commission File Number 001-37368

ADAPTIMMUNE THERAPEUTICS PLC
(Exact name of Registrant as specified in its charter)

England and Wales	**Not Applicable**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

60 Jubilee Avenue, Milton Park
Abingdon, Oxfordshire OX14 4RX
United Kingdom
(Address of principal executive offices)

(44) 1235 430000
(Registrant's telephone number, including area code)

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

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

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

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

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

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

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting 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 29, 2019, the number of outstanding ordinary shares par value £0.001 per share of the Registrant is630,762,860.

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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 ADP-A2M4 (MAGE-A4) and ADP-A2AFP (AFP) products through clinical development and the timing within which we can recruit patients and treat patients in all of 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");
- 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; 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, 2019	December 31, 2018
Assets		
Current assets		
Cash and cash equivalents	$ 34,574	$ 68,379
Marketable securities - available-for-sale debt securities	98,832	136,755
Accounts receivable, net of allowance for doubtful accounts of $0 and $0	3,809	192
Other current assets and prepaid expenses (including current portion of clinical materials)	37,918	25,769
Total current assets	**175,133**	**231,095**
Restricted cash	4,403	4,097
Clinical materials	2,690	3,953
Operating lease right-of-use assets, net of accumulated amortization	21,507	—
Property, plant and equipment, net of accumulated depreciation of $19,528 (2018: $15,924)	33,722	36,118
Intangibles, net of accumulated amortization	2,066	1,473
Total assets	$ **239,521**	$ **276,736**
Liabilities and stockholders' equity		
Current liabilities		
Accounts payable	4,344	4,083
Operating lease liabilities, current	2,338	—
Accrued expenses and other accrued liabilities	18,595	20,354
Deferred revenue	3,016	—
Total current liabilities	**28,293**	**24,437**
Operating lease liabilities, non-current	23,666	—
Other liabilities, non-current	571	5,414
Total liabilities	**52,530**	**29,851**
Stockholders' equity		
Common stock - Ordinary shares par value $0.001, 785,857,300 authorized and 630,672,578 issued and outstanding (2018: 701,103,126 authorized and 627,454,270 issued and outstanding)	943	939
Additional paid in capital	581,245	574,208
Accumulated other comprehensive loss	(8,199)	(9,763)
Accumulated deficit	(386,998)	(318,499)
Total stockholders' equity	**186,991**	**246,885**
Total liabilities and stockholders' equity	$ **239,521**	$ **276,736**

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,	
	2019	2018	2019	2018
Revenue	**$ 157**	**$ 9,038**	**$ 157**	**$ 17,234**
Operating expenses				
Research and development	(25,511)	(26,624)	(47,530)	(52,016)
General and administrative	(10,148)	(11,291)	(21,921)	(22,495)
Total operating expenses	**(35,659)**	**(37,915)**	**(69,451)**	**(74,511)**
Operating loss	**(35,502)**	**(28,877)**	**(69,294)**	**(57,277)**
Interest income	757	540	1,709	1,199
Other expense, net	(6,277)	(15,406)	(847)	(8,276)
Loss before income taxes	**(41,022)**	**(43,743)**	**(68,432)**	**(64,354)**
Income taxes	(65)	(102)	(67)	(229)
Net loss attributable to ordinary shareholders	**$ (41,087)**	**$ (43,845)**	**$ (68,499)**	**$ (64,583)**
Net loss per ordinary share - Basic and diluted				
Basic and diluted	**$ (0.07)**	**$ (0.08)**	**$ (0.11)**	**$ (0.11)**
Weighted average shares outstanding:				
Basic and diluted	629,355,975	565,197,217	628,655,278	563,804,832

See accompanying notes to unaudited condensed consolidated financial statements.

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

	Three months ended June 30,		Six months ended June 30,	
	2019	2018	2019	2018
Net loss	**$ (41,087)**	**$ (43,845)**	**$ (68,499)**	**$ (64,583)**
Other comprehensive loss, net of tax				
Foreign currency translation adjustments, net of tax of $0, $0, $0 and $0	4,842	6,107	1,299	3,582
Unrealized gains on available-for-sale debt securities				
Unrealized holding gains on available-for-sale debt securities, net of tax of $0, $0, $0 and $0	68	5,223	278	1,167
Reclassification adjustment for (gains) losses on available-for-sale debt securities included in net loss, net of tax of $0, $0, $0 and $0	(13)	1,310	(13)	2,473
Total comprehensive loss for the period	**$ (36,190)**	**$ (31,205)**	**$ (66,935)**	**$ (57,361)**

See accompanying notes to unaudited condensed consolidated financial statements.

ADAPTIMMUNE THERAPEUTICS PLC
UNAUDITED CONDENSED CONSOLIDATED STATEMENTS 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 2019	627,454,270	$ 939	$ 574,208	$ (9,607)	$ (156)	$ (318,499)	$ 246,885
Net loss	—	—	—	—	—	(27,412)	(27,412)
Issuance of shares upon exercise of stock options	840,432	1	35	—	—	—	36
Foreign currency translation adjustments	—	—	—	(3,543)	—	—	(3,543)
Unrealized holding gains on available-for-sale debt securities, net of tax of $-	—	—	—	—	210	—	210
Share-based compensation expense	—	—	3,479	—	—	—	3,479
Balance as of March 31, 2019	**628,294,702**	**$ 940**	**$ 577,722**	**$ (13,150)**	**$ 54**	**$ (345,911)**	**$ 219,655**
Net loss	—	—	—	—	—	(41,087)	(41,087)
Issuance of shares upon exercise of stock options	2,377,876	3	327	—	—	—	330
Foreign currency translation adjustments	—	—	—	4,842	—	—	4,842
Unrealized holding gains on available-for-sale debt securities, net of tax of $-	—	—	—	—	68	—	68
Reclassification from accumulated other comprehensive income of gains on available-for-sale debt securities included in net income, net of tax of $-	—	—	—	—	(13)	—	(13)
Share-based compensation expense	—	—	3,196	—	—	—	3,196
Balance as of June 30, 2019	**630,672,578**	**$ 943**	**$ 581,245**	**$ (8,308)**	**$ 109**	**$ (386,998)**	**$ 186,991**

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

	Common stock	Common stock	Additional paid in capital	Accumulated other comprehensive loss: Accumulated foreign currency translation adjustments	Accumulated other comprehensive loss: Accumulated unrealized gains (losses) on available-for-sale debt securities	Accumulated deficit	Total stockholders' equity
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)	562,119,334	854	455,401	(17,867)	(3,774)	(222,985)	211,629
Net loss						(20,738)	(20,738)
Issuance of shares upon exercise of stock options	2,740,626	4	1,530	—	—	—	1,534
Other comprehensive loss before reclassifications							
Foreign currency translation adjustments	—	—	—	(2,525)	—	—	(2,525)
Unrealized holding losses on available-for-sale debt securities, net of tax of $-	—	—	—	—	(4,056)	—	(4,056)
Reclassification from accumulated other comprehensive income of losses on available-for-sale debt securities included in net income, net of tax of $-	—	—	—	—	1,163	—	1,163
Share-based compensation expense	—	—	4,672	—	—	—	4,672
Balance as of March 31, 2018	**564,859,960**	**$ 858**	**$ 461,603**	**$ (20,392)**	**$ (6,667)**	**$ (243,723)**	**$ 191,679**
Net loss						(43,845)	(43,845)
Issuance of shares upon exercise of stock options	1,636,440	2	887	—	—	—	889
Other comprehensive loss before reclassifications							—
Foreign currency translation adjustments	—	—	—	6,107	—	—	6,107
Unrealized holding gains on available-for-sale debt securities, net of tax of $-	—	—	—	—	5,223	—	5,223
Reclassification from accumulated other comprehensive loss of losses on available-for-sale debt securities included in net income, net of tax of $-	—	—	—	—	1,310	—	1,310
Share-based compensation expense	—	—	3,739	—	—	—	3,739
Balance as of June 30, 2018	**566,496,400**	**$ 860**	**$ 466,229**	**$ (14,285)**	**$ (134)**	**$ (287,568)**	**$ 165,102**

See accompanying notes to unaudited condensed consolidated financial statements.

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

	Six months ended June 30,	
	2019	**2018**
Cash flows from operating activities		
Net loss	$ (68,499)	$ (64,583)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	3,642	3,499
Amortization	333	304
Share-based compensation expense	6,675	8,411
Realized (gain) loss on available-for-sale debt securities	(13)	2,473
Unrealized foreign exchange losses	1,048	2,915
Other	(153)	16
Changes in operating assets and liabilities:		
Increase in receivables and other operating assets	(16,851)	(11,602)
Decrease in non-current operating assets	1,263	87
Increase (decrease) in payables and deferred revenue	2,184	(24,162)
Net cash used in operating activities	**(70,371)**	**(82,642)**
Cash flows from investing activities		
Acquisition of property, plant and equipment	(1,202)	(3,139)
Acquisition of intangibles	(922)	(10)
Maturity or redemption of marketable securities	54,324	70,717
Investment in marketable securities	(15,983)	(33,556)
Net cash provided by investing activities	**36,217**	**34,012**
Cash flows from financing activities		
Proceeds from exercise of stock options	366	2,424
Net cash provided by financing activities	**366**	**2,424**
Effect of currency exchange rate changes on cash, cash equivalents and restricted cash	289	4,417
Net decrease in cash and cash equivalents	(33,499)	(41,789)
Cash, cash equivalents and restricted cash at start of period	72,476	88,296
Cash, cash equivalents and restricted cash at end of period	$ **38,977**	$ **46,507**

See accompanying notes to unaudited condensed consolidated financial statements.

ADAPTIMMUNE 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 primarily focused on providing novel cell therapies to patients, particularly for the treatment of solid tumors. The Company's 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 ("SPEAR T-cells") for administration to patients. Using its affinity engineered TCRs, the Company aims to become the first company to have a TCR T-cell approved for the treatment of a solid tumor indication.

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 $387.0 million as of June 30, 2019.

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 consolidated 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 February 27, 2019 (the "Annual Report"). The balance sheet as of December 31, 2018 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, 2019, the Company adopted new guidance on the accounting for leases, which has been codified within Accounting Standard Codification Topic 842, Leases ("ASC 842"). 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, 2019. Therefore, the comparative financial information for the three and six months ended June 30, 2018 and as of December 31, 2018 has not been restated and continues to be reported under previous guidance. The effect of adopting ASC 842 on the accumulated deficit, total stockholders' equity and net assets as at January 1, 2019 was $0.

(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.

(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 8, Fair value measurements.

(d) Leases

On January 1, 2019, the Company adopted a new standard, Accounting Standard Update 2016-02 – Leases, which is codified in ASC 842. The comparative financial information for the three and six months ended June 30, 2018 and as of December 31, 2018 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 determines whether an arrangement is a lease at contract inception by establishing if the contract conveys the right to use, or control the use of, identified property, plant, or equipment for a period of time in exchange for consideration. Leases may be classified as finance leases or operating leases. All the Company's leases are classified as operating leases as they were previously classed as these and the lease classification is not reassessed on adoption of ASC 842. Operating lease right-of-use (ROU) assets and operating lease liabilities recognized in the Condensed Consolidated Balance Sheet represent the right to use an underlying asset for the lease term and an obligation to make lease payments arising from the lease respectively.

Operating lease ROU assets and operating lease liabilities are recognized at the lease commencement date based on the present value of minimum lease payments over the lease term. Since the rate implicit in the lease is not readily determinable, the Company uses its incremental borrowing rates (the rate of interest that the Company would have to pay to borrow on a collateralized basis over a similar term for an amount equal to the lease payments in a similar economic environment) based on the information available at commencement date in determining the discount rate used to calculate the present value of lease payments. As the Company has no external borrowings, the incremental borrowing rates are determined using information on indicative borrowing rates that would be available to the Company based on the value, currency and borrowing term provided by financial institutions, adjusted for company and market specific factors. The lease term is based on the non-cancellable period in the lease contract, and options to extend the lease are included when it is reasonably certain that the Company will exercise that option. Any termination fees are included in the calculation of the ROU asset and lease liability when it is assumed that the lease will be terminated.

The Company accounts for lease components (e.g. fixed payments including rent and termination costs) separately from non-lease components (e.g. common-area maintenance costs and service charges based on utilization) which are recognized over the period in which the obligation occurs.

At each reporting date, the operating lease liabilities are increased by interest and reduced by repayments made under the lease agreements. The right-of-use asset is subsequently measured for an operating lease at the amount of the remeasured lease liability (i.e. the present value of the remaining lease payments), adjusted for the remaining balance of any lease incentives received, any cumulative prepaid or accrued rent if the lease payments are uneven throughout the lease term, and any unamortized initial direct costs.

The Company has operating leases in relation to property for office and research facilities. All of the leases have termination options, and it is assumed that the initial termination options for the buildings will be activated for most of these. The maximum lease term without activation of termination options is to 2041.

The Company has elected not to recognize a right-of-use asset and lease liability for short-term leases. A short-term lease is a lease with a lease term of 12 months or less and which does not include an option to purchase the underlying asset that the lessee is reasonably certain to exercise.

Operating lease costs are recognized on a straight line basis over the lease term, and they are categorized within Research and development and General and administrative expenses in the Condensed Consolidated Statement of Operations. The operating lease cash flows are categorized under Net cash used in operating activities in the Condensed Consolidated Statement of Cash Flows.

(e) New accounting pronouncements

Adopted in the period

Leases

On January 1, 2019, the Company adopted Accounting Standard Update 2016-02 – Leases, which is codified in ASC 842. 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, 2019. Therefore, the comparative information has not been adjusted and continues to be reported under previous guidance. The Company elected the package of practical expedients permitted under the transition guidance within the new standard, which among other things, allowed it to carry forward the historical lease classification of the Company's leases as operating leases. The effect on the accumulated deficit, total stockholders' equity and net assets as at January 1, 2019 was $0.

The adoption of ASC 842 has had a material impact on the Company's financial statements. At January 1, 2019 the Company recognized right-of-use assets and liabilities for operating leases following the adoption date of $22.2 million and $26.9 million respectively and derecognized $4.7 million of other liabilities and prepayments that had been recognized under previous guidance.

During the three months ended June 30, 2019, management performed further benchmarking of the incremental borrowing rate used in the determination of the right-of-use asset and the lease liability as more information became publicly available. This has highlighted that the Company is at the lower end of the range for comparable companies and as a result, management performed further analysis of the factors which were considered. Based on this additional analysis, the incremental borrowing rate has increased from a weighted-average of 4.65% to 7.2%. The change in the incremental borrowing rate has reduced the right-of-use asset and corresponding lease liability by $2.6 million. There is no impact on the Condensed Consolidated Statement of Operations and Condensed Consolidated Statement of Cash Flows.

To be adopted in future periods

Measurement of Credit Losses on Financial Instruments

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

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

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

Changes to the Disclosure Requirements for Fair Value Measurement

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

Note 3 — Revenue

Revenue from contracts with customers arises from one customer, which is GlaxoSmithKline ("GSK"), in one geographic location, which is the United Kingdom. Revenue comprises the following categories (in thousands):

	Three months ended June 30, 2019	Three months ended June 30, 2018	Six months ended June 30, 2019	Six months ended June 30, 2018
Development	$ 157	$ 9,038	$ 157	$ 17,234
	$ 157	**$ 9,038**	**$ 157**	**$ 17,234**

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. In 2019, GSK nominated a third target under the Collaboration and License Agreement. Development of this target commenced during the three months ended June 30, 2019.

The amount of the transaction price probable of being received that is allocated to performance obligations that are unsatisfied or partially satisfied at June 30, 2019 was $3.0 million. The revenue allocated to the third target program will be recognized over an estimated period of 18 months as the development of the target progresses.

The Company became entitled to invoice GSK $3.2 million upon the nomination of the third target. Under the terms of the GSK Collaboration and License Agreement, the Company may also be entitled to development and regulatory milestones. The development and regulatory milestones are per product milestones and are dependent on achievement of certain obligations, the nature of the product being developed, stage of development of product, territory in which an obligation is achieved and type of indication or indications in relation to which the product is being developed. In addition, for any program multiple products may be developed to address different HLA-types. These amounts have not been included within the transaction price as of June 30, 2019 because they are not considered probable.

The Company may also receive commercialization milestones upon the first commercial sale of a product based on the indication and the territory and mid-single to low double-digit royalties on worldwide net sales. These amounts have not been included within the transaction price as of June 30, 2019 because they are sales or usage-based royalties promised in exchange for a license of intellectual property, which will be recognized when the subsequent sale or usage occurs.

Development revenue recognized in the three and six months ended June 30, 2018 related to development of the second target program, PRAME, which ended in 2018, and the NY-ESO program, which was transferred to GSK on July 23, 2018.

The following table shows movements in deferred revenue for the six months ended June 30, 2019 (in thousands):

	Deferred revenue
Deferred revenue at January 1, 2019	$ —
Revenue in the period	(157)
Amounts invoiced in the period	3,217
Foreign exchange arising on consolidation	(44)
Deferred revenue at June 30, 2019	**$ 3,016**

Note 4 – Operating leases

The following table shows the lease costs for the three and six months ended June 30, 2019 (in thousands):

	Three months ended June 30, 2019	Six months ended June 30, 2019
Lease cost:		
Operating lease cost	$ 1,024	$ 2,014
Short-term lease cost	121	168
	$ 1,145	**$ 2,182**

	Six months ended June 30, 2019
Other information:	
Operating cash flows from operating leases (in thousands)	$ 2,194

	June 30, 2019
Weighted-average remaining lease term - operating leases	7.8 years
Weighted-average discount rate - operating leases	7.2%

The maturities of operating lease liabilities are as follows (in thousands):

	Operating leases
2019	$ 2,037
2020	4,110
2021	4,153
2022	4,158
2023	3,918
after 2023	16,302
Total lease payments	**34,678**
Less: Imputed interest	(8,674)
Present value of lease liability	**$ 26,004**

The Company has operating leases in relation to property for office and research facilities. The maximum lease term without activation of termination options is to 2041.

Note 5 — Other expense, net

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

	Three months ended June 30,		Six months ended June 30,	
	2019	2018	2019	2018
Foreign exchange losses	$ (6,403)	$ (14,022)	$ (1,013)	$ (5,605)
Gains (losses) on redemption or maturity of available-for-sale debt securities	13	(1,310)	13	(2,473)
Other	113	(74)	153	(198)
	$ (6,277)	**$ (15,406)**	**$ (847)**	**$ (8,276)**

Note 6 — Loss per share

The dilutive effect of 97,292,240 and 87,434,329 stock options outstanding as of June 30, 2019 and 2018, 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 7 — Accumulated other comprehensive income (loss)

The following amounts were reclassified out of other comprehensive income during the three and six months ended June 30, 2019 and 2018 (in thousands):

	Amount reclassified		Amount reclassified	
Component of accumulated other comprehensive income	Three months ended June 30, 2019	Three months ended June 30, 2018	Six months ended June 30, 2019	Six months ended June 30, 2018
Unrealized gains (losses) on available-for-sale securities				
Reclassification adjustment for (gains) losses on available-for-sale debt securities	$ (13)	$ 1,310	$ (13)	$ 2,473

The affected line in the Condensed Consolidated Statement of Operations for the amounts reclassified out of other comprehensive income above is “Other expense, net”.

Note 8 — 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, 2019 are as follows (in thousands):

	June 30, 2019	Fair value measurements using Level 1	Level 2	Level 3
Assets:				
Marketable securities:				
Corporate debt securities	$ 91,831	$ 91,831	$ —	$ —
Agency bond	3,999	—	3,999	—
Certificate of deposit	3,002	—	3,002	—
	$ 98,832	**$ 91,831**	**$ 7,001**	**$ —**

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 9 — Available-for-sale debt securities

As of June 30, 2019, the Company has the following investments in available-for-sale debt securities (in thousands):

	Remaining Contractual Maturity	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Aggregate Estimated Fair Value
Cash equivalents:					
Money market funds	Less than 3 months	$ 10,241	$ —	$ —	$ 10,241
		$ 10,241	**$ —**	**$ —**	**$ 10,241**
Marketable securities:					
Corporate debt securities	Less than 3 months	$ 35,703	$ 18	$ —	$ 35,721
Corporate debt securities	3 months to 1 year	56,027	85	(2)	56,110
Agency bond	3 months to 1 year	3,992	7	—	3,999
Certificate of deposit	Less than 3 months	3,002	—	—	3,002
		$ 98,724	**$ 110**	**$ (2)**	**$ 98,832**

Maturity information above is categorized by the period remaining after the reporting period until the maturity date. In the three and six months ended June 30, 2019, $13,000 of realized gains recognized on the maturity of available-for-sale debt securities were reclassified out of other accumulated other comprehensive loss. As of June 30, 2019 and December 31, 2018, the aggregate fair value of securities held by the Company in an unrealized loss position was $9.6 million and $117.2 million respectively, which consisted of 3 and 37 separate securities, respectively. No securities have been in an unrealized loss position for more than one year. As of June 30, 2019, 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 10 — Other current assets

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

	June 30, 2019	December 31, 2018
Corporate tax receivable	$ 26,328	$ 16,459
Prepayments	8,600	6,279
Clinical materials	1,755	1,087
VAT receivable	636	1,505
Other current assets	599	439
	$ 37,918	**$ 25,769**

Note 11 — Accrued expenses and other current liabilities

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

	June 30, 2019	December 31, 2018
Accrued clinical & development expenditure	$ 9,769	$ 9,637
Accrued employee expenses	5,678	7,553
Other accrued expenditure	2,739	2,422
Other	409	742
	$ **18,595**	$ **20,354**

Note 12 — Share-based compensation

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

	Three months ended June 30,		Six months ended June 30,	
	2019	2018	2019	2018
Research and development	$ 786	$ 2,071	$ 2,807	$ 4,285
General and administrative	2,410	2,008	3,868	4,126
	$ **3,196**	**$ 4,079**	**$ 6,675**	**$ 8,411**

The following table shows information about share options and options which have a nominal exercise price (similar to restricted stock units (RSUs)) granted:

	Three months ended June 30,		Six months ended June 30,	
	2019	2018	2019	2018
Number of options over ordinary shares granted	936,696	1,435,685	11,743,896	11,430,341
Weighted average fair value of ordinary shares options	$ 0.39	$ 1.18	$ 0.54	$ 0.80
Number of additional options with a nominal exercise price granted	459,240	151,056	6,957,366	6,703,692
Weighted average fair value of options with a nominal exercise price	$ 0.70	1.88	$ 0.93	$ 1.35

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

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our unaudited condensed consolidated financial statements and related notes included in this Quarterly Report. The information in this discussion contains forward-looking statements and information within the meaning of Section 27A of the Securities Act of 1933, as amended ("Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended, ("Exchange Act"), which are subject to the "safe harbor" created by those sections. These forward-looking statements include, but are not limited to, statements concerning our strategy, future operations, future financial position, future revenues, projected costs, prospects and plans and objectives of management. The words "believe," "may," "will," "estimate," "continue," "anticipate," "intend," "expect" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements that we make. These forward-looking statements involve risks and uncertainties that could cause our actual results to differ materially from those in the forward-looking statements, including, without limitation, the risks set forth in Part II, Item 1A, "Risk Factors" in this Quarterly Report and in our other filings with the U.S. Securities and Exchange Commission ("SEC"). The forward-looking statements are applicable only as of the date on which they are made, and we do not assume any obligation to update any forward-looking statements.

Overview

We are a clinical-stage biopharmaceutical company primarily focused on providing novel cell therapies to patients, particularly for the treatment of solid tumors. The Company's 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 ("SPEAR T-cells") for administration to patients. Using its affinity engineered TCRs, the Company aims to become the first company to have a TCR T-cell approved for the treatment of a solid tumor indication.

Update on Clinical Pipeline Progress

Wholly owned SPEAR T-cells

We have clinical trials ongoing with our wholly owned ADP-A2M4, ADP-A2M10, and ADP-A2AFP 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.

- **ADP-A2M4**

Phase 2 trial - SPEARHEAD-1

A Phase 2 clinical trial has been initiated in synovial sarcoma and MRCLS. The trial will take place at sites in the United States, Canada and Europe. The trial will include up to 60 patients at a selected dose of up to 10 billion transduced ADP-A2M4 SPEAR T-cells. Primary responses will be assessed by overall response rate by RECIST v1.1. The lymphodepletion regimen will be fludarabine (30mg/m^2/day) for 4 days and cyclophosphamide (600 mg/m^2/day) for 3 days.

Phase 1 multi-tumor trial

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. This trial is a first-in-human, open-label study utilizing a modified 3+3 design in up to 30 patients at a selected dose with escalating target doses of 100 million (Cohort 1), 1 billion (Cohort 2), 5 billion (Cohort 3), and up to 10 billion (Expansion Phase) transduced ADP-A2M4 SPEAR T-cells to evaluate safety. Patients are currently being enrolled in the Expansion Phase of the trial.

- To date, ADP-A2M4 continues to exhibit a favorable safety profile with no evidence of toxicity related to off-target binding or alloreactivity, and most adverse events were consistent with those experienced by cancer patients undergoing chemotherapy or other immunotherapies. Prolonged severe pancytopenia with aplastic anemia has been reported in one

patient treated with the highest lymphodepletion regimen (fludarabine (30mg/m^2/day) for 4 days and cyclophosphamide (1800 mg/m^2/day) for 3 days). Neurotoxicity and stroke were reported in a different patient who also received this lymphodepletion regimen. The protocol for this trial has been amended to mitigate the risk of prolonged severe pancytopenia and stroke in patients. These changes have been communicated to the FDA and acknowledged by the FDA. Further information on reported adverse events can be found in the Risk Factors section below**.**

- As of May 6, 2019, ten synovial sarcoma patients had been treated in the trial. Of these eight patients had been assessed with six showing evidence of tumor shrinkage. Three patients had confirmed partial responses and one patient had an unconfirmed partial response. Three patients had stable disease and one patient was assessed to have progressive disease. Evidence of anti-tumor activity was also seen in melanoma and ovarian cancer patients. A clinical update across the whole trial including these synovial sarcoma patients was provided on May 6, 2019 as part of a clinical and business update.

Radiation Sub-study

A radiation sub-study has now been initiated as part of the Phase 1 trial and is planned to enroll 10 patients across multiple solid tumor indications. The trial is being conducted at MD Anderson Cancer Center. Patients will receive low-dose radiation in up to five lesions prior to treatment with ADP-A2M4, at target doses of 1-10 billion SPEAR T-cells. The lymphodepletion regimen will be fludarabine (30mg/m^2/day) for 4 days and cyclophosphamide (600 mg/m^2/day) for 3 days.

ADP-A2M4CD8 - SURPASS Trial

A Phase 1 trial for a next generation SPEAR T-cell, ADP-A2M4CD8, has recently been initiated (the SURPASS Trial). This next generation SPEAR T-cell utilizes the same engineered T-cell receptor as ADP-A2M4, but with the addition of a CD8α homodimer. The addition of the CD8α homodimer has been shown in vitro to increase cytokine release, increase SPEAR T-cell potency and promote epitope spreading.

The SURPASS trial will enroll up to 30 patients across multiple solid tumor indications. Similar to our other trials, the SURPASS trial will be a three-cohort dose escalation study. Unlike the other trials, the stagger between patients will be shorter and the starting dose in the first cohort will be 0.8 to 1.2 billion SPEAR T-cells, instead of 100 million SPEAR T-cells, as was previously the case. Each dose cohort will enroll three patients and can be expanded to six patients if a dose limiting toxicity occurs. The dose ranges for the other two cohorts are: 1.2 to 3 billion and 3 to 6 billion SPEAR T-cells. After dose escalation is complete, there is an Expansion Phase with doses up to 10 billion cells. The lymphodepletion regimen will be fludarabine (30mg/m^2/day) for 4 days and cyclophosphamide (600 mg/m^2/day) for 3 days.

- **ADP-A2M10**

Two Phase 1 clinical trials are currently ongoing with ADP-A2M10 for the treatment of (i) NSCLC, and (ii) urothelial, melanoma and head and neck cancers in the United States, Canada, the United Kingdom and Spain. Enrollment in the trial is planned to close shortly and prior to the end of 2019. Expression of MAGE-A10 (the target peptide) has been lower than initially anticipated and the majority of MAGE-A10 expressing patients also express the MAGE-A4 peptide. A clinical update was provided on this trial on May 6, 2019. Most adverse events to date are consistent with those typically experienced by cancer patients undergoing cytotoxic chemotherapy or other cancer immunotherapies. As with ADP-A2M4 we have seen prolonged severe pancytopenia and aplastic anemia in one patient treated with the highest lymphodepletion regimen. The protocol for this trial has been amended to mitigate the risk of prolonged severe pancytopenia in patients. These changes have been communicated to the FDA and acknowledged by the FDA. Further information on reported adverse events can be found in the Risk Factors section below.

- **ADP-A2AFP**

We continue dosing patients in our Phase 1, open-label, dose-escalation study designed to evaluate the safety and anti-tumor activity of our alpha fetoprotein (“AFP”) therapeutic candidate for the treatment of hepatocellular carcinoma (“HCC”). The trial is open in the United States, United Kingdom and Spain. Data from the first HCC patient treated in Cohort 2 of the trial was presented at AACR and a further update will be provided in the first half of 2020. Most adverse events to date are consistent with those typically experienced by cancer patients undergoing cytotoxic chemotherapy or other cancer immunotherapies.

Ongoing GSK Collaboration Agreement Programs

- GSK has nominated a third target program under the GSK Collaboration and License Agreement that will evaluate and develop new SPEAR T-cells. This collaboration program has now started.

- GSK is currently entitled to nominate a fourth target program and, upon satisfying other conditions, may have the right to nominate a fifth program under the GSK Collaboration and License Agreement, in each case excluding our ongoing wholly-owned development programs.

Significant Events in the Three Months Ended June 30, 2019

- On May 15, 2019, we announced entry into a collaboration and license agreement with Alpine Immune Sciences, Inc. to develop next-generation SPEAR T-cell products which incorporate Alpine's secreted and transmembrane immunomodulatory protein technology. This collaboration will further enhance Adaptimmune's efforts to design and develop next-generation SPEAR T-cell therapies.

- On June 27, 2019, we announced that Adrian Rawcliffe, currently Chief Financial Officer (CFO) of the Company, will succeed James Noble as Chief Executive Officer (CEO). This transition will occur when James Noble retires from his executive duties and transitions to a non-executive director role on the Company's Board of Directors on September 1, 2019.

Subsequent Events since June 30, 2019

- On August 1, 2019, we announced further changes to our Executive Team with Dr Rafael Amado, President of Research and Development, leaving on August 12, 2019 and John Lunger being appointed as Chief Patient Supply Officer from August 1, 2019. We are recruiting for a Chief Medical Officer and a Chief Financial Officer.

Financial Operations Overview

New standards

On January 1, 2019, we adopted new accounting guidance on lease recognition, which has been codified within Accounting Standard Codification Topic 842, *Leases* ("ASC 842"). We 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, 2019. Therefore, the comparative information has not been adjusted and continues to be reported under previous guidance. The effect on the accumulated deficit, total stockholders' equity and net assets as at January 1, 2019 was $0.

Revenue

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. GSK has nominated its third target under the Collaboration and License Agreement. Development of this target commenced in the three months ended June 30, 2019, and the Company became entitled to $3.2 million following the nomination of the target. The development of the third target is a separate performance obligation, which will be recognized over the next 18 months as the development of the target progresses.

Future revenues will depend on the progress of the development programs within the Collaboration and License Agreement, and GSK's progress with the NY-ESO program, which are difficult to predict.

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 tomanufacture 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 manufactureof 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.

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, which may result in a payable tax credit at an effective rate of approximately 9.7% of qualifying expenditure.

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;
- 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, net

Other expense, net primarily 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.

Results of Operations

Comparison of Three Months Ended June 30, 2019 and 2018

The following table summarizes the results of our operations for the three months ended June 30, 2019 and 2018, together with the changes to those items (in thousands).

	Three months ended June 30,			
	2019	2018	Increase/decrease	
Revenue	**$ 157**	**$ 9,038**	**$ (8,881)**	**(98)%**
Research and development expenses	(25,511)	(26,624)	1,113	(4)%
General and administrative expenses	(10,148)	(11,291)	1,143	(10)%
Total operating expenses	**(35,659)**	**(37,915)**	**2,256**	**(6)%**
Operating loss	**(35,502)**	**(28,877)**	**(6,625)**	**23 %**
Interest income	757	540	217	40 %
Other income (expense), net	(6,277)	(15,406)	9,129	(59)%
Loss before income taxes	**(41,022)**	**(43,743)**	**2,721**	**(6)%**
Income taxes	(65)	(102)	37	(36)%
Loss for the period	**$ (41,087)**	**$ (43,845)**	**$ 2,758**	**(6)%**

Revenue

Revenue decreased by $8.8 million to $0.2 million in the three months ended June 30, 2019 compared to $9.0 million for the three months ended June 30, 2018.

The revenue recognized for the three months ended June 30, 2019 is due to the commencement of development on the third target nominated by GSK under the Collaboration and License Agreement. The development revenue for the three months ended June 30, 2018 was recognized due to the performance under the NY-ESO transition program and the PRAME development plan, which were completed in 2018.

Future revenues will depend on the progress of the third target, the development of programs for additional targets, and GSK's progress with the NY-ESO program, which are difficult to predict. We anticipate that $3.0 million of revenue for the third target will be recognized over the next 18 months.

Research and Development Expenses

Research and development expenses decreased by 4% to $25.5 million for the three months ended June 30, 2019 from $26.6 million for the three months ended June 30, 2018. Our research and development expenses comprise the following (in thousands):

	Three months ended June 30,			
	2019	2018	Increase/decrease	
Salaries, materials, equipment, depreciation of property, plant and equipment and other employee-related costs[1]	$ 16,718	$ 15,467	$ 1,251	8 %
Subcontracted expenditure	9,104	11,574	(2,470)	(21)%
Manufacturing facility expenditure	1,796	1,181	615	52 %
Share-based compensation expense	786	2,071	(1,285)	(62)%
Payments for in-process research and development	1,987	—	1,987	NA
Reimbursements for research and development tax and expenditure credits and government grants	(4,880)	(3,669)	(1,211)	33 %
	$ 25,511	**$ 26,624**	**$ (1,113)**	**(4)%**

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

The net decrease in our research and development expenses of $1.1 million for the three months ended June 30, 2019 compared to the same period in 2018 was primarily due to the following:

- a decrease of $2.5 million in subcontracted expenditures, including clinical trial expenses and contract research organization (CRO) costs and manufacturing expenses. This was primarily driven by a decrease in subcontracted manufacturing expenses and clinical trial costs due to the transfer of NY-ESO to GSK on July 23, 2018;
- a decrease in share-based compensation expense of $1.3 million due to options forfeited by leavers; and
- an increase in reimbursements for research and development tax and expenditure credits of $1.2 million due to an increased proportion of expenditure qualifying under the UK SME R&D Tax Credit Scheme.

offset by:

- an increase of $1.3 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 317 to 322
- an increase of $2.0 million in payments for in-process research and development after entering into a Collaboration Agreement relating to the development of next-generation SPEAR T-cell products with Alpine Immune Sciences, Inc. on May 14, 2019; and
- an increase in manufacturing of $0.6 million due to increased activity at our U.S. facility in Philadelphia and the development of a dedicated vector manufacturing capability in Stevenage, Hertfordshire, United Kingdom.

Our subcontracted costs for the three months ended June 30, 2019 were $9.1 million, compared to $11.6 million in the same period of 2018. This includes $4.1 million of costs associated with our ADP-A2M10, ADP-A2M4, and ADP-A2AFP SPEAR T-cells and $5.0 million of other development costs.

Our research and development expenses are highly dependent on the phases and progression of our research projects and will fluctuate depending on the outcome of ongoing clinical trials.

General and Administrative Expenses

General and administrative expenses decreased by 10% to $10.1 million for the three months ended June 30, 2019 from $11.3 million in the same period in 2018, due to a reduction in general corporate costs including travel and IT expenditure in the three months ended June 30, 2019. We expect that our general and administrative expenses will increase in the future as we expand our operations.

Other Expense, Net

Other expense, net was an expense of $6.3 million for the three months ended June 30, 2019 compared to an expense of $15.4 million for the three months ended June 30, 2018. Other 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 income has decreased, primarily due to movements in foreign exchange rates.

Income Taxes

Income taxes decreased to a charge of $65,000 for the three months ended June 30, 2019 from a charge of $102,000 for the three months ended June 30, 2018. Income taxes arise in the United States due to our U.S. subsidiary generating taxable profits. We incur losses in the United Kingdom.

Comparison of Six Months Ended June 30, 2019 and 2018

The following table summarizes the results of our operations for the six months ended June 30, 2019 and 2018, together with the changes to those items (in thousands).

	Six months ended June 30,			
	2019	2018	Increase/decrease	
Revenue	**$ 157**	**$ 17,234**	**$ (17,077)**	**(99)%**
Research and development expenses	(47,530)	(52,016)	4,486	(9)%
General and administrative expenses	(21,921)	(22,495)	574	(3)%
Total operating expenses	**(69,451)**	**(74,511)**	**5,060**	**(7)%**
Operating loss	**(69,294)**	**(57,277)**	**(12,017)**	**21 %**
Interest income	1,709	1,199	510	43 %
Other expense, net	(847)	(8,276)	7,429	(90)%
Loss before income taxes	**(68,432)**	**(64,354)**	**(4,078)**	**6 %**
Income taxes	(67)	(229)	162	(71)%
Loss for the period	**$ (68,499)**	**$ (64,583)**	**$ (3,916)**	**6 %**

Revenue

Revenue decreased by $17.0 million to $0.2 million in the six months ended June 30, 2019 compared to $17.2 million for the six months ended June 30, 2018.

The revenue recognized for the six months ended June 30, 2019 is due to the commencement of development for the third target nominated by GSK under the Collaboration and License Agreement. The development revenue for the six months ended June 30, 2018 was recognized due to the performance under the NY-ESO transition program and the PRAME development plan, which were completed in 2018.

Future revenues will depend on the progress of the development program for additional targets, and GSK's progress with the NY-ESO program, which are difficult to predict. We anticipate that $3.0 million of revenue for the third target will be recognized over the next 18 months.

Research and Development Expenses

Research and development expenses decreased by 9% to $47.5 million for the six months ended June 30, 2019 from $52.0 million for the six months ended June 30, 2018. Our research and development expenses comprise the following (in thousands):

	Six months ended June 30,			
	2019	2018	Increase/decrease	
Salaries, materials, equipment, depreciation of property, plant and equipment and other employee-related costs[1]	$ 33,407	$ 30,596	$ 2,811	9 %
Subcontracted expenditure	16,026	22,958	(6,932)	(30)%
Manufacturing facility expenditure	3,344	2,061	1,283	62 %
Share-based compensation expense	2,807	4,285	(1,478)	(34)%
Payments for in-process research and development	1,987	—	1,987	NA
Reimbursements for research and development tax and expenditure credits and government grants	(10,041)	(7,884)	(2,157)	27 %
	$ 47,530	**$ 52,016**	**$ (4,486)**	**(9)%**

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

The net decrease in our research and development expenses of $4.5 million for the six months ended June 30, 2019 compared to the same period in 2018 was primarily due to the following:

- a decrease of $6.9 million in subcontracted expenditures, including clinical trial expenses and contract research organization (CRO) costs and manufacturing expenses. This was primarily driven by a decrease in subcontracted manufacturing expenses and clinical trial costs due to the transfer of NY-ESO to GSK on July 23, 2018;
- a decrease in share-based compensation expense of $1.5 million due to options forfeited by leavers; and
- an increase in reimbursements for research and development tax and expenditure credits of $2.2 million due to an increased proportion of expenditure qualifying under the UK SME R&D Tax Credit Scheme.

offset by:

- an increase of $2.8 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 309 to 327;
- an increase of $2.0 million in payments for in-process research and development after entering into a Collaboration Agreement relating to the development of next-generation SPEAR T-cell products with Alpine Immune Sciences, Inc. on May 14, 2019; and
- an increase in manufacturing of $1.3 million due to increased activity at our U.S. facility in Philadelphia and the development of a dedicated vector manufacturing capability in Stevenage, Hertfordshire, United Kingdom.

Our subcontracted costs for the six months ended June 30, 2019 were $16.0 million, compared to $23.0 million in the same period of 2018. This includes $6.6 million of costs associated with our ADP-A2M10, ADP-A2M4, and ADP-A2AFP SPEAR T-cells and $9.4 million of other development costs.

Our research and development expenses are highly dependent on the phases and progression of our research projects and will fluctuate depending on the outcome of ongoing clinical trials.

General and Administrative Expenses

General and administrative expenses decreased by 3% to $21.9 million for the six months ended June 30, 2019 from $22.5 million in the same period in 2018 due to a reduction in general corporate costs including travel and IT expenditure in the six months ended June 30, 2019. We expect that our general and administrative expenses will increase in the future as we expand our operations.

Other Expense, Net

Other expense, net was an expense of $0.8 million for the six months ended June 30, 2019 compared to an expense of $8.3 million for the six months ended June 30, 2018. Other 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 income has decreased, primarily due to movements in foreign exchange rates.

Income taxes

Income taxes decreased to a charge of $67,000 for the six months ended June 30, 2019 from a charge of $229,000 for the six months ended June 30, 2018. Income taxes arise in the United States due to our U.S. subsidiary generating taxable profits. 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 Collaboration and License Agreement, government grants and research and development tax and expenditure credits. From inception through to June 30, 2019, we have raised:

- $513.8 million, net of issuance costs, through the issuance of shares, including $99.7 million raised through a registered direct offering in September 2018;
- $148.3 million upfront fees, milestones and exercise fees under our GSK Collaboration and License Agreement;
- $2.8 million of income in the form of government grants; and
- $24.6 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, 2019, we had cash and cash equivalents of $34.6 million and Total Liquidity of $133.4 million. We regularly assess Total Liquidity against our activities and make decisions regarding prioritization of those activities and deployment of Total Liquidity. We believe that our Total Liquidity will be sufficient to fund our operations, based upon our currently anticipated research and development activities and planned capital spending, through the third quarter of 2020.

Cash Flows

The following table summarizes the results of our cash flows for the six months ended June 30, 2019 and 2018 (in thousands).

	Six months ended June 30,	
	2019	2018
Net cash used in operating activities	$ (70,371)	$ (82,642)
Net cash provided by investing activities	36,217	34,012
Net cash provided by financing activities	366	2,424
Cash, cash equivalents and restricted cash	38,977	46,507

Operating Activities

Net cash used in operating activities decreased by $12.2 million to $70.4 million for the six months ended June 30, 2019 from $82.6 million for the six months ended June 30, 2018. The decrease in cash used in operations was primarily the result of a decrease in manufacturing expenses and clinical trial costs following the transfer of NY-ESO to GSK on July 23, 2018.

Net cash used in operating activities of $70.4 million for the six months ended June 30, 2019 comprised a net loss of $68.5 million and a net cash outflow of $13.4 million from changes in operating assets and liabilities, offset by non-cash items of $11.5 million. The non-cash items consisted primarily of depreciation expense on plant and equipment of $3.6 million, share-based compensation expense of $6.7 million and unrealized foreign exchange losses of $1.0 million.

Investing Activities

Net cash provided by investing activities of $36.2 million and $34.0 million for the six months ended June 30, 2019 and 2018, respectively consisted of:

- purchases of property and equipment of $1.2 million and $3.1 million for the six months ended June 30, 2019 and 2018, respectively;
- purchases of intangible assets of $0.9 million primarily relating to development of internal-use software for the six months ended June 30, 2019; and
- cash outflows from investment in marketable securities of $16.0 million and $33.6 million for the six months ended June 30, 2019 and 2018, respectively, and cash inflows from maturity or redemption of marketable securities of $54.3 million and $70.7 million for the six months ended June 30, 2019 and 2018, respectively.

Financing Activities

Net cash from financing activities of $0.4 and $2.4 million for the six months ended June 30, 2019 and 2018, respectively, consisted of proceeds from share option exercises.

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, 2019	December 31, 2018
Cash and cash equivalents	$ 34,574	$ 68,379
Marketable securities	98,832	136,755
Total Liquidity	**$ 133,406**	**$ 205,134**

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 2018 Annual Report on Form 10-K.

On May 14, 2019, we entered into a Collaboration Agreement relating to the development of next-generation SPEAR T-cell products with Alpine Immune Sciences, Inc. ("Alpine").

We paid an upfront exclusive license option fee of $2 million to Alpine in June 2019. Under the agreement, Adaptimmune will pay Alpine for ongoing research and development funding costs and development and commercialization milestone payments up to a maximum of $288 million may be payable if all possible targets are selected and milestones achieved. Alpine would also receive low single-digit royalties on worldwide net sales of applicable products.

We have made $2.3 million of payments to Alpine in the six months ended June 30, 2019, $2.1 million of which was recognized within "Research and development" expenses in the Condensed Consolidated Statement of Operations for the three and six months ended June 30, 2019.

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 2018 Annual Report on Form 10-K. There have been no material changes in the six months ended June 30, 2019.

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, 2019. Based on such evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that, as of June 30, 2019, 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 2019, we adopted new guidance on lease recognition, which has been codified within Accounting Standard Codification Topic 842,*Leases* ("ASC 842"). As a consequence of the new guidance, management implemented several new internal controls, including controls to identify lease arrangements and to ensure that they are appropriately measured, in the quarter ended March 31, 2019.

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, 2019 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II - OTHER INFORMATION

Item 1. Legal Proceedings.

As of June 30, 2019, 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 six months ended June 30, 2019, the years ended December 31, 2018, 2017, 2016 and six months ended December 31, 2015 and the year ended June 30, 2015, we incurred net losses of $68.5 million, $95.5 million, $70.1 million, $71.6 million, $23.0 million and $22.1 million, respectively. As of June 30, 2019, we had accumulated losses of $387.0 million. We expect to continue incurring significant losses as we continue with our research and development programs and to incur general and administrative costs associated with our operations. The extent of funding required to develop our product candidates is difficult to estimate given the novel nature of our 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 third SPEAR T-cell program and any future SPEAR T-cell programs under the GSK Collaboration and License Agreement) and achieving a level of revenues adequate to support our cost structure. We may never achieve profitability, and unless and until we do, we will continue to need to raise additional cash or alternative funding.

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

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

- completing preclinical development and advancing our SPEAR T-cells to clinic;
- delivering on the clinical development strategy for our SPEAR T-cells;
- progressing our clinical trials within predicted timeframes and without any substantial delays, for example as may be caused by delays in patient recruitment, regulatory requirements to hold or suspend any clinical trials or delays in obtaining approvals required to conduct clinical trials;
- demonstrating a favorable benefit (efficacy parameters): risk (safety) for our SPEAR T-cells 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;
- 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, 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.

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, 2019, we had $34.6 million of cash and cash equivalents and $98.8 million of marketable securities. We expect to use these funds to advance and accelerate the clinical development of our 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 for 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, nomination of further targets by GSK or changes to the third target program) 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 to us 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.

Raising additional capital may cause dilution to our existing shareholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

We may seek additional capital through a combination of public and private equity offerings, debt financings, strategic partnerships and alliances and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a shareholder. The incurrence of indebtedness would result in increased fixed payment obligations and could involve certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. If we

raise additional funds through strategic partnerships and alliances and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or product candidates, or grant licenses on terms unfavorable to us.

Risks Related to the Development of Our SPEAR T-cells

Our business is highly dependent on our wholly owned SPEAR T-cell candidates including ADP-A2M4, ADP-A2M4CD8, and ADP-A2AFP, 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 our ADP-A2M4, ADP-A2M4CD8, and ADP-A2AFP SPEAR T-cells will be sufficient for us to plan one or more pivotal clinical trials and obtain regulatory approval or marketing authorization. Negative results in any SPEAR T-cell clinical program may also impact our ability to obtain regulatory approval for other SPEAR T-cells, either at all or within anticipated timeframes because, although the SPEAR T-cell may target a different cancer peptide, the underlying technology platform and other aspects of our clinical programs are the same or substantially similar for all of our SPEAR T-cells. Similarly, negative results in the NY-ESO SPEAR T-cell clinical program, now fully transferred to GSK, may also impact our ability to obtain regulatory approval for other wholly owned SPEAR T-cells. Accordingly, a failure or delay in any one program may affect the ability to obtain regulatory approval to continue or conduct clinical programs for other SPEAR T-cells.

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

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

There is no guarantee that the FDA, or any other regulatory authority, will approve any IND (or equivalent application) for any of our future SPEAR T-cells, or for new indications for our SPEAR T-cells already in clinical trials, or that amendments to existing protocols will not be required. For example, we recently amended the protocols for all of our pending and on-going ADP-A2M4 and ADP-A2M10 clinical trials in response to reported serious adverse events of prolonged serious pancytopenia in our clinical trials for ADP-A2M4 and ADP-A2M10 in two patients treated with the highest lymphodepletion regimen. Such protocol amendments may delay our clinical trials, may require changes or resubmission of our INDs, or may result or be related to a halt in our planned or contemplated clinical trials.

We are continuing to expand our clinical trial foot print in Europe. This requires gaining the approval of country specific review bodies for GMO application and Clinical Trial Application (“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 human 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 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.

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.

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 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.

Results seen in third party clinical trials using products that are also used in our combination clinical trials, may impact on the further advancement of our clinical trials or clinical trials of our collaborators. For example, the FDA placed a clinical hold on three combination studies using an anti-PD-1 therapy used to treat multiple myeloma. There is no guarantee that further reviews of safety data with anti-PD-1 therapies will not result in delays or holds to our collaborator's clinical trials or the requirement to amend the protocol for such clinical trials or would not delay the start of any anti-PD-1 combination clinical trials that we may wish to start.

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

There is a significant risk at each stage of any clinical program that serious adverse events or low efficacy, as well as less favorable benefit:risk profiles, will prevent 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 neurotoxicity 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, potentially life-threatening and require medical intervention.

As of April 5, 2019 for ADP-A2AFP and April 15, 2019 for ADP-A2M4 and ADP-A2M10:

- The adverse events considered by investigators to be possibly related to ADP-A2AFP (n=3) include pyrexia, increase in alanine aminotransferase, increase in aspartate aminotransferase, increase in alkaline phosphatase, cognitive disorder, pain in extremity, muscular weakness. Serious adverse events reported with ADP-A2AFP whether considered related to the SPEAR T-cells or not include bile duct obstruction and abdominal pain.

- The adverse events occurring in >10% of subjects treated with ADP-A2M4 (n=23) and considered by investigators to be possibly related to ADP-A2M4 include cytokine release syndrome (CRS), fatigue, pyrexia, decreased appetite, rash, dyspnea, febrile neutropenia, headache, nausea, sinus tachycardia/tachycardia, anemia/red blood cells decreased, chills, diarrhea, hypotension, and tumor pain. Serious adverse events (SAE) reported with ADP-A2M4 in more than one subject whether considered related to the SPEAR T-cells or not, and any related SAE include CRS, pyrexia, atrial fibrillation, thrombocytopenia/platelet count decreased, and rash. There has also been one serious adverse event report of grade 2 encephalopathy considered related to ADP-A2M4 by the investigator which resolved after 2 days of treatment.

- The adverse events occurring in >10% of subjects treated with ADP-A2M10 (n=18) and considered by investigators to be possibly related to ADP-A2M10 include pyrexia, CRS, peripheral edema, chills, febrile neutropenia, leukopenia/white blood cells decreased, lymphopenia/lymphocyte count decreased, thrombocytopenia/platelet count decreased, rash and sinus tachycardia/tachycardia. Serious adverse events (SAE) reported with ADP-A2M10 in more than one subject whether considered related to the SPEAR T-cells or not, and any related SAE include CRS.

Since April 15, 2019, there were two SAE reports of severe prolonged pancytopenia with aplastic anemia (one patient receiving ADP-A2M4 and one patient receiving ADP-A2M10) considered by the investigator to be probably related to the SPEAR T-cells and to the lymphodepleting chemotherapy. Both of these patients died from complications of aplastic anemia. In another patient, there was one report of Grade 3 neurotoxicity considered by the investigator to be probably related to the ADP-A2M4 SPEAR T-cells and, in the same patient, a later grade 5 SAE of stroke that was considered by the investigator to be possibly related to the product. These reports were communicated to the FDA and we are responding to queries from the FDA in relation to these reports. All three patients received the highest lymphodepletion regimen (fludarabine (30mg/m^2/day) for 4 days and cyclophosphamide (1800 mg/m^2/day) for 2 days). The protocols for all of our ADP-A2M4 and ADP-A2M10 trials have now been amended to mitigate the future risk of prolonged pancytopenia

and stroke, including a reduction of the lymphodepletion regimen to a previously used regimen (fludarabine (30mg/m^2/day) for 4 days and cyclophosphamide (600 mg/m^2/day) for 3 days). In addition, patients with a prior history of stroke or central nervous system bleeding (or transient ischemic attack (TIA) or reversible ischemic neurologic deficit (RIND) within the prior 6 months of treatment) are now excluded. These protocol changes have been communicated to and acknowledged by the FDA. If further adverse events of a similar nature occur in patients, there is a risk that we or the FDA may impose a clinical hold until the adverse events are further evaluated or, alternatively, we or the FDA may suspend or require termination of these clinical 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.

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

SPEAR T-cells (including the NY-ESO SPEAR T-cell) and their potential associated risks are still under investigation. There is no guarantee that our SPEAR T-cells will work in the way that we currently anticipate or that affinity modification of T-cell receptors will produce the anticipated enhancements in activity. 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. Any delay in identification of suitable patients will result 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.

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 changed during the course of our clinical trials in melanoma with the NY-ESO SPEAR T-cell and as a result the clinical trial was 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.

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.

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, failure in quality systems applicable to manufacture, sterility failures, contamination during process;

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

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

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

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

- Inability to procure starting materials or to manufacture starting materials (including at our UK vector facility), 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 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 these 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

- 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, for that product to be released for use in Europe and then for that SPEAR T-cell product to be transported back to the site in Europe for administration to the patient. The supply and manufacturing chain required to achieve this is very complex and could be subject to failures at any point in the supply and manufacturing chain. Any inability to set up acceptable manufacturing and supply chains to enable treatment of patients in Europe could result in a delay to those trials starting in Europe or could result in a delay in patient treatment, requirement to re-apherese a patient or a requirement to re-manufacture patient material.

As our SPEAR T-cells progress through preclinical programs and clinical trials towards approval and commercialization, it is expected that various aspects of the manufacturing and administration process will be altered in an effort to optimize processes and results. We have already identified some improvements to our manufacturing and administration processes, but these changes may not achieve the intended objectives, may not be transferable to third parties or able to be used at larger scales and could cause our SPEAR T-cells to perform differently or affect the results of planned clinical trials or other future clinical trials. In addition, such changes may require amendments to be made to regulatory applications or comparability tests to be conducted which may further delay the timeframes under which modified manufacturing processes can be used for any SPEAR T-cell. If SPEAR T-cells manufactured under the new process has a worse safety or efficacy profile than the prior investigational product or the process is less reproducible than the previous process, we may need to re-evaluate the use of that manufacturing process, which could significantly delay or even result in the halting of our clinical trials.

Developing a commercially viable process is a difficult and uncertain task, and there are risks associated with scaling to the level required for advanced clinical trials or commercialization, including, among others, increased costs, potential problems with process scale-out, process reproducibility, stability issues, lot consistency, loss of product, and timely availability of reagents or raw materials or contract manufacturing services or facilities. A failure to develop such a commercially viable process within anticipated timescales may prevent or delay progression of our T-cell therapies into pivotal clinical trials and ultimately commercialization. In addition, we may ultimately be unable to reduce the expenses associated with our SPEAR T-cells to levels that will allow us to achieve a profitable return on investment. We have entered into an alliance with Universal Cells, Inc. that, if successful, will enable us to treat patient populations with an off-the-shelf product. However, there is no guarantee that the research program with Universal Cells, Inc. will be successful, will be carried out within the timescales currently anticipated, or even if successful 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 which is capped at £10 million in the United Kingdom and $5 million in the United States. However, because our level of insurance is capped, it may be insufficient to fully compensate us if any of these events were to occur in the future.

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

In order to commercially produce our products, we will need to comply with the FDA's cGMP requirements at both our Navy Yard facility, vector 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 authorization 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 US manufacturing facility and plan to manufacture vector at a UK vector 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 either facility is operated. This may result in a delay in our ability to manufacture SPEAR T-cells at our own facility or in our ability to supply vector material for use in the SPEAR T-cell manufacturing process. In addition, there is no guarantee that any SPEAR T-cells or vector produced in any of our facilities will be able to meet regulatory requirements or that we will be able to recruit and maintain sufficient staff to enable manufacture of products within required timescales. Any failure to meet regulatory requirements or produce SPEAR T-cells and vector according to regulatory requirements could result in delays to our clinical programs, potential side effects and even fatalities to patients and may result in withdrawal of regulatory approval for our manufacturing facility.

The outcome of clinical trials is uncertain and 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 may 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. Any such hold will require addressing by us and our collaborators and will inevitably delay progression of the clinical trials concerned, if such clinical trials progress at all.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. Success in preclinical programs and early clinical trials does not ensure that later clinical trials will be successful. Moreover, the results of preclinical programs and early clinical trials of SPEAR T-cells may not be predictive of the results of later-stage clinical trials. To date, we have only obtained interim results from Phase 1/2 clinical trials that are uncontrolled, involve small sample sizes and are of shorter duration than might be required for regulatory approval. There may be other reasons why our

early clinical trials are not 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. 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 demonstrating 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 SPEAR T-cell 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 authorization 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.

As of April 5, 2019 for ADP-A2AFP and April 15, 2019 for ADP-A2M4 and ADP-A2M10:

- The adverse events considered by investigators to be possibly related to ADP-A2AFP (n=3) include pyrexia, increase in alanine aminotransferase, increase in aspartate aminotransferase, increase in alkaline phosphatase, cognitive disorder, pain in extremity, muscular weakness. Serious adverse events reported with ADP-A2AFP whether considered related to the SPEAR T-cells or not include bile duct obstruction and abdominal pain.

- The adverse events occurring in >10% of subjects treated with ADP-A2M4 (n=23) and considered by investigators to be possibly related to ADP-A2M4 include cytokine release syndrome (CRS), fatigue, pyrexia, decreased appetite, rash, dyspnea, febrile neutropenia, headache, nausea, sinus tachycardia/tachycardia, anemia/red blood cells decreased, chills, diarrhea, hypotension, and tumor pain. Serious adverse events (SAE) reported with ADP-A2M4 in more than one subject whether considered related to the SPEAR T-cells or not, and any related SAE include CRS, pyrexia, atrial fibrillation, thrombocytopenia/platelet count decreased, and rash. There has also been one SAE report of grade 2 encephalopathy considered related to ADP-A2M4 by the investigator which resolved after 2 days of treatment.

- The adverse events occurring in >10% of subjects treated with ADP-A2M10 (n=18) and considered by investigators to be possibly related to ADP-A2M10 include pyrexia, CRS, peripheral edema, chills, febrile neutropenia, leukopenia/white blood cells decreased, lymphopenia/lymphocyte count decreased, thrombocytopenia/platelet count decreased, rash and sinus tachycardia/tachycardia. Serious adverse events (SAE) reported with ADP-A2M10 in more than one subject whether considered related to the SPEAR T-cells or not, and any related SAE include CRS.

Since April 15, 2019, there were two SAE reports of severe prolonged pancytopenia with aplastic anemia (one patient receiving ADP-A2M4 and one patient receiving ADP-A2M10) considered by the investigator to be probably related to the SPEAR T-cells and to the lymphodepleting chemotherapy. Both of these patients died from complications of aplastic anemia. In another patient, there was one report of Grade 3 neurotoxicity considered by the investigator to be probably related to the ADP-A2M4 SPEAR T-cells and, in the same patient, a later grade 5 SAE of stroke that was considered by the investigator to be possibly related to the product. These reports were communicated to the FDA and we are responding to queries from the FDA in relation to these reports. All three patients received the highest lymphodepletion regimen (fludarabine (30mg/m^2/day) for 4 days and cyclophosphamide (1800 mg/m2/day) for 2 days). The protocols for all of our ADP-A2M4 and ADP-A2M10 trials have now been amended to mitigate the future risk of prolonged pancytopenia and stroke, including a reduction of the lymphodepletion regimen to a previously used regimen (fludarabine (30mg/m^2/day) for 4 days and cyclophosphamide (600 mg/m^2/day) for 3 days). In addition, patients with a prior history of stroke or central nervous system bleeding (or transient ischemic attack (TIA) or reversible ischemic neurologic deficit (RIND) within the prior 6 months of treatment) are now excluded. These protocol changes have been communicated to and acknowledged by the FDA. If further adverse events of a similar nature occur in patients, there is a risk that we or the FDA may impose a clinical hold until the adverse events are further evaluated or, alternatively, we or the FDA may suspend or require termination of these clinical trials.

CRS has been reported in subjects in our SPEAR T-cell trials. A subset of these reported CRS events has been Grade 3 or 4 in severity. Subjects with more severe CRS symptoms have generally responded to treatment with the anti-IL6 or anti-IL6 receptor therapy. All of our protocols now allow for use of this therapy for the treatment of cytokine release syndrome. The anti-IL6 receptor antibody (tocilizumab) has been shown to control cytokine release syndrome without abrogating the anti-tumor response.

Any unacceptable toxicities arising in ongoing clinical programs could result in suspension or termination of those clinical programs. The more SAEs that are reported the greater the risk of suspension of termination of clinical programs, even where the SAEs are unrelated to each other or to our SPEAR T-cells. 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 delivery therapies to some patients.

Use of SPEAR T-cells in combination with other third party products or therapies may increase or exacerbate side effects that have been seen with our SPEAR T-cells alone or may result in new side effects that have not previously been identified with our SPEAR T-cells alone. Any undesirable side effects seen in combination trials may affect our ability to continue with and obtain regulatory approval for the combination therapy, but may also impact our ability to continue with and obtain regulatory approval for SPEAR T-cell therapies alone.

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

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

In particular, eligible patients must be screened for the target peptide and HLA type, which may reduce the number of patients who can be recruited for any clinical program. For example, low target peptide expression levels in the NY-ESO SPEAR T-cell and ADP-A2M10 programs 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. 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.

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 or "reference" 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 our 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 or result in clinical holds being imposed on ongoing trials 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 or a collaborator, IRBs for the institutions in which such trials are being conducted, the Data Monitoring Committee for such trial, or by the FDA or other regulatory authorities due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a SPEAR T-cell, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. If we or our collaborators experience termination of, or delays in the completion of, any clinical trial of our SPEAR T-cells, the commercial prospects for our SPEAR T-cells will be harmed, and our ability to generate product revenue will be delayed. In addition, any delays in completing our clinical trials will increase our costs, slow our product development and approval process and jeopardize our ability to commence product sales and generate revenue.

Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may ultimately lead to the denial of regulatory approval of our SPEAR T-cells.

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

The regulatory approval process and the amount of time it takes us to obtain regulatory approvals for our SPEAR T-cells will depend on the data that are obtained in our ongoing clinical trials and in one or more future registration or pivotal clinical trials. We may attempt to seek approval on a per indication basis for our SPEAR T-cells on the basis of a single pivotal trial or on the basis of data from a Phase 2 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 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. For example, clinical trials may be required in paediatric populations before any marketing approval can be obtained, which can be time consuming and costly. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. The FDA and foreign regulatory authorities also have substantial discretion in the drug and biologics approval process. The number and types of preclinical programs and clinical trials 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;
- 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 authorization applications in other countries. Regulatory authorities in jurisdictions outside of the United States have requirements for approval of SPEAR T-cells with which we must comply prior to marketing in those jurisdictions. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our SPEAR T-cells in certain countries. If we fail to comply with the regulatory requirements in international markets and/or receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our SPEAR T-cells will be harmed.

We may 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, where obtained we may be unable to maintain breakthrough therapy designation or, obtain or maintain the benefits associated with such designations.

We obtained breakthrough therapy status in the United States and PRIME status in Europe for the NY-ESO SPEAR T-cell for the treatment of certain patients with inoperable or metastatic synovial sarcoma who have received prior chemotherapy. We may seek breakthrough therapy or fast track designations for our other SPEAR T-cells in the United States or equivalent regulations elsewhere in the world.

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

Breakthrough therapy designation does not change the standards for product approval. There can be no assurance that we will receive breakthrough therapy designation for any SPEAR T-cell or any particular indication. Additionally, other treatments from competing companies may obtain the designations and impact our ability to develop and commercialize our SPEAR T-cells, which may adversely impact our business, financial condition or results of operation.

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

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

In Europe, the EMA has implemented the so-called "PRIME" (PRIority MEdicines) status in order support the development and accelerate the approval of complex innovative medicinal products addressing an unmet medical need. The PRIME status enables early dialogue with the relevant EMA scientific committees and, possibly, some payers; and thus reinforces the EMA's scientific and regulatory support. It also opens accelerated assessment of the marketing authorization application (150 days instead of 210 days). The PRIME status,

which is decided by the EMA, is reserved to medicines that may benefit from accelerated assessment, i.e. medicines of major interest from a public health perspective, in particular from a therapeutic innovation perspective.

In 2016, the EMA granted PRIME status to NY-ESO SPEAR T-Cell for the treatment of certain patients with metastatic synovial sarcoma who have received prior chemotherapy.

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

Any regulatory approvals that we receive for our SPEAR T-cells will require surveillance to monitor the safety and efficacy of the SPEAR T-cell. The FDA may also require a risk evaluation and mitigation strategy in order to approve our SPEAR T-cells, which could entail requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or a comparable foreign regulatory authority approves our SPEAR T-cells, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export and recordkeeping for our SPEAR T-cells will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration and listing, as well as continued compliance with cGMPs and cGCPs for any clinical trials that we conduct post-approval. We and our contract manufacturers will be subject to periodic unannounced inspections by the FDA to monitor and ensure compliance with cGMPs. We must also comply with requirements concerning advertising and promotion for any SPEAR T-cells for which we obtain marketing approval. Promotional communications with respect to prescription drugs, including biologics, are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved labeling. Thus, we will not be able to promote any SPEAR T-cells we develop for indications or uses for which they are not approved. Later discovery of previously unknown problems with our SPEAR T-cells, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on our ability to conduct clinical trials, including full or partial clinical holds on ongoing or planned trials;
- restrictions on such products' manufacturing processes;
- restrictions on the marketing of a product;
- restrictions on product distribution;
- requirements to conduct post-marketing clinical trials;
- untitled or warning letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- 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 centralized procedure (EMA's scientific assessment and European Commission's approval), 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.

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, the CHMP may ultimately not agree that the requirements for such conditional marketing authorization have been satisfied. This would delay the commercialization of our SPEAR T-cells as we would have to wait for a complete data package before submitting the marketing authorization application.

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 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.

The European criteria for orphan designation are different from the U.S. criteria. On the one hand, the prevalence criterion is five in 10,000 individuals in the European Economic Area (EU plus Iceland, Liechtenstein and Norway). On another hand, no therapy is available for the rare condition or, if such a therapy exists, the future orphan product must bring a significant benefit over that therapy. The significant benefit may be any benefit to patients, including improved safety, improved efficacy, better quality of life or better patient compliance to treatment, provided that it is significant. It must be demonstrated by means of a comparison with the other available therapies, including the medicinal products already approved for the same rare condition. The Committee for Orphan Medicinal Products, or COMP, examines if the orphan criteria are met, and the orphan status is granted by a decision of the European Commission. The meeting of the criteria for orphan designation is examined again by the COMP at the time of approval of the medicinal product. If the criteria for orphan designation are no longer met at that time, the European Commission withdraws the orphan status.

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 authorization 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 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. In Europe, the orphan exclusivity may be lost vis-à-vis another drug in cases the manufacturer is unable to assure sufficient quantity of the drug to meet patient needs or if that other product is proved to be clinically superior to the approved orphan product. A drug is clinically superior if it is safer, more effective or makes a major contribution to patient care.

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).

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. While such mechanisms are in place, 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 significant toxicity and potentially patient fatality. We will need to invest in enhanced systems, such as bar coding, to further 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 significant toxicity and potentially 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 further 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.

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.

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 United Kingdom, United States 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 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 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 Anti-Kickback Statute and analogous state law requirements;

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

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

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

- state and foreign law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to: items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance issued by the federal government or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. California and a few other states have passed laws that require pharmaceutical companies to comply with the April 2003 Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers and/or the Pharmaceutical Research and Manufacturers of America Code on Interactions with Healthcare Professionals. In addition, several states impose other marketing restrictions or require pharmaceutical companies to make marketing or price disclosures to the state. There are ambiguities as to what is required to comply with these state requirements and if we fail to comply with an applicable state law requirement we could be subject to penalties.

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

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

As a company that carries out extensive research and development activities, we benefit from the U.K. research and development tax credit regime for small and medium sized companies, whereby our principal research subsidiary company, Adaptimmune Limited, is able to surrender the trading losses that arise from its research and development activities for a payable tax credit of up to approximately 33.4% of eligible research and development expenditures. Qualifying expenditures largely comprise employment costs for research staff, consumables and certain internal overhead costs incurred as part of research projects. Subcontracted research expenditures are eligible for a cash rebate of up to approximately 21.7%. The majority of our pipeline research, clinical trials management and manufacturing development activities, all of which are being carried out by Adaptimmune Limited, are eligible for inclusion within these tax credit cash rebate claims.

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

We may also benefit in the future from the United Kingdom's "patent box" regime, which would allow certain profits attributable to revenues from patented products to be taxed at a rate of 10%. As we have many different patents covering our products, future upfront

fees, milestone fees, product revenues, and royalties could be taxed at this favorably low tax rate. When taken in combination with the enhanced relief available on our research and development expenditures, we expect a long-term lower rate of corporation tax to apply to us. If, however, there are unexpected adverse changes to the United Kingdom research and development tax credit regime or the "patent box" regime, or we are unable to qualify for such advantageous tax legislation, our business, results of operations and financial condition may be adversely affected.

Risks Related to the Commercialization of Our SPEAR T-cells

The market opportunities for 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.

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;
- 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 in our manufacturing process, 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.

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.

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 on GSK in relation to the performance of programs under the GSK Collaboration and License Agreement and associated payments.

Commercialization of the NY-ESO SPEAR T-cell therapy and payments made by GSK in relation to the NY-ESO SPEAR T-cell therapy depend on GSK's progression of the NY-ESO program through development. GSK has nominated a third target program under the GSK Collaboration and License Agreement that will evaluate and develop new SPEAR T-cells. GSK is currently entitled to nominate a fourth target program and, upon satisfying other conditions, may have the right to nominate a fifth program under the GSK Collaboration and License Agreement, in each case excluding our ongoing wholly-owned development programs. We have no control over whether GSK will elect to progress additional targets under the collaboration arrangements and therefore trigger additional payments from GSK under the GSK Collaboration and License Agreement. 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 will impact our ability to receive further payments under the GSK Collaboration and License Agreement.

The current development plans or any future development plan agreed upon between GSK and us, including those relating to the third target program, may be unsuccessful or fail to result in candidate therapies that are feasible for further development or commercialization. For example, the second target program was terminated by GSK and us due to low presentation of peptide in certain indications. 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 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.

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.

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.

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") and other third parties to provide services related to the manufacture, supply, and processing of our SPEAR T-cells. If one or more of these third parties 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) or provide their services in the future, we may be forced to find an alternative third-party service provider, which we may not be able to do on commercially reasonable terms, if at all. Failure to identify a suitable alternative service provider could impact our business, financial condition or results of operations.

We rely on a limited number of third-party manufacturers and third party service providers for clinical trial product supplies and services 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.

- We may not own, or may have to share, the intellectual property rights to any improvements made by our third-party manufacturers in the manufacturing process for our SPEAR T-cells. Our third party manufacturers may use processes which infringe or potentially infringe third party intellectual property rights which may result in inability to use such processes going forward, an increase in the pricing of such processes or a need to change a different process.

- Our third party manufacturers may fail to perform testing and analysis services accurately, in a manner that can be interpreted or on a timely basis. This could delay or prevent release of our SPEAR T-cell product and as a result delay clinical trials and patient treatment.

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

- Our third-party manufacturers may cease to be able to do business with us (whether for insolvency or other reasons, including takeover, merger or acquisition) at a time when we are unable to source such manufacture elsewhere or at our own manufacturing facility.

- Increased costs, unexpected delays, equipment failures, lack of reproducibility, labor shortages, natural disasters, power failures and numerous other factors which are outside of our control or which may be imposed by our CMOs.

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

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

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

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

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

Our TCR technology was originally developed by Avidex, which was subsequently acquired by Medigene in 2006. We were formed as a new, separate company and licensed our TCR technology for T-cell therapy from Medigene in July 2008. Immunocore was subsequently formed as a new separate company and acquired the TCR technology for soluble TCRs from Medigene later in 2008 to develop soluble TCR proteins. Certain of our shareholders also hold shares in Immunocore.

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

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

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 authorization applications. We cannot provide assurances that, upon inspection, such regulatory authorities will determine that any of our clinical trials comply with the cGCP regulations. In addition, our clinical trials must be conducted with biologic product produced under cGMPs and will require a large number of subjects. Our failure or any failure by these third parties to comply with these regulations or to support BLA for approval of any of our SPEAR T-cells for the treatment of a sufficient number of patients may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of these third parties violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

Any third parties conducting our clinical trials are not and will not be our employees and, except for remedies available to us under our agreements with such third parties which could be limited, we cannot control whether or not they devote sufficient time and resources to our ongoing clinical trials and preclinical programs. These third parties may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug or biologic development activities, which could affect their performance on our behalf. If these third parties do not successfully carry out their contractual duties or

obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to complete development of, obtain regulatory approval of, or successfully commercialize our SPEAR T-cells. As a result, our financial results and the commercial prospects for our SPEAR T-cells would be harmed, our costs could increase and our ability to generate revenue could be delayed.

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

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

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

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

We rely on third parties for equipment and components necessary to manufacture our SPEAR T-cells.

As we further develop our manufacturing process, the manufacture of our SPEAR T-cells may require access to specialized or customized equipment and components from third parties. Such third parties may refuse to supply such equipment and components 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 manufacture our SPEAR T-cells.

Some of the equipment and components 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. While other equipment and components may be available to perform the same or similar operational steps, such alternative equipment and components may be less efficient, more costly, and may result in production delays that may detrimentally impact timescales for the manufacture and supply of our SPEAR T-cells. Even where alternative equipment and components are available, such alternatives 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.

We have formed and may form or seek collaboration agreements or enter into additional licensing arrangements with third parties and either fail to realize the benefits of such relationships or incur substantial additional costs in performing such relationships.

We have formed and may form or seek further third party alliances, create joint ventures or collaborations or enter into additional licensing arrangements with third parties that we believe will complement or augment our development, manufacturing and commercialization efforts with respect to our SPEAR T-cell therapies and any future products. For any of these third party alliances we are reliant on performance of a third party to achieve the end aims of the alliances. For example, we have a collaboration agreement with Universal Cells Inc. ("Universal") under which Universal is required to perform certain collaboration activities. Any delays in the performance of these activities or any requirement to amend or modify those activities will result in delay to the overall program. Any of these relationships may require us to incur non-recurring and other charges, increase our near and long-term expenditures, issue securities that dilute our existing stockholders or disrupt our management and business. There is no guarantee that such third party relationships will result in any positive improvements to our SPEAR T-cells or associated manufacturing processes or that performance of such third party relationships will occur in accordance with expected timelines. Such third party alliances may result in us incurring additional costs or requiring additional resources over and above the costs and resources committed to those alliances. In addition, we face significant competition in seeking appropriate partners and the negotiation process is time-consuming and complex. Moreover, we may not be successful in our efforts to establish third party arrangements for our SPEAR T-cells which may impact our ability to further develop our SPEAR T-cells or delay the further development of our SPEAR T-cells.

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.

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.

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

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

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

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

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

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

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.

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 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, Adrian Rawcliffe, our CFO and CEO designate; Dr. Helen Tayton-Martin, our Chief Business Officer; William Bertrand, our Chief Operating Officer; and John Lunger, our Chief Patient Supply Officer. We do not hold key-man insurance for our senior managers.

Our business is dependent on our ability to recruit experienced and suitably trained employees or consultants, and to retain such employees on a long-term basis. In particular, we are recruiting for a new Chief Medical Officer, following the announcement that Dr. Rafael Amado will be leaving the Company on August 12, 2019, and also for a Chief Financial Officer. There is no guarantee that we will be able to secure candidates for either role on suitable timelines or at all and this may compromise our ability to progress our development and research programs in accordance with currently anticipated timelines.

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 Dr. Tayton-Martin; mutual three months' or two months' notice periods in the case of senior managers and mutual one-month notice periods for all other employees. In the United States, the employment agreements provide for at-will employment except that, under their employment agreements, Mr. Lunger, Mr. Rawcliffe and Mr. Bertrand must provide 60 days' written notice. This means that any of our employees in the United States, except for Mr. Lunger, Mr. Rawcliffe and Mr. Bertrand, could leave our employment at any time, with or without notice. Our success also depends on our ability to continue to attract, retain and motivate highly skilled junior, mid-level and senior managers as well as junior, mid-level and senior scientific and medical personnel.

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, 2019, we had 404 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 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;
- 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 active area of research and a number of immune-related products have been identified in recent years that are alleged to modulate the immune system. Many of these products utilize dendritic cells, a form of immune cell that presents cancer target peptides to T cells and that can in turn result in T-cell activation. More recently, bi-specific antibodies and checkpoint inhibitors (for instance PD-1/PD-L1 antibodies) have been identified as having utility in the treatment of cancer. Bi-specific antibodies commonly target both the cancer peptide and the TCR, thus bringing both cancer cells and T cells into close proximity to maximize the chance of TCR binding and hence an immune response to the cancer cells. Checkpoint inhibitors on the other hand work by targeting receptors that inhibit T-cell effectiveness and proliferation and essentially activate T cells. Other immunotherapies that are being actively investigated include: antibody-drug complexes, TCR-mimic antibodies, oncolytic viruses, cancer vaccines. A variety of cell-based autologous and allogeneic ("off-the-shelf") approaches are also being researched and developed, including but not limited to: CAR-T cell, TCR T-cell, GammaDelta T-cell, CAR-NK cell, NK cell, NKT cell and CTL.

- **CAR-T in hematological malignancies:** Engineered T-cell therapeutics have been identified using antibody recognition systems engineered into T cells, so-called CAR-T cells. A number of targets in hematological malignancies have been well characterized including, but not limited to: BCMA, CD4, CD5, CD19, CD22, CD20, CD33, CD38, CD70, CS1 and CD123. Two CD-19 directed CAR-T cell products have been approved by the U.S. Food and Drug Administration ("FDA") Kymriah™ (tisagenlecleucel) and Yescarta™ (axicabtagene ciloleucel) as well as by the European Medicines Agency (EMA) in the European Union. More recently, Kymriah™ has been approved by the MHLW in Japan. A number of companies and academic institutions are developing CAR-T cell products including but not limited to Allogene Therapeutics, Atara Bio, Autolus, Baylor College of Medicine, bluebird bio, CASI Pharmaceuticals, Celyad, Celgene, Cellectis, CRISPR Therapeutics, Fate Therapeutics, Intrexon, Janssen (JNJ with Nanjing Legend), Juno Therapeutics, Kite Pharma (Gilead), Linea Rx, Mustang Bio, Novartis, Precigen, Refuge Biotechnologies Inc, Servier, Sorrento Therapeutics, Xenetic Biosciences 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, IL13rα2, Lewis Y, L1-CAM, Mesothelin, MUC16, PSCA, PSMA and ROR1. Competitors include but are not limited to: Allogene Therapeutics, Amgen, Atara Bio, Aurora Biopharma, Avid Biotics / Xyphos, Baylor College of Medicine, Cell Medica, Bellicum, BioNTech, Carisma Therapeutics (formerly CARMA Therapeutics), Carsgen, Celgene (with Obsidian Therapeutics) Cellectis Therapeutics, Celyad, CRISPR Therapeutics, Endocyte (a Novartis Company), Fate Therapeutics, Formula Therapeutics, Fred Hutchinson Cancer Research Center, Helix BioPharma, Juno Therapeutics, Lyell Immunopharma, MaxCyte, Memorial Sloan Kettering Cancer Center, Minerva Biotechnologies, Mustang bio, OncoSec Immunotherapies, Oncternal Therapeutics, Poseida Therapeutics, Senti Biosciences, Sorrento Therapeutics, Symvivo, Targazyme and Tmunity.

- **CARs & TCR-mimics targeting peptide-HLA complexes:** Most CAR-T therapies in development are directed towards suitable antigen targets. Another area of development is the creation of CAR-T that selectively binds to the peptide-HLA (pHLA) complex (the natural binding site for endogenous TCR). Furthermore, competitors are also looking at pHLA antibodies or TCR mimic antibodies that can either be engineered in T-cells or developed as standalone antibody therapies in cancer indications (both hematologic malignancies and solid tumors). Targets of such pHLA CAR-T or TCR mimic antibodies include: AFP, CD19, BCMA, NY-ESO-1, p53 and WT1. A number of pharmaceutical, biotechnology, and academic institutions are researching and developing CARs & TCR-mimics targeting the peptide-HLA complex, including but not limited to: Adicet Bio / Regeneron, Altor Bioscience, Cancer Research Technology/CRUK, Eureka Therapeutics, Gritstone Oncology, Morphosys, Xencor and Ziopharm Oncology.

- **TCR T-cells:** TCR T-cells are being developed by competitors that are directed towards a multitude of targets including: AFP, CD20, HPV-16 E6/E7, KRAS, MAGE-A1, MAGE-A3, MAGE A3/A6, MART1, NRAS, NY-ESO-1, p53, PRAME, TGFβRII frameshift antigen WT1, as well as personalized neoantigens. Juno Therapeutics (a Celgene Company) has

developed an engineered TCR therapeutic candidate where the end TCR is purported to have enhanced affinity through stem-cell selection. Juno's candidate JTCR016 (WT1-specific TCR), in collaboration with Fred Hutchinson Cancer Research Center and the National Cancer Institute (NCI), is currently undergoing a Phase 1/2 trial in NSCLC and mesothelioma setting as well as a separate Phase 1/2 in AML. Medigene AG has reported development of a PRAME TCR therapeutic candidate (MDG1011), which has begun a Phase 1/2 clinical investigation in AML, MM and myelodysplastic syndromes. In addition to Juno there is a growing number of TCR companies that are adopting approaches to TCR affinity enhancement, for example Axis Therapeutics, Takara, Takara Bio, Fred Hutchinson Cancer Centre and Immatics. In addition other TCR-focused competitors include, but are not limited to: 3T, Adaptive Biotechnologies (with Genentech), AgenTus, Atreca, Baylor College, Bellicum, BioNTech, bluebird bio, Captain T cell, Cellular Biomedicine Group Inc, Cell Medica Ltd, Cytovant Sciences, GigaMune, GSK, Immunocellular Therapeutics, Immunocore, Intellia Therapeutics, Inc. (with Ospedale San Raffaele), Juno Therapeutics, Kiromic, Kite Pharma (Gilead), Lion TCR LTD, MD Anderson Cancer Center, MediGene AG, NCI, Neon Therapeutics, PACT Pharma, Parker Institute, Refuge Biotechnologies Inc., Roswell Park Cancer Institute, Scancell (with BioNTech), Tactiva Therapeutics, Takara Bio Inc, Takeda (T-CIRA), TCR Cure, T-Cure, TCR x immunotherapies, T-Knife, Tmunity, University of Leiden, Zelluna (with Oslo University Hospital) and Ziopharm Oncology.

There are a number of different approaches being developed for allogeneic or "off-the-shelf" immunotherapy products including stem-cell derived products, HLA-matched products, healthy-donor derived products and use of cells with no or limited HLA type (for example GammaDelta T-cell, or NK cells). Competitors include Century Therapeutics (with FujiFilm Cellular Dynamics), Editas, Fate Therapeutics, Takeda (in collaboration with CiRA), Thyas, Editas, UCLA and T-CiRA.

In addition to adoptive cell therapy approaches aforementioned, our competitors are also investigating other cell-based approaches, including the potential of GammaDelta T-cell, CAR-Macrophages, CAR-NK cell, NK cell, NKT cell, CTLs, TILs, Marrow-infiltrating lymphocytes (MILs), Multi-tumor-associated antigen (TAA)-specific T-cells and virus-specific T-cells either preclinically or in a clinical setting (both hematologic malignancies and solid tumors). In this space there are a number of potential competitors, including, but not limited to: Adicet Bio, Atara Bio, Aurora BioPharma, Cell Medica, Cellular Biomedicine Group Inc, CytomX, Celgene, Fate Therapeutics, Fortress Biotech, Gadeta (with Kite Pharma), Gamma Delta Therapeutics (with Takeda), Gamida cell, Genocea, Glycostem Therapeutics, iCell Gene Therapeutics, Immatics, Iovance Biotherapeutics (formerly Lion Bio), KSQ Therapeutics, MD Anderson Cancer Center, Multimmune, NantKwest, NexImmune, Nkarta, Sorrento Therapeutics, Marker Therapeutics, Tessa Therapeutics, TC Biopharm (with bluebird bio), Torque Therapeutics, Unum Therapeutics, WindMIL Therapeutics and Ziopharm Oncology. Although Immunocore is focused on soluble TCRs rather than engineered SPEAR T-cells, we could also face competition from Immunocore if it develops or acquires products directed at the same targets or indications as our TCR therapeutic product candidates. Moreover, many of our employees have come from a shared background within Immunocore and there is an awareness within Immunocore of certain of our confidential information on the technology platform controlled through confidentiality agreements. This knowledge could be used by Immunocore to facilitate its own developments or to target competitive products against our products placing it in a preferable position as compared to third party competitors.

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

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

ensuring that any impact on our operations is limited. Depending on the terms of Brexit, the United Kingdom could lose the benefits of global trade agreements negotiated by the European Union on behalf of its members, which may result in increased trade barriers which could make our doing business worldwide more difficult. In addition, currency exchange rates in the pound sterling and the euro with respect to each other and the U.S. dollar have already been adversely affected by Brexit. Should this foreign exchange volatility continue it could cause volatility in our financial results.

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

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

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

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

We are exposed to risks related to currency exchange rates.

We conduct a significant portion of our operations within the United Kingdom in both U.S. dollars and pounds sterling and our arrangements with GSK are denominated in pounds sterling. Changes in currency exchange rates have had and could have a significant effect on our operating results. Exchange rate fluctuations between the U.S. dollar and local currencies create risk in several ways, including the following: weakening of the pound sterling may increase the cost of overseas research and development expenses and other costs outside the United Kingdom; strengthening of the U.S. dollar may decrease the value of any future revenues denominated in other currencies. Effects of exchange rates on transactions and cash deposits held in a currency other than the functional currency of a subsidiary can distort our financial results; and commercial pricing and profit margins are affected by currency fluctuations.

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

The rules governing passive foreign investment companies, or PFICs, can have adverse effects for U.S. federal income tax purposes. The tests for determining PFIC status for a taxable year depend upon the relative values of certain categories of assets and the relative amounts of certain kinds of income. The determination of whether we are a PFIC depends on the particular facts and circumstances (such as the valuation of our assets, including goodwill and other intangible assets) and may also be affected by the application of the PFIC rules, which are subject to differing interpretations. Based on our estimated gross income, the average value of our assets, including goodwill and the nature of our active business, we do not believe that the Company was classified as a PFIC for U.S. federal income tax purposes for the U.S. taxable year ended December 31, 2018. There can be no assurance, however, that we will not be considered to be a PFIC for this taxable year or any particular year in the future because PFIC status is factual in nature, depends upon factors not wholly within our control, generally cannot be determined until the close of the taxable year in question and is determined annually.

If we are a PFIC, U.S. holders of our ADSs would be subject to adverse U.S. federal income tax consequences, such as ineligibility for any preferred tax rates on capital gains or on actual or deemed dividends, interest charges on certain taxes treated as

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

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

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

The price of our ADSs may be volatile.

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

- the commencement, enrollment or results of our planned clinical trials;
- the loss of any of our key scientific or management personnel;
- announcements of the failure to obtain regulatory approvals or receipt of a complete response letter from the FDA;
- 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;
- 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, 2019, an aggregate of 54,795,774 options over our ordinary shares had vested and become exercisable. If a large number of our ADSs are sold in the public market after they become eligible for sale, the sales could reduce the trading price of our ADSs and impede our ability to raise capital in the future.

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

As a U.S. public company whose ADSs trade on Nasdaq, we have incurred and will continue to incur significant legal, accounting, insurance and other expenses. We are subject to the reporting requirements of the Exchange Act, which requires, among other things, that we file with the SEC annual, quarterly and current reports with respect to our business and financial condition and must comply with the Nasdaq listing requirements and other applicable securities rules and regulations. In addition, the Sarbanes-Oxley Act, as well as rules subsequently adopted by the SEC and the Nasdaq to implement provisions of the Sarbanes-Oxley Act, impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. Further, pursuant to the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010, the SEC has adopted and will adopt additional rules and regulations, such as mandatory “say on pay” voting requirements, that we must comply with. We expect the rules and regulations applicable to public companies to substantially increase our legal and financial compliance costs and to make some activities more time-consuming and costly. Our insurance costs have increased, particularly for directors and officers liability insurance, and we may be required to incur further substantial increased costs to maintain the same or similar coverage or be forced to accept reduced coverage in future. To the extent these requirements divert the attention of our management and personnel from other business concerns, they could have a material adverse effect on our business, financial condition and results of operations. The increased costs will increase our net loss and may require us to reduce costs in other areas of our business. These laws and regulations could also make it more difficult and expensive for us to attract and retain qualified persons to serve on our board of directors, our board committees or as our executive officers. Furthermore, if we are unable to satisfy our obligations as a public company, we could be subject to delisting of the ADSs from Nasdaq, fines, sanctions and other regulatory action and potentially civil litigation.

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

We must maintain effective internal control over financial reporting in order to accurately and timely report our results of operations and financial condition. In addition, as a U.S. public company, the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, requires, among other things, that we assess the effectiveness of our disclosure controls and procedures and the effectiveness of our internal control over financial reporting at the end of each fiscal period. Pursuant to Section 404 of the Sarbanes-Oxley Act, we are required to furnish a report by our management on our internal control over financial reporting, and we are required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. The rules governing the standards that must be met for our management to assess our internal control over financial reporting pursuant to Section 404 of the Sarbanes-Oxley Act are complex and require significant documentation, testing and possible remediation. These stringent standards require that our audit committee be advised and regularly updated on management's review of internal control over financial reporting.

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

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

We are incorporated under the laws of England and Wales. The rights of holders of our ordinary shares and, therefore, certain of the rights of holders of ADSs, are governed by English law, including the provisions of the Companies Act 2006, and by our articles of association. These rights differ in certain respects from the rights of shareholders in typical U.S. corporations organized in, for example, Delaware. Some of our directors, officers and members of senior management reside outside the United States, and a substantial portion of our assets and all or a substantial portion of the assets of such persons are located outside the United States. As a result, it may be difficult for you to serve legal process on us or our directors and executive officers or have any of them appear in a U.S. court. The United States and the United Kingdom do not currently have a treaty providing for the recognition and enforcement of judgments, other than arbitration awards, in civil and commercial matters. The enforceability in the United Kingdom of any judgment of a U.S. federal or state court will depend on the particular facts of the case as well as the laws and any treaties in effect at the time, including conflicts of laws principles (such as those bearing on the question of whether a U.K. court would recognize the basis on which a U.S. court had purported to exercise jurisdiction over a defendant). In this context, there is doubt as to the enforceability in the United Kingdom, in original actions or in actions for enforcement of judgments of U.S. courts, of civil liabilities based solely on the federal securities laws of the United States. In addition, awards for punitive damages in actions brought in the United States or elsewhere may be unenforceable in the United Kingdom. An award for monetary damages under the U.S. securities laws would likely be considered punitive if it did not seek to compensate the claimant for loss or damage suffered and was intended to punish the defendant.

Provisions in the U.K. City Code on Takeovers and Mergers 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.

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.

Item 6. Exhibits.

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

Exhibit Number	Description of Exhibit
3.1*	Articles of Association of Adaptimmune Therapeutics plc (incorporated by reference to Exhibit 3.1 to our Current Report on Form 8K filed with the SEC on June 16, 2016).
10.1†**	Collaboration Agreement dated May 14, 2019 between Adaptimmune Limited and AIS Operating Co., Inc., f/k/a Alpine Immune Sciences, Inc.
10.2*	Employment Agreement dated as of June 26, 2019 by and between Adaptimmune, LLC and Adrian Rawcliffe (incorporated by reference to Exhibit 10.1 to our Current Report on Form 8-K filed with the SEC on June 27, 2019).
10.3*	James Noble Letter Agreement dated June 26, 2019 (incorporated by reference to Exhibit 10.2 to our Current Report on Form 8-K filed with the SEC on June 27, 2019).
10.4*	James Noble Variation Agreement dated June 26, 2019 (incorporated by reference to Exhibit 10.3 to our Current Report on Form 8-K filed with the SEC on June 27, 2019).
10.5*	James Noble Letter of Appointment dated June 26, 2019 (incorporated by reference to Exhibit 10.4 to our Current Report on Form 8-K filed with the SEC on June 27, 2019).
31.1**	Certification of Principal Executive Officer pursuant to Rule 13a-14(a) and Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2**	Certification of Principal Financial Officer pursuant to Rule 13a-14(a) and Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1**	Certification of Principal Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2**	Certification of Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101**	The following financial information from Adaptimmune Therapeutics plc's Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2019, formatted in iXBRL (Inline eXtensible Business Reporting Language): (i) Unaudited Condensed Consolidated Balance Sheets as of June 30, 2019 and December 31, 2018, (ii) Unaudited Condensed Consolidated Statements of Operations for the three and six months ended June 30, 2019 and 2018, (iii) Unaudited Condensed Consolidated Statements of Comprehensive Loss for the three and six months ended June 30, 2019 and 2018, (iv) Unaudited Condensed Consolidated Statements of Change in Equity for the three and six months ended June 30, 2019 and 2018, (v) Unaudited Condensed Consolidated Statements of Cash Flows for the six months ended June 30, 2019 and 2018 and (vi) Notes to the Unaudited Condensed Consolidated Financial Statements.

* Previously filed.

** Filed herewith.

† Certain confidential information contained in this agreement has been omitted because it (i) is not material and (ii) would be competitively harmful if publicly disclosed.

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

Date: August 1, 2019

/s/ James Noble
James Noble
Chief Executive Officer

Date: August 1, 2019

/s/ Adrian Rawcliffe
Adrian Rawcliffe
Chief Financial Officer

CERTAIN CONFIDENTIAL INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY [***], HAS BEEN OMITTED BECAUSE IT IS BOTH (i) NOT MATERIAL AND (ii) WOULD BE COMPETITIVELY HARMFUL IF PUBLICLY DISCLOSED

CONFIDENTIAL – FINAL

COLLABORATION AGREEMENT

BETWEEN

ADAPTIMMUNE LIMITED

AND

AIS OPERATING CO., INC.

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COLLABORATION AGREEMENT

THIS COLLABORATION AGREEMENT ("**Agreement**") is made and entered into on 14 May 2019 (" **Effective Date**") BETWEEN

(A) **ADAPTIMMUNE LIMITED** having its principal place of business at 60 Jubilee Avenue, Milton Park, Abingdon, Oxon, OX14 4RX, United Kingdom ("**Adaptimmune**"); and

(B) **AIS OPERATING CO., INC.** , f/k/a Alpine Immune Sciences, Inc., having its principal place of business at 201 Elliot Avenue West, Suite 230, Seattle, WA 98119, United States ("**Alpine**").

Alpine and Adaptimmune are sometimes referred to herein individually as a " **Party**" and collectively as the " **Parties**."

BACKGROUND:

(A) Adaptimmune is a biotechnology company that is engaged in research and development of TCR therapies for pharmaceutical therapy use.

(B) Alpine is a biotechnology company that has proprietary variant Ig Domain technology which can be used to identify and engineer immune proteins to assist, activate or otherwise modulate immune cell interactions.

(C) Alpine and Adaptimmune desire to collaborate in certain Research Programs (as defined below) to conduct research and preclinical development of products that combine Adaptimmune's TCR therapies with Alpine's SIP/TIP technology.

(D) Following the Completion of each Research Program, Adaptimmune will have the Option to obtain an Exclusive License to further develop and commercialize Products arising therefrom (all capitalized terms as defined below).

(E) Based on the foregoing premises and the mutual covenants and obligations set forth below, the Parties agree as follows.

THE PARTIES AGREE:

1. DEFINITIONS

Capitalized terms used in this Agreement, whether used in the singular or plural, shall have the meanings set forth below or elsewhere herein, unless otherwise specifically indicated herein.

Acceptance	is defined in Clause 3.1.3;
Accounting Standard	means, either (a) International Financial Reporting Standards (" **IFRS**") or (b) US generally accepted accounting principles ("**GAAP**"), in either case, which standards or principles (as applicable) are currently used at the applicable time, and as consistently applied, by the applicable Party;
Acquiring Third Party	means a Third Party (including in each case any entity which directly or indirectly controls, is controlled by, or is under common control with such Third Party) which, as at the date of the Change of Control, controls or owns [***];
Adaptimmune Background IP	means all Intellectual Property Rights that (a) are Controlled by Adaptimmune or its Affiliates as of the Effective Date, or (b) created or developed by Adaptimmune or its Affiliates during the Term other than in the performance of this Agreement;

Adaptimmune Foreground IP	is defined in Clause 10.1.2(a);
Adaptimmune Indemnitees	is defined in Clause 14.2;
Adaptimmune Licensed IP	means any of the Adaptimmune Background IP or Adaptimmune Foreground IP or Joint Foreground IP co-owned by Adaptimmune, subject to Clause 6.6, that is necessary or reasonably useful for the performance of the Research Program;
Adaptimmune Platform Technology	shall mean technology created or developed by Adaptimmune outside of the performance of this Agreement, whether prior to or after the Effective Date, including [***];
Adjusted Net Sales	means, with respect to each Product, [***] (a) [***], and (b) [***] of Net Sales of such Product in such period;
Affiliate	means, with respect to a Party, any Person that, directly or indirectly (through one or more intermediaries) controls, is controlled by, or is under common control with a Party. For purposes of this Clause, "control" means the direct or indirect ownership of more than fifty percent (50%) of the voting stock or other voting interests or interest in the profits of the Party;
Agreement	means this Agreement;
Alliance Manager	means the individual appointed by each Party as the principal point of contact for communication between the Parties under this Agreement and appointed in accordance with Clause 2.1.3;
Alpine Background IP	means all Intellectual Property Rights that (a) are Controlled by Alpine or its Affiliates as of the Effective Date, or (b) created or developed by Alpine or its Affiliates during the Term other than in the performance of this Agreement;
Alpine Foreground IP	is defined in Clause 10.1.2(b);
Alpine Indemnitees	is defined in Clause 14.1;
Alpine Licensed IP	means any of the Alpine Background IP, Alpine Foreground IP or Joint Foreground IP co-owned by Alpine, subject to Clause 6.6, which either (a) [***]; or (b) [***];
Alpine Patents	means the Patents set out in Exhibit 6;
Alpine Platform Technology	means the platform technology created or developed by Alpine outside of the performance of this Agreement, whether prior to or after the Effective Date, including its [***];
Anticorruption Laws	is defined in Clause 17.1.1;
Applicable Laws	means all applicable international, multinational, national, regional, state, provincial and local laws, rules, regulations, ordinances, declarations, requirements, directives, guidance, policies and guidelines which are in force during the Term and in any jurisdiction in which any Clinical Trial or other activity under this Agreement is performed or in which any Product is manufactured, sold or supplied to the extent in each case applicable to any Party to this Agreement, including, as applicable to activities hereunder, the regulations and

	regulatory guidance promulgated by the FDA, the Consolidated Guidance E6 on Good Clinical Practice adopted by the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, as ratified by the FDA and the Clinical Trials Directive (Directive 2001/20/EC of 4th April 2001) and the respective implementing legislation, the conditions and requirements imposed by the related ethics committee and any of the foregoing which relate to ethical business conduct, the import or export of goods, technical data or other items, and data protection and privacy rules, as any of the foregoing may be amended from time to time;
Background IP	means, as applicable, the Alpine Background IP and the Adaptimmune Background IP;
Biosimilar	means any drug or biological product that is subject to review under an abbreviated approval pathway as a biosimilar, follow-on biologic or generic biological product, as those terms are commonly understood under the FD&C Act or the PHS Act and related rules and regulations, or the corresponding or similar laws, rules and regulations of any other jurisdiction and where such drug or biological product obtains Regulatory Approval based on, or in part on, reference to any data or Regulatory Approval applicable to a Product hereunder;
Bona Fide Internal Program	is defined in Clause 3.1.3;
Change of Control	means with respect to a Party, (a) the sale or disposition to a Third Party of all or substantially all of the business or assets of such Party to which the subject matter of this Agreement relates, including all of or substantially all of the Licensed IP under which such Party has granted rights to the other Party under this Agreement; or (b) (i) the acquisition by a Third Party of more than fifty percent (50%) of the issued voting shares or stock in such Party, or (ii) the acquisition, merger or consolidation of such Party with or into a Third Party. A Change of Control will not include an acquisition, merger or consolidation or similar transaction of a Party in which the holders of the voting shares in such Party immediately prior to such acquisition, merger, consolidation or transaction, will beneficially own, directly or indirectly, at least fifty percent (50%) of the voting shares in the Third Party or the surviving entity in such acquisition, merger, consolidation or transaction, as the case may be, immediately after such acquisition, merger, consolidation or transaction;
Clinical Trial	means a Phase I Clinical Trial, Phase II Clinical Trial, Phase III Clinical Trial, or Phase IV Clinical Trial, as the case may be, and any clinical studies specifically including pediatric subjects, or any other equivalent trial in which any Product is administered to a human subject;
CMC	means chemistry, manufacturing and control;
Combination Therapy	Is defined in Clause 6.3.1;

Commercially Reasonable Efforts	means, on a Party-by-Party basis, that level of effort and resources required to carry out a particular task or obligation in an active and sustained manner, consistent with the general practice followed by the Party in the exercise of its reasonable business discretion relating to other pharmaceutical therapies or products owned by it, or to which it has exclusive rights, which are of similar market potential at a similar stage in their development or life, taking into account issues of patent coverage, safety and efficacy, therapy profile, the competitiveness of any therapy in development and in the marketplace, supply chain management considerations, the proprietary position of the product or therapy, the regulatory structure involved, the profitability of the applicable therapies (including pricing and reimbursement status achieved), and other relevant factors, including technical, legal, scientific and/or medical factors;
Competing Product	means a cell therapy comprising [***]
Completion	is defined in Clause 3.5;
Confidential Information	is defined in Clause 11.1;
Control or **Controlled by**	means the rightful possession by a Party, whether directly or indirectly and whether by ownership, license (other than pursuant to this Agreement) or otherwise, as of the Effective Date or during the Term, of the right (excluding where any required Third-Party consent cannot be obtained) to grant a license, sublicense or other right to exploit any Intellectual Property Rights as provided herein, without violating the terms of any agreement with any Third Party;
Covers or **Covered** or **Covering**	means, with respect to a particular Patent or Intellectual Property Right and in reference to a particular compound, process or Product (whether alone or in combination with one or more other ingredients) that the use, manufacture, sale, supply, import, offer for sale of such compound or product or use of such process would infringe a valid claim of such Patent in the absence of any license granted under this Agreement, or in the case of a patent application would infringe the claim of such patent application if such patent application was a granted patent;
Development Candidate	means, with respect to a given Research Program, the first Product, if any, resulting from such Research Program and selected by Adaptimmune, considering JSC and JPT input, as meeting the applicable criteria [***];
Disclosing Party	is defined in Clause 11.1;
Dispute	is defined in Clause 16.1;
Effective Date	is defined in the Preamble;
EMA	means the European Medicines Agency and any successor thereto;
Enforcement	is defined in Clause 10.4.3;
EU	means the member states of the European Union and Switzerland, or any successor entity thereto performing similar functions, and for the purposes of this Agreement shall also be deemed to include the UK;
EU Major Market	means any one of [***];

[***]	[***]
Exclusive License	is defined in Clause 6.3.1;
FDA	means the US Food and Drug Administration, or any successor entity thereto performing similar functions;
Field	[***]
First Commercial Sale	means, with respect to a particular Product, the first sale of such Product to a Third Party following the obtaining of Marketing Approval for such Product in any country, excluding, however, any shipment or invoicing or other distribution of such Product for use (a) in a Clinical Trial, (b) on a named-patient basis, (c) for compassionate use, (d) under Treatment IND, or (e) in any nonregistrational studies (e.g. an investigator-initiated trial);
Foreground IP	means any Intellectual Property Rights created or developed in the performance of this Agreement, including under any Research Program;
GMP	means all current Good Manufacturing Practices applicable to biopharmaceuticals in the US and/or in the EU, as are in effect from time to time during the Term and in each case as applicable to the activities being carried out under this Agreement;
Governmental Official	is defined in Clause 17.1.2;
GLP	means all applicable current Good Laboratory Practice standards for laboratory activities for pharmaceuticals, as set forth in the FDA's Good Laboratory Practice regulations as defined in 21 C.F.R. Part 58 and/or the Good Laboratory Practice principles of the Organization for Economic Co-Operation and Development ("**OECD**"), and such standards of good laboratory practice as are required by the EU and other organizations and governmental agencies in countries in which the relevant activity under this Agreement is being performed;
GXP	means any of the following as applicable to this Agreement: GLP and GMP;
IND	means an investigational new drug application filed with the FDA pursuant to 21 CFR Part 312 before the commencement of Clinical Trials of a Product, or any comparable or equivalent filing (including any Clinical Trial Authorization filed in the EU) with any relevant regulatory authority in any other jurisdiction required before the commencement of any Clinical Trial in such jurisdiction;
Indemnitee	is defined in Clause 14.3;
Indemnitor	is defined in Clause 14.3;
Infringement	is defined in Clause 10.4.1;
Initial Program Targets	means [***];
Initial Research Programs	means the two Research Programs described in Exhibit 1;

Intellectual Property Rights	means Patents, rights to discoveries, inventions, copyrights and related rights, trademarks, trade names and domain names, rights in designs, rights in computer software, database rights, rights in confidential information (including know-how) and any other intellectual property rights, in each case whether registered or unregistered and including all applications (or rights to apply) for, and renewals or extensions of, such rights and all similar or equivalent rights or forms of protection which subsist or will subsist now or in the future in any part of the world;
Joint Foreground IP	is defined in Clause 10.1.2(c);
JPT	is defined in Exhibit 4;
JSC	is defined in Exhibit 4;
Licensed IP	means, as applicable, the Alpine Licensed IP and the Adaptimmune Licensed IP;
Loss or **Losses**	is defined in Clause 14.1;
MAA or **Marketing Approval Application**	means a BLA, sBLA, NDA, sNDA and any equivalent thereof in the US or any other country or jurisdiction. As used herein: "**BLA**" means a Biologics License Application and amendments thereto filed pursuant to the requirements of the FDA, as defined in 21 C.F.R. § 600 et seq., for FDA approval of a Product; "**sBLA**" means a supplemental BLA; and "**NDA**" means a New Drug Application and amendments thereto filed pursuant to the requirements of the FDA, as defined in 21 C.F.R. § 314 et seq., for FDA approval of a Product and "**sNDA**" means a supplemental NDA;
[***]	[***]
Milestone Events	is defined in Clause 8.3;
Milestones	is defined in Clause 8.3;
Net Sales	means, with respect to a particular Product for any period, the amount which reflects the gross amount invoiced for such Product sold by Adaptimmune or its Affiliates or Sublicensees less the following deductions in relation to each Product, to the extent in each case such deductions are actually made and accounted for within Adaptimmune's or its Affiliates' or Sublicensees' accounts: (a) credits, reserves or allowances granted for damaged, outdated, returned, rejected, withdrawn or recalled Product; (b) trade, quantity and cash discounts allowed; (c) discounts, refunds, rebates, chargebacks, retroactive price adjustments, and any other similar allowances which effectively reduce the net selling price; (d) that portion of the sales value associated with, and reasonably attributable to, drug delivery systems or other associated therapy requirements (including screening assays, companion diagnostics and other associated assays) and to the extent invoiced with a Product;

(e) allowance for distribution expenses;

(f) taxes imposed in connection with the sales and disposition of such Product and actually paid by Adaptimmune or its Affiliates or Sublicensees;

(g) duties and any other governmental charges or levies imposed upon the import or export, or manufacture or sale of a Product, including the annual fee imposed on the pharmaceutical manufacturers by the US government (but, for clarity, excluding income or franchise taxes); and

(h) any other similar and customary deductions which are in accordance with the Accounting Standards and which are consistently used by Adaptimmune, its Affiliates or Sublicensees in connection with its public financial reporting requirements.

The supply of Products for use (a) in a Clinical Trial, (b) on a named-patient basis, (c) for compassionate use, (d) under Treatment IND, or (e) in any nonregistrational studies (e.g. an investigator-initiated trial) shall not constitute a Net Sale.

The supply of Products to Affiliates or Sublicensees will not constitute a Net Sale, but the subsequent resale of Product to a Third Party that is not a Sublicensee shall be included within the computation of Net Sales.

[***]

Non-Prosecuting Party means, with respect to a Patent, the Party other than the Prosecuting Party for such Patent;

Non-Publishing Party is defined in Clause 12.3.1;

Option Is defined in Clause 6.2;

Option Period is defined in Clause 6.2;

Other Program Target means any Target, other than the Initial Program Targets, which has been Accepted in accordance with clause 3.1.3;

Other Research Program means any Research Program, other than the Initial Research Programs, established to develop a SIP or TIP for an Other Program Target following the Acceptance of such Other Program Target in accordance with Clause 3.1.3;

Party or **Parties** is defined in the Preamble;

Patent(s) means any and all patents and patent applications and any patents issuing therefrom or claiming priority therefrom, worldwide, together with any extensions (including patent term extensions and supplementary protection certificates) and renewals thereof, reissues, reexaminations, substitutions, confirmation patents, registration patents, invention certificates, patents of addition, renewals, divisionals, continuations, and continuations-in-part of any of the foregoing;

Patent Expert is defined in Clause 10.1.2;

Person	means an individual, sole proprietorship, partnership, limited partnership, limited liability partnership, corporation, limited liability company, business trust, joint stock company, trust, unincorporated association, joint venture or other similar entity or organization;
Phase I Clinical Trial	means a human clinical trial, the principal purpose of which is preliminary determination of safety, pharmacokinetics and pharmacodynamics parameters of a Product in healthy individuals or patients, as described in 21 C.F.R. § 312.21(a), or similar clinical study in a country other than the US;
Phase II Clinical Trial	means a human clinical trial, the principal purpose of which is to explore a variety of doses, dose response, and duration of effect, and to provide a preliminary determination of clinical safety and efficacy of a Product for a particular therapeutic indication or therapeutic indications in a target patient population, as described in 21 C.F.R. § 312.21(b), or similar clinical study in a country other than the US; provided, that, to the extent there is any ambiguity as to whether a given human clinical trial constitutes a Phase II Clinical Trial or a "Phase I(b)" clinical trial [***];
Phase III Clinical Trial	means a human clinical trial (including a pivotal or registration trial), the principal purpose of which is to (a) demonstrate clinically and statistically the efficacy and safety of a Product for its intended one or more indications, (b) define contraindications, warnings, precautions and adverse reactions that are associated with the Collaboration Product in the dosage range to be prescribed, and (c) to obtain Regulatory Approval of such Product for such indication(s), as further defined in 21 C.F.R. § 312.21(c) or a similar clinical study in a country other than the US; provided, that, (i) to the extent there is any ambiguity as to whether a given human clinical trial constitutes a Phase III Clinical Trial or a "Phase II(b)" clinical trial, [***] and (ii) [***];
Post-Acquisition Internal Program	is defined in Clause 3.1.3;
Product	means, with respect to a specific Research Program and Program Target, an adoptive cell therapy comprising both "X" plus "Y" (as combined, the "**Basic Product**") and optionally "Z", where Z may be coformulated, engineered in, or otherwise sold together as a kit with the Basic Product and for a single price (any such therapy which includes a Basic Product plus Z, a "**Combination Product**"), where: • "**X**" means a TCR-engineered human T-cell developed by Adaptimmune or its Affiliates (a "**TCR-T**"), which TCR-T may be the TCR-T identified as of the date of Option exercise under such Research Program and included within the Development Candidate, or identified after exercise of the Option, in each case, alone or including one or more other moieties or excipients in such TCR-T; • "**Y**" means the specific form of a SIP or a TIP that was developed during such Research Program for combining with a TCR-T; and • "**Z**" means any other active agent or moiety owned or Controlled by Adaptimmune or its Affiliates or Sublicensees, or to which Adaptimmune, its Affiliates or Sublicensees has access.

Program Target	means the Initial Program Targets and any Other Program Target;
Prosecute or **Prosecute and Maintain** or **Prosecution and Maintenance**	means, with respect to a Patent, all activities associated with the preparation, filing, prosecution and maintenance of such Patent , as well as activities associated with re-examinations, reissues, applications for patent term adjustments and extensions, supplementary protection certificates and the like with respect to that Patent, together with the conduct of interferences, derivation proceedings, pre- and post-grant proceedings, the defense of oppositions and other similar proceedings with respect to that Patent;
Prosecuting Party	means, with respect to a Patent, the Party responsible for Prosecution such Patent, under Clause 10.2;
Public Disclosure	is defined in Clause 12.2.2;
Publication	is defined in Clause 12.3.1;
Publishing Party	is defined in Clause 12.3.1;
Receiving Party	is defined in Clause 11.1;
Regulatory Approval	means the technical, medical and scientific licenses, registrations, authorizations and approvals required for marketing or use of a Product (including approvals of, BLAs, IND applications, pre- and post-approvals, and labeling approvals and any supplements and amendments to any of such approvals) from any national, supra-national, regional, state or local regulatory agency, department, bureau, commission, council or other governmental entity, necessary for the development, manufacture, distribution, marketing, promotion, offer for sale, use, import, export or sale of a Product in a regulatory jurisdiction. In the US, Regulatory Approval means approval of any Marketing Approval Application or equivalent by the FDA. Regulatory Approval shall include obtaining any pricing reimbursement or other pricing approval requirement;
Regulatory Authority	means the FDA, EMA, any other regulatory authority or governmental body with regulation or governance over the performance of any part of the activities under this Agreement;
Release	is defined in Clause 12.1;
Replaced Product	is defined in Clause 8.3.5;
Replacement Product	is defined in Clause 8.3.5;
Research License	is defined in Clause 6.1;
Research Plan	means, with respect to a given Research Program, the activities required for completion of such Research Program;
Research Program	means, with respect to each Target, a program for the development of a Product directed to such Target and covering all development activities up to (but not including) the filing of the first IND or other regulatory or ethical equivalent for a Product;
Research Term	means a period of [***] years, the first year starting on the Effective Date;
Requesting Party	is defined in Clause 12.2.2;

Reviewing Party	is defined in Clause 12.2.2;
Royalty	is defined in Clause 8.4.1;
Royalty Report	is defined in Clause 8.4.6;
Royalty Term	is defined in Clause 8.4.4;
Rules	is defined in Clause 16.2.1;
SAE	means a serious adverse effect resulting from any Clinical Trial or administration of a Product;
SIP	means a secreted immunomodulatory protein;
Sublicensee	means a Third Party or Affiliate who has been granted a sublicense under any license under this Agreement;
SUSAR	means a suspected unexpected serious adverse reaction resulting from any Clinical Trial or administration of any product or therapy to a human being;
Target	means a biological target for which a SIP or TIP may be developed under any Research Program for purposes of modulation of the activity or function of such target, including the Initial Program Targets;
TCR	means T-cell receptor;
Term	is defined in Clause 15.1;
Third Party	means any entity other than Adaptimmune or Alpine or an Affiliate of either of them;
Third-Party Claims	is defined in Clause 14.1;
Third-Party Infringement Claim	is defined in Clause 10.5.1;
Third-Party Rights Agreement	is defined in Clause 3.1.3.
Title 11	is defined in Clause 15.3;
TIP	means a transmembrane immunomodulatory protein;
UK	means the United Kingdom;
US	means the United States of America and its territories and possessions;

Valid Claim	means, with respect to a particular country, (a) (i) an issued claim in an issued and unexpired Patent in the Alpine Licensed IP or (ii) an issued claim in an issued and unexpired Patent in the Adaptimmune Licensed IP where such claim covers the composition of matter of a TCR-T (or any component thereof) that is incorporated in the applicable Product, in each case ((i) and (ii)) in such country that has not lapsed or been disclaimed, revoked, held unenforceable, unpatentable or invalid by a decision of a court or other governmental agency of competent jurisdiction, unappealable or unappealed within the time allowed for appeal, and that has not been admitted to be invalid or unenforceable through re-examination, re-issue, disclaimer or otherwise, or lost in an interference proceeding, or (b) a claim of a pending patent application in such country that has been pending less than seven (7) years from the earliest date on which such patent application claims priority (direct or indirect, in whole or in part) and which claim was filed and is being prosecuted in good faith and has not been cancelled, withdrawn or abandoned or finally rejected by an administrative agency action from which no appeal can be taken;
Valid Claim Expiration	is defined in Clause 8.4.4;
VAT	means, (a) in the EU, value added tax calculated in accordance with Council Directive 2006/112/EC and, (b) in a jurisdiction outside the EU, any equivalent tax;
Year	means any consecutive twelve (12)-month period, the first Year starting on the Effective Date of this Agreement.

2. GOVERNANCE

2.1 **Governance Generally**.

2.1.1 **JSC and JPT**. The Parties agree to set up (a) a Joint Steering Committee ("**JSC**") to oversee performance of this Agreement and manage the relationship between the Parties, and (b) a Joint Project Team ("**JPT**") to oversee the performance of each Research Program. Further ad hoc committees may be set up as required by the Parties.

2.1.2 The formation, composition, decision making, duration and characterization of the JSC and JPT are set out further in Exhibit 4.

2.1.3 **Alliance Managers**. Within thirty (30) days after the Effective Date, each Party shall appoint an Alliance Manager to be the principal point of contact for communications under this Agreement. The Alliance Managers shall facilitate the flow of information and collaboration between the Parties and assist in the resolution of pending issues and potential disputes in a timely manner, and the Parties to reach consensus and avert escalation of such issues or potential disputes. Either Party may replace its Alliance Manager at any time upon prior written notice (including by email) to the other Party's Alliance Manager. Each Party shall ensure that its Alliance Manager has the necessary availability, training and experience to diligently and properly perform the obligations required of an Alliance Manager under this Agreement.

3. RESEARCH PROGRAM

3.1 **Research Program**.

3.1.1 Adaptimmune and Alpine will perform up to [***] Research Programs, each directed to a different Program Target.

3.1.2 The first [***] Research Programs and the Research Plans related thereto are described in Exhibit 1 and will start from the Effective Date of this Agreement ("**Initial Research Programs**").

3.1.3 During the first [***] months following the Effective Date, Adaptimmune has the right to request a further [***] Research Programs. Any request will be made in writing, specifying the Target proposed for such Research Program, and shall be submitted to the JSC for review. Within [***] following any such submission, the JSC shall confer and discuss to determine whether to accept such proposed Target and request for Research Program, taking into account factors such as scientific feasibility and regulatory and intellectual property considerations relating to the development of a Product directed to such proposed Target, and Alpine's representatives shall inform the JSC whether (A) Alpine has entered into an agreement with a Third Party in relation to the proposed Target that would prevent the grant of rights necessary for the conduct of such Research Program or would otherwise prevent the development or commercialization of Products relating to such Target in the Field (any such agreement, a "**Third-Party Rights Agreement**"), or (B) a Change of Control of Alpine [***]. If the JSC unanimously (including Alpine's members), decides to accept such request for a new Research Program directed to such proposed Target ("**Acceptance**"), such new Research Program shall be deemed an " **Other Research Program**" and such proposed Target shall be deemed an "**Other Research Target**". [***]

3.1.4 Following Acceptance of each Other Research Program in accordance with Clause 3.1.3 above, the Parties will use Commercially Reasonable Efforts to agree (and in any case aim to agree within a maximum period of [***] after Acceptance) on a Research Plan for such Other Research Program, which shall set forth (a) the Other Research Target under such Research Program, (b) the initial SIP or TIP that will be combined with a TCR-T to develop a Product under such Research Program, (c) the various phases of research and preclinical development activities for such Product as required to enable the filing of an IND by Adaptimmune, (d) the criteria for the Adaptimmune to determine, with the consideration of JSC input, whether to advance the research or preclinical development of such Product from one phase to a subsequent phase pursuant to the Research Plan, and (e) any other relevant details and requirements similar to those set out for the Initial Research Programs in Exhibit 1.

3.1.5 The start date for any Other Research Program will be the date of agreement to the applicable Research Plan by the Parties, unless otherwise provided in the Research Plan.

3.2 **Performance of Research Program**

3.2.1 Under each Research Program, each Party shall use Commercially Reasonable Efforts to perform any part of the Research Program assigned to it, including making resources available as and when required and supplying any product, equipment or materials as and when required and specified under the Research Plan for such program. Each Party will provide all data and deliverables as required to be generated by it in accordance with the Research Program. The costs and expenses incurred in the conduct of the Research Programs shall be allocated between the Parties in accordance with Clause 8.1.

3.2.2 The Parties may enter into a supply agreement or quality agreement to supplement

the terms of this Agreement, as necessary, with terms relating to manufacture and supply, quality and/or any other terms necessary or reasonably useful for the development of any Product. The Parties will negotiate any such supplemental agreement in good faith and on a timely basis to prevent any unreasonable delay to activities performed under the Research Program.

3.2.3 [***]

3.3 **Changes to Research Program**.

3.3.1 The Parties, directly or via the JPT, will work together to propose to the JSC modifications to the Research Plan as required during its performance and as data from the Research Programs arise. The JSC will be responsible for amending the Research Plan as necessary in relation to any changes; provided that any amendment to a Research Plan that material changes a Party's personnel and/or resources necessary for performance of such Research Program must be mutually agreed by the Parties in writing (i.e. the JSC cannot make such decisions).

3.3.2 Subject to Clause 3.3.3 below, [***]

3.3.3 [***]

3.4 **Subcontractors**. Each Party may subcontract portions of its work under the Research Program to (i) any Affiliate or (ii) Third Parties; provided in the case of a Third Party, (a) there are no reasonably based objections from the other Party regarding the use of said subcontractor, and (b) such subcontract is in writing and is consistent with the terms and conditions of this Agreement including the confidentiality provisions of Article 11 and (c) any rights granted to such subcontractor are restricted to only those rights necessary for performance by such subcontractor of the portions of work on behalf of the subcontracting Party. The subcontracting Party will remain fully responsible (at its cost) for all acts or omissions of any subcontractor it appoints (including any acts or omissions which result in a breach of the terms of this Agreement) and shall ensure that each subcontractor complies with the terms and conditions of this Agreement. Each Party shall notify the other Party in writing at least thirty (30) calendar days in advance of any subcontractor appointments other than Affiliates. In addition, each Party may audit any subcontractor appointed by the other Party prior to such subcontractor being appointed to perform any part of any Research Program, and on provision of written notice within fifteen (15) calendar days of such Party becoming aware of such subcontractor appointment. Such audit will occur as soon as reasonably practicable and in any event in accordance with any timelines set out in the applicable Research Program. Each Party will provide the other Party with reasonable assistance to enable the conduct of such audits (including interacting with such subcontractors to substantiate the need and right to conduct such audits). To the extent any audit identifies any noncompliance with Applicable Laws (including noncompliance with GXP), the appointing Party shall use reasonable efforts to procure correction of such noncompliance by subcontractor or shall use an alternative subcontractor where correction of such noncompliance is not possible or practicable. Each Party will put in place written Quality Agreements with any subcontractor performing GXP activities prior to them supplying materials or services supporting any relevant GXP activities under any Research Program, to the extent such Quality Agreements are reasonably required in order to comply with Applicable Laws. The other Party may request copies of such Quality Agreement to the extent necessary to satisfy its internal standard operating procedures or to satisfy obligations to any Regulatory Authority or under Applicable Laws.

3.5 **Completion of any Research Program**. The term for a particular Research Program shall commence on the start date for such Research Program and as set forth in Clause 3.1.5, and shall continue, unless earlier terminated in accordance with Article 15, until the completion or waiver (by the JSC and JPT) of all the tasks set out in the Research Program and delivery of all data and deliverables thereunder ("**Completion**"). The final report for each Research Program shall identify the Product resulting therefrom, and include such data and research records that have been compiled and which may be required to support an IND filing for such Product as specified in the applicable Research Plan. To the extent any final report does not include any data generated under such Research Program and reasonably required to support the filing of an IND for such Product, upon Adaptimmune's reasonable request, Alpine will promptly provide any such additional data and information. [***]

3.6 **Reports and Records**.

3.6.1 **Progress Reports**. Each Party shall keep the other Party regularly informed of its activities (if any) under each Research Program and shall provide to the other Party's representatives on the JPT regular written summary updates at each JPT meeting. If reasonably necessary for a Party to perform its work under a Research Program, that Party may request that the other Party provide more detailed information and data regarding the updates it earlier provided, and the other Party shall promptly provide the requesting Party with information and data as is reasonably available and reasonably necessary to conduct a Research Program, and such other information as the Parties agree. All such reports, information and data provided by a Party shall be considered such Party's Confidential Information.

3.6.2 **Research Records**. Each Party shall maintain records of its performance of each, if any, Research Program (or cause such records to be maintained) in sufficient detail and in good scientific manner as will properly reflect all work done and results achieved by or on behalf of such Party in the performance of such Research Program. All laboratory notebooks shall be maintained for no less than five (5) years after creation of the relevant notebook entry. All other records shall be maintained by each Party during the applicable Research Program and for a minimum of three (3) years thereafter. All such records of a Party shall be considered such Party's Confidential Information. Records shall not be destroyed by either Party without prior written notification of such destruction being provided to other Party, and other Party being given the opportunity to take over the storage and responsibility for such records.

3.7 **Research Efforts**. Each Party shall assign such scientific and technical personnel and allocate such other resources as are reasonably necessary for performing the activities as are assigned to it in each Research Program, and shall perform such activities in accordance with all Applicable Laws (including GXP, as applicable) in each case to the extent applicable to performance of the relevant Research Program activities by such Party, the terms and conditions of this Agreement, and within generally accepted professional standards. Each Party shall be solely responsible for the safety and health of its employees, consultants and visitors, and for compliance with all Applicable Laws related to health, safety and the environment, including providing its employees, consultants and visitors with all required information and training concerning any potential hazards involved in performing such activities and any precautionary measures to protect its employees from any such hazards at its own facilities and as regards its or its subcontractors performance of the Research Program. Each Party shall use Commercially Reasonable Efforts to train its personnel assigned to perform activities under this Agreement and ensure that any personnel so assigned shall be capable of professionally and competently performing the activities assigned to it in each Research Program.

4. REGULATORY

4.1 **Regulatory Matters**. Upon and following Adaptimmune's exercise of its Option with respect to a Research Program, the following shall apply:

4.1.1 As between the Parties, Adaptimmune shall be responsible for holding and applying for any Regulatory Approvals or MAAs in relation to the applicable Product and for sponsoring any Clinical Trials (including holding the IND). Adaptimmune shall have sole decision making authority in relation to any sponsorship of any Clinical Trials or progression of any applicable Products through Clinical Trials and including the decision on whether to apply for any MAAs.

4.1.2 Adaptimmune shall be primarily responsible, and act as the sole point of contact, for communications with Regulatory Authorities in connection with the development, commercialisation, and manufacturing of such applicable Product. To the extent

Alpine is required to provide any information or response to a Regulatory Authority, such response will be discussed with Adaptimmune to the extent practicable and Adaptimmune shall provide only such information as is necessary to comply with its legal obligations unless otherwise mutually agreed to by the Parties. Alpine shall provide to Adaptimmune a copy of any material correspondence in relation to a Product (or anything which is likely to affect the safety or regulatory approval of any Product) received from a Regulatory Authority, and where reasonably possible provide Adaptimmune an opportunity to comment on such correspondence.

4.1.3 Alpine hereby grants Adaptimmune the right to reference and utilize all toxicology and safety data developed by Alpine for any and all Products, as may reasonably be requested by Adaptimmune relating to regulatory matters (including preparation and filing for any INDs and MAAs and obtaining and maintaining Regulatory Approvals).

4.1.4 Nothing in this Clause 4.1 shall require any Party to breach its obligations to any Regulatory Authority under Applicable Law.

4.2 **Safety Event Reporting**. Additionally, each Party shall provide to the other Party prompt written notice of any material safety events pertaining to any Product of which it becomes aware, including any SUSARs, SAEs or other material events which might have general applicability to the development of any Product or the use of the Alpine Technology to develop any Product. The Parties will agree to the terms of a pharmacovigilance agreement if reasonably required to facilitate such safety event reporting.

4.3 **Product Recall**. Adaptimmune shall be responsible for investigating any SUSAR or other complaint in relation to any Product. Adaptimmune shall be responsible for carrying out any product recall for any Product, but shall keep the JSC and JPT, as relevant, informed of the status and process for such recall including any material correspondence with any Regulatory Authority. The costs associated with any recall of any Product shall be borne by Adaptimmune.

5. DEVELOPMENT; COMMERCIALISATION

5.1 **Development Generally**. Upon and following the Completion of a Research Program and Adaptimmune's exercise of its Option with respect to a Development Candidate, Adaptimmune shall (a) have the sole responsibility for development of such Development Candidate from filing of an IND through clinical studies into a pharmaceutical Product containing such Development Candidate for use in the Field, and (b) use Commercially Reasonable Efforts to develop such Product in the Field.

5.2 **Development Updates**. Starting from the Adaptimmune's exercise of its Option, Adaptimmune shall keep Alpine informed on a [***] basis of its development of such Product through to the first regulatory approval.

5.3 **Commercialisation Generally**. With respect to each Research Program as to which it exercises its Option, Adaptimmune shall (a) be primarily responsible for and have sole decision making authority in relation to the commercialisation, manufacture and promotion of the applicable Product following filing of IND, and (b) use Commercially Reasonable Efforts to commercialize and promote such Product in the Field following regulatory approval thereof.

5.4 **Commercialisation Updates**. Starting from the First Commercial Sale of a Product, Adaptimmune shall keep Alpine informed on a regular basis [***] of its commercialisation activities of such Product.

6. LICENSES

6.1 **Research License**. With respect to each Initial Research Program, commencing on the Effective Date, and with respect to each Other Research Program, commencing on the Parties' agreement of the Research Plan with respect thereto, and in each case, continuing in full force

and effect until the earlier of expiry of applicable Option Period or exercise of applicable Option, each Party hereby grants to the other Party a royalty-free, nontransferable (except to such other Party's agents performing the Research Program), nonexclusive license in the Field under such Party's Licensed IP solely for the purposes of and to the extent necessary for performing such Research Program (collectively, the "**Research License**"). The Research License shall be specific to the research and preclinical development activities and responsibilities of the applicable Party under the Research Program.

[***].

6.2 **Exclusive Option**. Alpine hereby grants to Adaptimmune an exclusive option to obtain an Exclusive License in accordance with Clause 6.3 below, as of the Effective Date, with respect to Products arising under each of the Initial Research Programs and any other Products using the SIP or TIP from the Initial Research Programs. Effective as of the date of Acceptance of any Target for any Other Research Program in accordance with Clause 3.1.3, Alpine hereby grants to Adaptimmune an exclusive option to obtain an Exclusive License in accordance with Clause 6.3 below with respect to Products arising under such Other Research Program and any other Products using the SIP or TIP from such Other Research Program. Each such option whether in relation to the Initial Research Programs or Other Research Programs shall be an "**Option**". Each Option shall expire on the earlier of [***] (such period from commencement until expiration of the Option, the "**Option Period**"). Subject to earlier termination of this Agreement, prior to the expiry of any Option Period, Adaptimmune may exercise such Option in its sole discretion by providing written notice of its intent to exercise to Alpine's Alliance Manager (including by electronic mail, provided such is acknowledged by Alpine's Alliance Manager). During the applicable Option Period, Alpine will not enter into any Third-Party agreement or arrangement that would conflict with or prevent the grant of any Exclusive License to Adaptimmune on exercise of such Option by Adaptimmune. On expiry of the Option Period without exercise, the Option shall expire and Alpine shall cease to have any obligation to grant an Exclusive License to Adaptimmune in relation to any Product arising from the applicable Research Program.

6.3 **Exclusive License**.

6.3.1 As from the date of receipt of notice of exercise of an Option by Alpine with respect to a Research Program, Alpine shall and hereby grants to Adaptimmune (a) a worldwide exclusive license under the Alpine Licensed IP to make, have made, develop, have developed, use, import and have imported, sell, have sold and offer for sale any Products arising from such Research Program and any other Products using the SIP or TIP arising from such Research Program (solely as permitted under Clauses 6.3.2 and 6.3.3), in each case in the Field (each, an "**Exclusive License**"), and (b) a worldwide exclusive license under the Alpine Licensed IP to make, have made, develop, have developed, use, import and have imported, sell, have sold and offer for sale any Product described in subclause (a) as part of a combination therapy (as distinct from a Combination Product) administered in connection with the administration of another active agent (a "**Combination Therapy**"). For clarity, it is agreed that the exclusive license under Clause 6.3.1(b) does not include any exclusive license under any of the Alpine Licensed IP, which is specific to any part of the Combination Therapy other than the Product.

6.3.2 [***].

6.3.3 [***].

6.4 **Competing Products; Target Exclusivity**. [***]

6.5 **Sublicenses**. Each Party shall have the right to sublicense the licenses and rights granted under Clauses 6.1 and 6.3(a) to its Affiliates by providing fifteen (15) days' advance written notice to the other Party; (b) subject to the terms and conditions in Clause 3.4, to any Third-Party subcontractors by providing fifteen (15) days' advance written notice to the other Party, [***] (c) [***]. Any sublicense granted pursuant to this Clause 6.5 must be consistent with the terms and conditions of this Agreement and in the form of a written agreement, and any sublicensing Party shall provide a copy of each such sublicense agreement to the other Party within fifteen (15) days following execution thereof, provided that such sublicensing Party may redact any terms that are unrelated to this Agreement.

Each Party shall be responsible for all actions and omissions of any of its Sublicensees, including where such actions and omissions result in a breach of the terms of this Agreement.

6.6 **New Intellectual Property**. Subject to the last sentence of this Clause 6.6, any intellectual property acquired or in-licensed by a Party following the Effective Date and during the Term that would be subject to a license set forth in Clause 6.1 or 6.3, and for which the Party granting such license under this Agreement (or any of its Affiliates) would be obligated to pay a Third Party due to the other Party's use of such intellectual property or the use of which would be subject to terms and conditions additional to those set forth in this Agreement, shall only be included in such license if such other Party agrees in writing to pay such amounts due to such Third Party and/or comply with such terms and conditions, as applicable. The Party acquiring or licensing such intellectual property shall notify the other Party in writing within thirty (30) days of acquiring or licensing such intellectual property, which notice shall specify the applicable terms and conditions, including any payments therefor. It is understood and agreed that any intellectual property acquired or licensed by a Party following the Effective Date and during the Term that (a) would be subject to a license set forth in Clause 6.1 or 6.3, and (b) is reasonably necessary for Adaptimmune's use of any Alpine Platform Technology, shall be included in the license set forth in Clause 6.1 pursuant to the terms of this Agreement without any further negotiation of the Parties and shall not be subject to this Clause 6.6.

6.7 **No Additional Licenses**. Except as expressly provided in this Agreement, nothing in this Agreement shall grant either Party any right, title or interest in and to the know-how, Patents or other Intellectual Property Rights of the other Party (either expressly or by implication or estoppel).

7. TECHNOLOGY TRANSFER

7.1 In addition to any technology transfer contemplated by any Research Program, following completion of any Research Program and Adaptimmune's exercise of its Option in relation to such Research Program, Alpine will:

7.1.1 [***]

7.1.2 [***].

To the extent required, the details of what technical assistance and transfer of technology will be required from Alpine will be agreed upon by the Parties as part of a technology transfer plan to be initially prepared by Adaptimmune and approved by the JPT.

8. FINANCIAL TERMS

8.1 **Research and Development Costs.**

8.1.1 For each of the Initial Research Programs, Adaptimmune shall pay to Alpine the amount of [***] once every [***], [***] per year per Initial Research Program to fund Alpine's activities under each Initial Research Program; provided, that if Adaptimmune materially changes such Initial Research Program, Adaptimmune shall be responsible for the costs of implementing such material changes, such costs to be mutually agreed, including those set forth in Clause 3.3. The first payments for the Initial Research Programs shall be due and payable by Adaptimmune as of the Effective Date. For each Other Research Program, Adaptimmune shall pay to Alpine the amount of [***] once every [***] per year per Other Research Program to fund Alpine's activities under each Other Research Program; provided, that (a) [***] (b) if Adaptimmune materially changes such Other Research Program (it being understood and agreed that any change requested by Adaptimmune pursuant to Clause 3.3.2 shall not be a material change for purposes of this Clause 8.1.1), Adaptimmune shall be responsible for the costs of implementing such material changes, such costs to be mutually agreed. [***].

8.1.2 The research funding provided under Clause 8.1.1 shall be used by Alpine towards its costs of carrying out its activities under the associated Research Program. Where any Research Program terminates or all Alpine activities under any Research Program have completed, the research funding required to be paid by Adaptimmune under this Clause 8.1 will be pro-rated up to the date of effective termination or completion.

8.1.3 Save as otherwise explicitly provided in this Clause 8.1, each Party will fund their own development costs and activities arising under this Agreement. In particular, each Party will fund the completion of its activities under any Research Program and Adaptimmune will fund its preclinical testing and any Clinical Trials it sponsors.

8.2 **Upfront Payments**. Adaptimmune will pay to Alpine the amounts set out in Exhibit 2. Payments will be made as provided in Exhibit 2.

8.3 **Milestones**. Adaptimmune will pay to Alpine the milestone payments set out in Exhibit 2 (" **Milestones**") on achievement on the events set out in Exhibit 2 ("**Milestone Events**"). The following terms shall apply to the payment of Milestones under this Clause 8.3.

8.3.1 Milestones shall be due only once for each Research Program and shall apply in relation to the first Product from such Research Program to achieve the Milestone Event. Should the same or additional Product achieve the same Milestone Event more than once (for example for multiple indications), no additional Milestones shall be payable by Adaptimmune.

8.3.2 Milestones shall be due and payable regardless of whether it is Adaptimmune or any Affiliate or Sublicensee achieving such Milestone Event or any other Third Party achieving such Milestone Event on behalf of Adaptimmune or its Affiliates or Sublicensee.

8.3.3 If, for any reason, a particular Milestone Event specified is achieved with respect to a given Product without one or more preceding Milestone Events with respect to such Product having been achieved, then upon the achievement of such Milestone Event, both the Milestones applicable to such achieved Milestone Event and the Milestones applicable to all preceding unachieved Milestone Event(s) shall be due and payable.

8.3.4 In the event that in any Clinical Trials two or more Milestone Events are merged or combined with any other Milestone Event, for example a Phase II Clinical Trial is combined with a Phase III Clinical Trial, the Milestone will be payable once when the earlier of the two combined Milestone Events shall be deemed to be achieved.

8.3.5 If any Product within a Research Program is replaced for any reason by a different Product, then Milestones already paid for the achievement of any Milestone Events by the first Product (the "**Replaced Product**") shall not be due and payable for a second time by the achievement of same Milestone Events by the second Product (the "**Replacement Product**"). For clarity, Milestones shall be due for the achievement of any Milestone Event by the Replacement Product for which a Milestone was not previously paid for the Replaced Product.

8.3.6 With respect to each Milestone Event, Adaptimmune shall inform Alpine within [***] days of the achievement of such Milestone Event. Alpine shall issue an invoice for payment of the applicable Milestone and Adaptimmune shall pay such invoice within [***] days of receipt of the relevant invoice.

8.4 **Royalties**.

8.4.1 On a Product-by-Product basis, at the end of each calendar quarter during the Royalty Term, pursuant to the terms and conditions set forth in Clause 8.4.6 and subject to Clause 8.4.2, Adaptimmune shall pay to Alpine a running royalty equal to [***] of worldwide Adjusted Net Sales for such Product in such calendar quarter (" **Royalty**").

8.4.2 Royalties shall be payable on Net Sales of each Product in each country during the Royalty Term.

8.4.3 **Payment Offsets**. The following payment offsets will apply in relation to the payment of any Royalty with respect to a particular Product:

(a) In any calendar quarter that such Product is not Covered by a Valid Claim of a Patent within the Licensed IP in a country where such Licensed Product is sold, the applicable Royalty set forth in Clause 8.4.1 with respect to such Product in such country shall be reduced by [***].

(b) [***].

(c) Following the first commercial sale of a Biosimilar to such Product by a Third Party (other than any of Adaptimmune's Sublicensees) in a country after Valid Claim expiration but during the Royalty Term, the applicable Royalty set forth in Clause 8.4.1 due and payable by Adaptimmune shall be reduced [***] in such country.

(d) Notwithstanding the foregoing, during any calendar quarter in the Royalty Term for a Product in a country, the Royalty offset provisions in this Clause 8.4.3, individually or in combination, shall not reduce by more than [***], the Royalties that would otherwise have been due to Alpine under Clause 8.4.1 with respect to the Adjusted Net Sales of such Product in such country during such calendar quarter.

8.4.4 **Royalty Term**. The Royalty obligations set forth in Clause 8.4.1 above will, on a country-by-country and Product-by-Product basis, commence upon the First Commercial Sale of such Product in such country and expire upon the earlier [***].

8.4.5 **Term of the Exclusive License**. The term of the Exclusive License shall extend, on a country-by-country and Product-by-Product basis, until the later of [***].

8.4.6 **Royalty Reports**. Following First Commercial Sale of a Product, Adaptimmune shall provide a report to Alpine within [***] days after the end of each calendar quarter (" **Royalty Report**"). [***]. On receipt of such Royalty Report, Alpine will provide an invoice for the Royalty and Adaptimmune shall pay such Royalty within forty five (45) days of receipt of such invoice.

9. PAYMENTS

9.1 **Mode of Payment**.

9.1.1 All payments hereunder shall be made by wire transfer in immediately available funds to the account listed below (or such other account as the receiving Party shall designate before such payment is due):

If to Alpine:

[***]
[***]
[***]
[***]
[***]
[***]

9.1.2 Adaptimmune will be responsible for any bank costs or charges associated with any transfer of sums or reimbursement of costs including any currency conversion costs or transfer costs.

9.2 **Currency of Payments**. All payments under this Agreement shall be made in US dollars, unless otherwise expressly provided in this Agreement. Net Sales shall be reported in US dollars irrespective of the currency in which such sales were invoiced. Adaptimmune will make the conversion to US dollars using the conversion rates it typically uses for its accounts and in accordance with its application of the Accounting Standards.

9.3 **Taxes**. Each Party shall comply with Applicable Laws regarding filing and reporting for tax purposes. Neither Party shall treat their relationship under this Agreement as a pass through entity for tax purposes. If any payments made by Adaptimmune under this Agreement are subject to withholding taxes under Applicable Laws of any state, federal, provincial or foreign government, Adaptimmune shall be authorised to withhold such taxes as are required under such Applicable Laws, pay such taxes to the appropriate government authority, and remit the balance due to Alpine net of such taxes. Adaptimmune shall secure and deliver to Alpine an official receipt for taxes paid. The Parties will fully cooperate with each other to enable each Party to more accurately determine its own tax liability and to minimize such liability to the extent legally permissible and administratively reasonable. Each Party shall provide and make available to the other Party any exemption certificates, resale certificates, information regarding out of state or out of country sales or use of equipment, materials or services, and any other information reasonably requested by the other Party to support the provisions of this Clause 9.3, including the appropriate organization of invoice formats and supporting documents to allow maximization of reclamation of VAT and other transaction taxes.

9.4 **Late Payment**. In relation to any undisputed amount required to be paid by Adaptimmune hereunder which is not paid by the payment date due, Alpine may charge interest at a monthly rate equal to [***]; provided, however, that in no event will such rate exceed the maximum legal interest rate then in effect. Such interest shall be computed on the basis of a month of thirty (30) days for the actual number of days such payment is overdue.

9.5 **Records**. Adaptimmune shall keep and maintain records of its sales of Products in sufficient detail to enable Alpine to verify the accuracy of Royalties due from Adaptimmune and pursuant to an inspection under Clause 9.6. Adaptimmune shall keep such records for a period of five (5) years from the end of the calendar year in which the relevant Product sales were made.

9.6 **Inspections**. Alpine shall be entitled to appoint an independent Third Party qualified accountant or a person possessing similar professional status and associated with an independent accounting firm acceptable to Adaptimmune to verify the level of Net Sales accounted for and Manufacturing Costs incurred by Adaptimmune and the payment of Royalty in accordance with this Agreement. Adaptimmune shall make its records available as set forth in this Clause. The accounting firm shall enter into appropriate obligations with Adaptimmune to treat all information it receives during its inspection under obligations of nondisclosure and nonuse no less restrictive than those set forth in Article 11. Such audit right shall apply no more than once in any calendar year and shall only relate to the previous three (3) calendar years' records (to the extent not previously audited by Alpine). The independent Third Party shall only be entitled to report to Alpine as to whether or not the Net Sales and Manufacturing Costs of any Product are materially accurate. Where any inspection identifies any shortfall in the Royalty required to Alpine, Adaptimmune shall make up such shortfall within thirty (30) days of receiving notice of such shortfall. Where any inspection identifies an overpayment in the Royalties required to Alpine, Adaptimmune shall be entitled to deduct the amount of such overpayment

from the next payment or payments made to Alpine. Alpine shall pay the cost of any inspection unless such inspection identifies a shortfall in Royalty in the preceding calendar year in excess of five percent (5%), in which case Adaptimmune shall pay the reasonable costs of the Third Party carrying out such inspection.

10. INTELLECTUAL PROPERTY; OWNERSHIP

10.1 **Disclosure; Ownership; Inventorship; Assignment and Cooperation**.

10.1.1 **Disclosure**. During the Term, each Party shall promptly disclose to the other Party in writing any Foreground IP (whether or not patentable) conceived or reduced to practice by or for the disclosing Party in the course of performance of this Agreement. Such disclosure may be made directly by each Party or via designated patent representatives for each Party.

10.1.2 **Ownership**. As between the Parties:

(a) Adaptimmune shall solely own any Foreground IP which solely relates to the Adaptimmune Platform Technology, including any Foreground IP which solely claims or Covers any improvement to the Adaptimmune Platform Technology ("**Adaptimmune Foreground IP**"). Alpine hereby assigns and agrees to assign to Adaptimmune any rights it has in the Adaptimmune Foreground IP;

(b) Alpine shall solely own any Foreground IP which solely relates to the Alpine Platform Technology including any Foreground IP which solely claims or Covers any improvement to the Alpine Platform Technology ("**Alpine Foreground IP**"). Adaptimmune hereby assigns and agrees to assign to Alpine any rights it has in the Alpine Foreground IP; and

(c) The Parties shall jointly own any Foreground IP other than that set out in Clauses 10.1.2(a) and 10.1.2(b) (" **Joint Foreground IP**"). Without limiting the foregoing, each Party retains an undivided one-half interest in and to the Joint Foreground IP (including Patents therein). Each Party hereby assigns and agrees to assign its rights in any Joint Foreground IP to the other Party to the extent necessary to ensure such joint ownership. [***]

In the event of any dispute as to whether any Foreground IP solely relates to either the Adaptimmune Platform Technology or Alpine Platform Technology under Clauses 10.1.2(a) or 10.1.2(b) and where such dispute is not resolved by reference to senior executives in accordance with Clause 16.1, an independent patent expert ("**Patent Expert**") shall be appointed by the Parties to resolve such dispute. The decision of the Patent Expert shall be binding on the Parties in the absence of manifest error or fraud. The Patent Expert shall be mutually agreed between the Parties in writing within thirty (30) days of expiry of the thirty (30)-day resolution period in Clause 16.1. Where the Parties cannot agree such Patent Expert, the Patent Expert shall be appointed by the American Arbitration Association under its Supplementary Rules for the Resolution of Patent Disputes. Any Patent Expert shall be a patent attorney and have at least twenty (20) years' experience in relation to pharmaceutical or biotechnology patent matters. The fees of the Patent Expert shall be shared equally between the Parties and the Parties shall use reasonable efforts to ensure resolution occurs as quickly as possible after referral to such Patent Expert. The Parties shall reasonably cooperate with the Patent Expert, including providing such information as may reasonably be required by the Patent Expert to reach a decision.

Nothing in this clause shall affect or impact any ownership of either Party in relation to such Party's Background IP.

10.1.3 **Assignment; Cooperation**. Each Party shall execute such further documentation as may be necessary or appropriate, and provide reasonable assistance and

cooperation, to implement the provisions of this Article 10. Each Party shall, to the extent legally practicable and possible under relevant national or local laws, cause all of its employees, Affiliates and any Third Parties working pursuant to this Agreement on its behalf, to assign (or otherwise convey rights) to such Party any Patents and Know-How or other Foreground IP discovered, conceived or reduced to practice by such employee, Affiliate or Third Party, and to cooperate with such Party in connection with obtaining patent protection therefor.

10.2 **Patent Prosecution**.

10.2.1 **Adaptimmune Controlled Prosecution and Maintenance**.

(a) Adaptimmune shall, at its sole discretion and expense, have the sole right (but not the obligation) to Prosecute and Maintain Patents within the Adaptimmune Background IP.

(b) Adaptimmune shall, at its sole discretion and expense, have the first right (but not the obligation) to Prosecute and Maintain Patents within the Joint Foreground IP, to the extent such Patents include [***]. Without limiting the foregoing, if (i) Adaptimmune elects not to Prosecute and Maintain any Patents under this Clause 10.2.1(b), and (ii) such Patent(s) relates solely [***], then Adaptimmune shall provide written notice to Alpine of its election at least [***] prior to any upcoming deadline in any patent office with respect to such Patent. In such event, Alpine shall have the right, but not the obligation, to assume the responsibility for the prosecution and maintenance of such Patent at its sole expense, in which event Adaptimmune shall cause the files for such Patent to be transferred to such counsel as Alpine may designate and shall take such actions as Alpine may reasonably request to preserve Alpine's ability to effectively prosecute and maintain such Patent.

(c) Adaptimmune shall, at its sole discretion and expense, have the sole right (but not the obligation) to Prosecute and Maintain Patents within the Adaptimmune Foreground IP.

10.2.2 **Alpine Controlled Prosecution and Maintenance**.

(a) Alpine shall, at its sole discretion and expense, have the sole right (but not the obligation) to Prosecute and Maintain Patents within the Alpine Background IP.

(b) Alpine shall, at its sole discretion and expense, have the sole right (but not the obligation) to Prosecute and Maintain Patents within the Alpine Foreground IP, excluding any Patents falling within Clause 10.2.1(b) above. [***]

10.2.3 **Jointly Controlled Prosecution and Maintenance**. In relation to any Joint Foreground IP not Prosecuted and Maintained by Adaptimmune under Clauses 10.2.1(b), the Parties shall mutually agree upon which Party shall have the right to Prosecute and Maintain such Patents.

10.3 **Comments from Non-Prosecuting Party.** The Prosecuting Party will provide the Non-Prosecuting Party with copies of any filed patent application, filings and other material correspondence with applicable governmental authorities relating to any Joint Foreground IP, and will keep the Non-Prosecuting Party reasonably informed of the status of such Prosecution and Maintenance, including providing Non-Prosecuting Party with copies of all communications received from or filed in patent offices within a reasonable period of time after receipt by Prosecuting Party. Prosecuting Party shall also consult with Non-Prosecuting Party regarding such activities and shall reasonably consider Non-Prosecuting Party's input with respect thereto. The Prosecuting Party shall be responsible for the fees of Prosecution and Maintenance of the Joint Foreground IP for which it is responsible.

10.4 **Enforcement Rights for Infringement by Third Parties**.

10.4.1 **Notice**. Each Party shall promptly notify, in writing, the other Party upon learning of any (a) actual or suspected infringement, or (b) any claim of invalidity, unenforceability, or noninfringement, of the Patents within any Background IP or Foreground IP to the extent such actual or suspected infringement is with respect to a product which is competitive with any Product (each an "**Infringement**").

10.4.2 **Enforcement Actions**.

(a) The Parties shall consult in good faith as to potential strategies to terminate suspected or potential Infringement. In the absence of any agreement otherwise, the Prosecuting Party in relation to the relevant Patent or Party owning or Controlling the relevant intellectual property right in the case of Foreground IP or Background IP shall have the first right, but not the obligation, to seek to abate any actual or suspected Infringement by a Third Party, or to file suit against any Third Party for Infringement. If the Prosecuting Party or owning or Controlling Party does not, within one hundred twenty (120) days of receipt of a notice under Clause 10.4.1, take steps to abate the Infringement, or to file suit to enforce against such Infringement, then other Party shall have the right, but not the obligation, to take action to enforce against such Infringement; provided that if Prosecuting Party is diligently pursuing ongoing settlement discussions at the end of such one hundred and twenty (120) day period then Non-Prosecuting Party shall not be permitted to exercise such right unless such settlement discussions cease without reaching settlement or Prosecuting Party ceases to pursue such discussions diligently.

(b) The Non-Prosecuting Party shall reasonably cooperate with the Party controlling any such action to abate or enforce pursuant to this Clause 10.4.2 (as may be reasonably requested by the controlling Party and at the controlling Party's expense), including, if necessary, by being joined as a party; provided that the noncontrolling Party shall be reimbursed by the controlling Party as to any costs or expenses incurred, and shall have the right to be represented by its own counsel at its own expense. The Party controlling any such action shall keep the other Non-Prosecuting Party updated with respect to any such action, including providing copies of all documents received or filed in connection with any such action.

10.4.3 **Settlement**. The Party controlling any such enforcement action described in Clause 10.4.2 (an " **Enforcement**"), at its sole discretion, may take reasonable actions to terminate any alleged infringement without litigation; provided, that if any such arrangement would adversely affect the noncontrolling Party's rights under this Agreement or impose any obligation or requirement on the noncontrolling Party, then that arrangement is subject to the noncontrolling Party's prior written consent, which consent shall not to be unreasonably withheld, conditioned or delayed.

10.4.4 **Costs and expenses**. The Party controlling any Enforcement shall bear all of its costs and expenses, including litigation expenses, related to such Enforcement actions.

10.4.5 **Damages**. Unless otherwise mutually agreed by the Parties in writing, and subject to the respective indemnity obligations of the Parties set forth in Article 14, all damages, amounts received in settlement (including royalty, milestone or other payments), judgment or other monetary awards recovered in Enforcement with respect to activities of the Third Party that occurred prior to the effective date of such award shall be shared as follows:

(a) first, to reimburse the controlling Party for costs and expenses incurred under Clause 10.4.4; and

(b) then, any remainder amount shall be apportioned [***] to the controlling Party and [***] to the noncontrolling Party.

10.5 **Third-Party Infringement Claims**.

10.5.1 **Notice**. In the event that a Third Party shall make any claim, give notice, or bring any suit or other inter parties proceeding against Alpine or Adaptimmune, or any of their respective Affiliates, subcontractors or customers, for infringement or misappropriation of any Intellectual Property Rights with respect to the research, development, making, using, selling, offering for sale, import or export of any Product or with respect to any Program Target ("**Third-Party Infringement Claim**"), in each case, the Party receiving notice of a Third-Party Infringement Claim shall promptly notify the other Party in writing and provide all evidence in its possession pertaining to the claim or suit that it is entitled to disclose.

10.5.2 **Defense**. The Parties shall consult as to potential strategies to defend against any Third Party Infringement Claim, consistent with the overall goals of this Agreement, including by being joined as a party. The Parties shall cooperate with each other in all reasonable respects in the defense of any Third Party Infringement Claim or raising of any counterclaim related thereto. Subject to the respective indemnity obligations of the Parties set forth in Article 14, (a) Adaptimmune shall be primarily responsible for defending such Third-Party Infringement Claim (including selection of counsel, venue, and directing all aspects, stages, motions, and proceedings of litigation) to the extent such Third-Party Infringement Claim relates to [***] or any Adaptimmune Platform Technology; and (b) subject to Clause 10.5.2(a), Alpine shall be primarily responsible for defending such Third-Party Infringement Claim (including selection of counsel, venue, and directing all aspects, stages, motions, and proceedings of litigation) to the extent such Third-Party Infringement Claim relates to the Alpine Platform Technology. If the Party with primary responsibility does not, within one hundred twenty (120) days of receipt of a notice under Clause 10.5.1, take steps to defend the Third-Party Infringement Claim, then to the extent that such Third-Party Infringement Claim is brought against the other Party, the other Party shall have the right, but not the obligation, to take action to enforce or defend against such Third-Party Infringement Claim; provided that if the Party with primary responsibility is diligently pursuing ongoing settlement discussions at the end of such one hundred and twenty (120)-day period, then other Party shall not be permitted to exercise such right unless such settlement discussions cease without reaching settlement or such responsible Party ceases to pursue such settlement discussions diligently. At the controlling Party's request and expense, the noncontrolling Party shall cooperate with the controlling Party in connection with any such defense and counterclaim, provided that the noncontrolling Party shall be reimbursed by the controlling Party as to any reasonable and documented costs or expenses, and shall have the right to be represented by its own counsel at its own expense. Any counterclaim or other similar action by a Party, to the extent such action involves any enforcement of rights under the Background IP or Foreground IP, will be treated as an Enforcement subject to Clause 10.4. Nothing in this Clause shall prevent any Party from complying with the terms of any court order relating to or arising out of any Third-Party Infringement Claim.

10.5.3 **Settlement**. If any such defense under Clause 10.5.2 would adversely affect the other Party's rights under this Agreement or impose a financial obligation upon the other Party or grant rights in respect, or affect the validity or enforceability, of the other Party's Intellectual Property Rights or any Foreground IP, then any settlement, consent judgment or other voluntary final disposition of such Third-Party Infringement Claim shall not be entered into without the consent of the other Party (such consent not to be unreasonably withheld, conditioned or delayed).

10.5.4 **Costs and Expenses**. The Party controlling the defense of any Third-Party Infringement Claim shall bear all costs and expenses, including litigation expenses, to defend against any Third-Party Infringement Claim.

11. CONFIDENTIALITY

11.1 **Confidential Information, definition**. In this Agreement, "**Confidential Information**" means any nonpublic, proprietary information (of whatever kind and in whatever form or medium, including copies thereof), tangible materials or other deliverables (a) disclosed by or on behalf of a Party in connection with this Agreement, whether prior to or during the Term and whether disclosed orally, electronically, by observation or in writing, or (b) created by, or on behalf of, either Party and provided to the other Party, or created jointly by the Parties, in the course of this Agreement. The Party or Parties creating or disclosing information in accordance with (a) and (b) shall be the owner of such Confidential Information, provided that, to the extent a Party is allocated ownership of Intellectual Property Rights under Article 10 that embodies or contains any Confidential Information, such Confidential Information shall be deemed to be owned by such Party, regardless of which Party initially disclosed or created such Confidential Information. The owner of any Confidential Information shall be deemed to be the "**Disclosing Party**" of such Confidential Information, and the other Party shall be deemed to be the "**Receiving Party**" of such Confidential Information.

11.2 **Nonuse and Nondisclosure of Confidential Information**. During the Term, and for [***] after the date of expiration or termination of this Agreement, a Receiving Party shall (i) except to the extent permitted by this Agreement or otherwise agreed to by the Disclosing Party in writing, keep confidential and not disclose to any Third Party any Confidential Information of the Disclosing Party; (ii) except in connection with activities contemplated by, the exercise of rights permitted by or in order to further the purposes of, this Agreement or otherwise agreed to by the Disclosing Party in writing, not use for any purpose any Confidential Information of the Disclosing Party; and (iii) take all reasonable precautions to protect the Confidential Information of the Disclosing Party, including all precautions the Receiving Party employs with respect to its own confidential information of a similar nature, but in any case no less than a reasonable standard of care.

11.3 **Exclusions Regarding Confidential Information**. Notwithstanding anything set forth in this Article 11 to the contrary, the obligations of Clause 11.2 above shall not apply to the extent that a Receiving Party can demonstrate that the Confidential Information of the Disclosing Party:

(a) was already known to the Receiving Party, other than under an obligation of confidentiality, at the time of receipt by the Receiving Party;

(b) was generally available to the public or otherwise part of the public domain at the time of its receipt by the Receiving Party;

(c) became generally available to the public or otherwise part of the public domain after its receipt by the Receiving Party other than through any act or omission of the Receiving Party or those to whom the Receiving Party discloses in breach of this Agreement;

(d) was received by the Receiving Party without an obligation of confidentiality from a Third Party having the right to disclose such information without restriction;

(e) was independently developed by or for the Receiving Party without use of or reference to the Confidential Information of the Disclosing Party; or

(f) was released from the restrictions set forth in this Agreement and imposed on the Receiving Party by express prior written consent of the Disclosing Party.

11.4 **Authorised Disclosures of Confidential Information**. Notwithstanding the foregoing, a Receiving Party may use and disclose the Confidential Information of the Disclosing Party as follows:

(a) if required by law, rule or governmental regulation or by judicial order, including as may be required in connection with any filings made with, or by the disclosure policies of, a major stock exchange; provided that the Receiving

Party seeking to disclose the Confidential Information of the Disclosing Party (i) uses all reasonable efforts to inform the Disclosing Party of such requirement in writing prior to making any such disclosures and cooperates with the Disclosing Party's efforts to avoid or limit disclosure, or to seek a protective order, confidential treatment or other appropriate remedy (including redaction), (ii) whenever possible, requests confidential treatment of such information that is disclosed, and (iii) limits the disclosure of such Confidential Information to the extent so required and to otherwise continue to comply with the obligations of confidentiality and nonuse set forth in Clause 11.2;

(b) to the extent such use and disclosure is reasonably required in the Prosecution and Maintenance of a Patent within the Foreground IP in accordance with this Agreement; provided that such proposed disclosure is provided to the other Party in writing in advance and the other Party approves such disclosure;

(c) as reasonably necessary to obtain or maintain any Regulatory Approval, including to conduct preclinical studies and Clinical Trials and for pricing approvals, for any Products, provided, that, the disclosing Party shall take all reasonable steps to limit disclosure of the Confidential Information outside such Regulatory Agency and to otherwise continue to comply with the obligations of confidentiality and nonuse set forth in Clause 11.2;

(d) to take any lawful action that is reasonably necessary to protect its interest under, or to enforce compliance with the terms and conditions of, this Agreement;

(e) to the extent necessary, to any of its Affiliates, vendors, consultants, agents, attorneys, contractors and clinicians, provided that any such Affiliate or Third Party is under written agreements of confidentiality and nonuse at least as restrictive as those set forth in this Article 11; or

(f) to any of its actual or potential Sublicensees or [***] involved in such activities, for the limited purpose of evaluating such transaction, collaboration or license and under appropriate conditions of confidentiality..

11.5 **Terms of this Agreement**. The Parties agree that this Agreement and the terms hereof will be considered Confidential Information of both Parties. Each Party agrees not to, and to cause its Affiliates not to, disclose to any Third Party any terms of this Agreement [***].

11.6 **No License**. As between the Parties, any Confidential Information disclosed hereunder shall remain the property of the Disclosing Party and as further provided in Clause 11.1. Disclosure of Confidential Information to the Receiving Party shall not constitute any grant, option or license to the Receiving Party, beyond those licenses expressly granted under Article 6, under any patent, trade secret or other rights now or hereinafter held by the Disclosing Party.

11.7 **Change of Control**.

11.7.1 In the event of a Change of Control of Alpine by an Acquiring Third Party, Alpine will adopt reasonable procedures to (i) prevent use of Adaptimmune's Confidential Information [***] by such Acquiring Third Party [***]; (ii) otherwise ensure compliance with the confidentiality obligations set out in this Article 11; and (iii) keep the Adaptimmune's Confidential Information [***]. Any disclosure of Adaptimmune Confidential Information to Acquiring Third Party [***]. Alpine will provide written notice to Adaptimmune of any Change of Control within [***] days after the Change of Control is consummated.

11.7.2 In the event of a Change of Control of Adaptimmune by an Acquiring Third Party prior to Adaptimmune's exercise of its Option for a given Research Program, Adaptimmune will (a) [***]; and (b) provide written notice to Alpine of such Change of Control within [***] days after the Change of Control is consummated. Any disclosure of Alpine's Confidential Information with respect to such Research

Program to an Acquiring Third Party will be subject to prior written agreement by Alpine and may require the Acquiring Third Party to agree to terms of nondisclosure and nonuse that are at least as restrictive as those set out in this Article 11 with Alpine.

11.7.3 In the event of a Change of Control of Adaptimmune by an Acquiring Third Party following Adaptimmune's exercise of its Option for a given Research Program, Adaptimmune will [***].

12. PUBLICITY; PUBLICATIONS; USE OF NAME

12.1 **Publicity**. The Parties shall agree and issue a joint press release, as set out in Exhibit 5, concerning the execution of this Agreement on a mutually agreed date. The text of any other press releases, public announcements or PowerPoint presentations concerning this Agreement, the subject matter hereof, or the research, development or commercial results of Products hereunder (a "**Release**") shall be addressed pursuant to Clauses 12.2–12.4, inclusive, as applicable.

12.2 **Releases required by Law or Regulation; Investor Presentations; Other Releases** .

12.2.1 Each Party may issue any Release it is required to issue by Applicable Law (including requirements of any law or rule imposed by the US Securities and Exchange Commission or any securities exchange). For clarification, where any Party reasonably believes, after consultation with outside legal counsel or General Counsel, that any Release is required in order for it to comply with any securities exchange requirement, including a required release of any material information or an obligation to correct any market misstatement, such Party shall be entitled to issue such Release in accordance with such reasonable belief, without providing the other Party with any prior notification of such Release.

12.2.2 Each Disclosing Party acknowledges that the Receiving Party hereunder may, from time to time desire, but not be legally required, to publicly disclose through a (i) press release; or (ii) media appearance, public announcement or presentation, such as presentations to analysts or shareholders (collectively, "**Public Disclosures**") the terms of this Agreement, or significant development or commercialization activity regarding any Products, to keep its investors reasonably informed of the achievement of milestones, significant events in the development and regulatory process of Products, and commercialization activities and the like, and that such Public Disclosures may pertain to Confidential Information of the Disclosing Party that is not otherwise permitted to be disclosed under Article 11 or this Article 12. With respect to any such Public Disclosures, except for the initial press release described in Clause 12.1, the Receiving Party (the "**Requesting Party**") shall provide the Disclosing Party (the " **Reviewing Party**") with a draft of the Content (as defined in the next sentence) of the draft press release, presentation, and the like at least ten (10) business days in advance of the issuance of the press release, or scheduled date of the investor presentation. The word "**Content**" in this Clause means any information relating to the activities contemplated by this Agreement, and does not include any other business information of the Requesting Party or information pertaining to the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995 relating to "forward-looking statements." The Reviewing Party may notify the Requesting Party of any reasonable objections or suggestions that such Party may have regarding the Content in the Public Disclosure provided for review under this Clause, and the Requesting Party shall reasonably consider any such objections or suggestions that are provided within ten (10) business days. The principles to be observed with respect to Public Disclosures shall include accuracy, compliance with applicable law and regulatory guidance documents, reasonable sensitivity to potential negative reactions of a regulatory authority, reasonable sensitivity to commercial information of value to competitors, and the need to keep investors informed regarding the Requesting Party's business. The Requesting Party shall use commercially reasonable efforts

to adopt the reasonable requests of the Reviewing Party with respect to its Confidential Information and shall restrict the use of the Confidential Information of the Reviewing Party that is disclosed in Investor Presentations, under written agreements of confidentiality at least as restrictive as those set forth in this Agreement.

12.2.3 Any Release not required by Applicable Law and not falling within Clause 12.2.2 shall require the consent of the other Party, not to be unreasonably withheld, conditioned or delayed.

12.2.4 Notwithstanding the foregoing, (a) Adaptimmune retains the right to issue any Release, without consent of Alpine, relating solely to the Adaptimmune Platform Technology and not including any of the Confidential Information of Alpine, and (b) Alpine retains the right to issue any Release, without consent of Adaptimmune, relating solely to the Alpine Platform Technology and not a specific TIP or SIP included within a Product, or any of the Confidential Information of Adaptimmune.

12.3 **Publications**. Notwithstanding Clause 12.2, both Parties recognise that the publication or disclosure of scientific papers, presentations, abstracts or any other written or oral presentations regarding results of and other information regarding the Products may be beneficial to both Parties, provided that such publications or presentations are subject to reasonable controls to protect Confidential Information, the patentability of inventions and other commercial considerations. Accordingly, the following shall apply:

12.3.1 Any proposed paper, presentation, or other public disclosure regarding any Product or Research Program (" **Publication**") by either Party ("**Publishing Party**") shall be provided to the other Party (" **Non-Publishing Party**") for review. The Non-Publishing Party shall review such proposed Publication within twenty (20) calendar days of receipt and may comment on and/or object to any content of the proposed Publication.

12.3.2 The Parties shall work together to resolve any comments and objections of the Non-Publishing Party on a timely basis and neither Party shall unreasonably withhold its consent to any proposed Publication, save that (a) a Non-Publishing Party may request deletion of any of its Confidential Information from any such proposed Publication, and (b) upon a Non-Publishing Party request, the Publishing Party shall delay such proposed Publication for maximum of sixty (60) days to permit such Non-Publishing Party to obtain patent protection for any of its Confidential Information.

12.3.3 [***].

12.4 **No Use of Names**. Except as expressly provided herein, no right, express or implied, is granted by the Agreement to from either Party to the other Party use in any manner the name of any other trade name, symbol, logo or trademark of such Party or its Affiliates, in connection with the performance of this Agreement.

13. REPRESENTATIONS

13.1 **Mutual Representations and Warranties**. Each Party represents and warrants to the other Party that as of the Effective Date:

13.1.1 it is validly organized under the laws of its jurisdiction of incorporation;

13.1.2 it has obtained all necessary consents, approvals and authorizations of all governmental authorities and other persons or entities required to be obtained by it in connection with this Agreement;

13.1.3 the execution, delivery and performance of this Agreement have been duly authorised by all necessary corporate action on its part;

13.1.4 it has the legal right and power to enter into this Agreement and to fully perform its obligations hereunder;

13.1.5 the performance of its obligations under this Agreement will not conflict with such Party's charter or incorporation documents or any Third-Party agreement, contract or other arrangement to which such Party is a party;

13.1.6 it will comply with all Applicable Laws in the performance of this Agreement;

13.1.7 it has not received any written letter threatening infringement or alleging any infringement in relation to any of its Background IP that to its actual knowledge will be required for performance of any Research Program, and it has no actual knowledge that its Background IP infringes the rights of any Third Party or has been misappropriated by any Third Party;

13.1.8 it will not use in the performance of this Agreement any person or personnel (whether directly or through a subcontractor) that has been debarred or otherwise prevented or restricted from performing any clinical research or has been convicted of any offence related to any Clinical Trial in any jurisdiction or otherwise prevented from performing any Clinical Trial by any Regulatory Authority; and

13.1.9 it has the legal right and power to extend the rights and licenses granted to the other Party hereunder.

13.2 Alpine represents and warrants that the list of Patents set out in Exhibit 6 is a complete and accurate list of the Patents Covering the Alpine Platform Technology within the Alpine Licensed IP as at the Effective Date and that it is the owner of such Patents.

13.3 **Disclaimers**. EXCEPT AS OTHERWISE EXPRESSLY STATED IN THIS AGREEMENT, NEITHER PARTY MAKES ANY REPRESENTATION OR WARRANTY OF ANY KIND WITH RESPECT TO PATENTS, KNOW-HOW, MATERIALS OR CONFIDENTIAL INFORMATION SUPPLIED BY IT TO THE OTHER PARTY HEREUNDER, AND EXPRESSLY DISCLAIMS ALL WARRANTIES, EXPRESS OR IMPLIED, INCLUDING WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE AND NONINFRINGEMENT. IN PARTICULAR, BOTH PARTIES ACCEPT THAT, GIVEN THE NATURE OF THE PRODUCTS BEING GENERATED UNDER THIS AGREEMENT, THERE CAN BE NO GUARANTEE THAT ANY PRODUCT CAN BE SUCCESSFULLY GENERATED OR THAT IF GENERATED, THE PRODUCT WILL BE CAPABLE OF OBTAINING REGULATORY APPROVAL.

14. INDEMNIFICATION

14.1 **Indemnification by Adaptimmune**. Subject to Clause 14.3, Adaptimmune shall indemnify, defend and hold Alpine, its Affiliates and their respective directors, officers, and employees and the successors and assigns of any of the foregoing (collectively, "**Alpine Indemnitees**") harmless from and against any and all liabilities, damages, settlements, penalties, fines, costs or expenses (including reasonable attorneys' fees and other reasonable expenses of litigation) (collectively, "**Loss**" or "**Losses**") to the extent arising out of or in connection with any Third-Party claims, suits, actions, demands or judgments ("**Third-Party Claims**") resulting from (a) the negligence or wilful misconduct of Adaptimmune or its Affiliates, Sublicensees or any of their subcontractors; (b) any violation of Applicable Laws by Adaptimmune or its Affiliates, Sublicensees or any of their subcontractors; (c) any breach of this Agreement, including any breach of the warranties under Article 13, by Adaptimmune or its Affiliates Sublicensees or any of their subcontractors; and (d) the clinical development, manufacture or commercialization of any Product following exercise of the relevant Option therefor; except, in each case, to the extent such Third-Party Claim results from any activities for which Alpine is obligated to indemnify the Adaptimmune Indemnitees under Clause 14.2.

14.2 **Indemnification by Alpine**. Subject to Clause 14.3, Alpine shall indemnify, defend and hold Adaptimmune, its Affiliates and their respective directors, officers, and employees and the

successors and assigns of any of the foregoing (collectively, " **Adaptimmune Indemnitees**") harmless from and against any and all Losses to the extent arising out of or in connection with any Third-Party Claims resulting from (a) the negligence or wilful misconduct of Alpine or its Affiliates, Sublicensees or subcontractors; and (b) any violation of Applicable Laws by Alpine or its Affiliates, Sublicensees or subcontractors; and (c) any breach of this Agreement, including any breach of the warranties under Article 13, by Alpine or its Affiliates, Sublicensees or any of their subcontractors; except, in each case, to the extent such Third-Party Claim results from any activities for which Adaptimmune is obligated to indemnify the Alpine Indemnitees under Clause 14.1.

14.3 **Procedure**. If a Party intends to claim indemnification under this Agreement (the " **Indemnitee**"), it shall promptly notify the other Party (the "**Indemnitor**") in writing of such alleged Loss and the Third Party Claim. The Indemnitor shall have the right to control the defense thereof with counsel of its choice as long as such counsel is reasonably acceptable to Indemnitee. Any Indemnitee shall have the right to retain its own counsel at its own expense for any reason in connection with such Third Party Claim, provided, however, that if the Indemnitee shall have reasonably concluded, based upon a written opinion from outside legal counsel, that there is a conflict of interest between the Indemnitor and the Indemnitee in the defense of such action, the Indemnitor shall pay the fees and expenses of a separate counsel to represent the Indemnitee in relation to such Third Party Claim. The Indemnitee, its employees and agents, shall reasonably cooperate with the Indemnitor and its legal representatives in the investigation of any Third-Party Claims covered by this Agreement. The obligations of this Article 14 shall not apply to any settlement of any Third-Party Claims if such settlement is effected without the consent of both Parties, which shall not be unreasonably withheld or delayed. The failure to deliver written notice to the Indemnitor within a reasonable time after the commencement of any such action shall not relieve the Indemnitor of any obligation to the Indemnitee under this Clause 14.3, except if such failure is prejudicial to the Indemnitor's ability to defend such action. It is understood that only Alpine and Adaptimmune may claim indemnity under this Agreement (on its own behalf or on behalf of its Indemnitees), and other parties may not directly claim indemnity hereunder.

14.4 **Insurance**.

14.4.1 **Insurance Coverage**. Each Party shall obtain and maintain comprehensive general liability insurance customary in the industry for companies of similar size conducting similar business and developing similar products as those of the Parties under this Agreement.

14.4.2 **Evidence of Insurance**. No earlier than thirty (30) days after signing this Agreement, each Party shall provide, upon request therefor, the other Party with its certificate of insurance evidencing the insurance coverage set forth in Clause 14.4.1.

14.5 **Limitation of Damages**. NEITHER PARTY HERETO WILL BE LIABLE FOR INDIRECT, INCIDENTAL, CONSEQUENTIAL, SPECIAL, EXEMPLARY, OR PUNITIVE DAMAGES, INCLUDING LOST PROFITS, ARISING FROM OR RELATING TO THIS AGREEMENT, REGARDLESS OF ANY NOTICE OF SUCH DAMAGES, EXCEPT IN RESPECT OF ANY BREACH OF (1) A PARTY'S OBLIGATIONS UNDER ARTICLE 10 OR 11, OR (2) INDEMNIFICATION OBLIGATIONS UNDER THIS ARTICLE 14 FOR THIRD-PARTY CLAIMS. FOR THE AVOIDANCE OF DOUBT, NOTHING IN THIS CLAUSE SHALL LIMIT OR EXCLUDE ANY LIABILITY TO A THIRD PARTY FOR FRAUD BY ANY PARTY OR ANY LIABILITY ARISING AS A RESULT OF PERSONAL INJURY OR DEATH CAUSED BY NEGLIGENCE OF ANY PARTY. NOTHING IN THIS CLAUSE 14.5 SHALL LIMIT EITHER PARTY'S RIGHT TO PURSUE AND OBTAIN EQUITABLE RELIEF.

15. TERM AND TERMINATION

15.1 **Term**. The term of this Agreement (the " **Term**") shall commence on the Effective Date and, unless sooner terminated as provided in this Article 15, shall continue in full force and effect:

15.1.1 on a Research Program-by-Research Program basis, until the expiration of the Option Period for such Research Program, where the Option is not exercised therefor, or

15.1.2 following the effective date of any Exclusive License with respect to a Research Program, on a country-by-country and Product-by-Product basis, [***].

15.2 **Termination by Either Party for Material Breach**. Either Party may terminate this Agreement (i) in its entirety, (ii) with respect to any Exclusive License granted by such Party, (iii) with respect to a given Research Program, or (iv) on a country-by-country basis, by written notice delivered to the other Party for any material breach of this Agreement by the other Party if such material breach is not cured within ninety (90) days (thirty (30) days for payment defaults) after the breaching Party receives written notice of such breach from the nonbreaching Party describing such breach and demanding its cure; provided, that if such breach is not capable of being cured within such ninety (90)-day (or thirty (30)-day) period, the cure period shall be extended for such amount of time that the Parties may agree in writing is reasonably necessary to cure such breach, so long as (1) the breaching Party is making Commercially Reasonable Efforts to do so, and (2) the Parties agree on an extension within such ninety (90)-day (or thirty (30)-day) period. For clarity, this Agreement may be terminated in its entirety under this Clause 15.2 only if the material breach affects the fundamental purpose of this Agreement. Notwithstanding anything to the contrary herein, if the allegedly breaching Party in good faith either disputes (a) whether a breach is material or has occurred or (b) the alleged failure to cure or remedy such material breach, and provides written notice of that dispute to the other Party within the above time periods, then the matter will be addressed under the dispute resolution provisions in Article 16 and the notifying Party may not so terminate this Agreement until it has been determined under Article 16 that the allegedly breaching Party is in material breach of this Agreement, and such breaching Party further fails to cure such breach within ninety (90) days (or such longer period as determined by the arbiter of such dispute resolution) after the conclusion of that dispute resolution procedure.

15.3 **Termination by Either Party for Insolvency or Bankruptcy**. Either Party may terminate this Agreement effective ten (10) business days after delivery of written notice to the other Party upon the liquidation, dissolution, winding-up, insolvency, bankruptcy, or filing of any petition therefor, appointment of a receiver, custodian or trustee, or any other similar proceeding, by or of the other Party where such petition, appointment or similar proceeding is not dismissed or vacated within ninety (90) calendar days. All rights and licenses granted pursuant to this Agreement are, for purposes of Clause 365(n) of Title 11 of the United States Code or any foreign equivalents thereof ("**Title 11**"), licenses of rights to "intellectual property" as defined in Title 11. Each Party in its capacity as a licensor hereunder agrees that, in the event of the commencement of bankruptcy proceedings by or against such bankrupt Party under Title 11, (a) the other Party, in its capacity as a licensee of rights under this Agreement, shall retain and may fully exercise all of such licensed rights under this Agreement (including as provided in this Clause 15.3) and all of its rights and elections under Title 11, and (b) the other (licensee) Party shall be entitled to a complete duplicate of all embodiments of such intellectual property, and such embodiments, if not already in its possession, shall be promptly delivered to the other (licensee) Party (i) upon any such commencement of a bankruptcy proceeding, unless the bankrupt Party elects to continue to perform all of its obligations under this Agreement, or (ii) if not delivered under (i), immediately upon the rejection of this Agreement by or on behalf of the bankrupt Party.

15.4 [***]

15.5 **Termination by either Party for Patent challenge**. Either Party may terminate any Exclusive License under which a license has been granted to the other Party to use any of such Party's Licensed IP, if the other Party or its Affiliates commences proceedings (whether before a regulatory or administrative body or a court) anywhere in the world, or voluntarily assists any Third Party in commencing or participating in such proceedings (whether before a regulatory or administrative body or a court) alleging that any claim in any Patent within such Licensed IP that is licensed to the other Party by such Party (including the Adaptimmune Background IP or Alpine Background IP, as applicable) is invalid, unenforceable or otherwise not patentable, and such proceedings are not withdrawn within thirty (30) days after receipt of a written notice to withdraw. Notwithstanding the foregoing, a license-granting Party shall have no right to

terminate any Exclusive License pursuant to this Clause 15.5 if any proceedings are brought as a defense (including an affirmative defense) in relation to a claim of infringement brought against the other Party or its Affiliates.

15.6 **Accrued Rights and Obligations**. Expiration or termination of this Agreement in its entirety, or with respect to a particular Exclusive License, a given Research Program, or a given country for any reason, shall not release either Party hereto from any liability which, as of the effective date of such expiration or termination, had already accrued to the other Party or which is attributable to a period prior to such termination, nor preclude either Party from pursuing any rights and remedies it may have hereunder or at law or in equity which accrued or are based upon any event occurring prior to the effective date of such expiration or termination.

15.7 **Effects of Termination**. The effects of termination set forth in this Clause 15.7 shall apply either with respect to this Agreement in its entirety or only with respect to a specific Research Program, Exclusive License or country, in all cases as applicable.

15.7.1 **Termination of Licenses**.

(a) Upon termination of the Agreement in its entirety by either Party, all licenses and options granted under this Agreement shall terminate as of the effective date of such termination save as explicitly otherwise provided to survive termination of this Agreement. Performance of all Research Programs shall cease as of effective date of termination.

(b) Upon termination of any Exclusive License by either Party, such Exclusive License shall terminate as of the effective date of such termination save as explicitly otherwise provided to survive termination of this Agreement. All other Exclusive Licenses and the remaining terms of this Agreement shall continue in full force and effect following such termination.

(c) Upon termination of any Research Program by either Party, such Research Program and the associated Development License shall terminate as of the effective date of such termination save as explicitly otherwise provided to survive termination of this Agreement. All other Research Programs and Development Licenses and the remaining terms of this Agreement shall continue in full force and effect following such termination. The Option granted under Clause 6.2 in relation to such Research Program shall terminate as of the effective date of termination.

(d) Upon termination of this Agreement in relation to any Product or to any country, the Exclusive License shall only terminate in relation to such Product or to such country (save as explicitly otherwise provided to survive termination) and shall otherwise remain in full force and effect.

15.7.2 **Termination of Target Exclusivity**. Upon (a) early termination of this Agreement in its entirety by Adaptimmune or by Alpine, (b) expiration of the Option Period with respect to any Research Program without exercise of the Option, or (c) the early termination of any Exclusive License by either Adaptimmune or Alpine with respect to one or more countries, the provisions of Clause 6.4 shall cease to apply to the Program Target that is the subject of such Research Program(s) or Exclusive License(s) with respect to such terminated country(ies).

15.7.3 **Clinical Trials**. The Parties shall ensure that where the expiry or any early termination of this Agreement impacts the conduct or completion of any Clinical Trial under an Exclusive License, that any such Clinical Trial shall be wound down in accordance with the protocol for such Clinical Trial and in such a way as to minimize any patient harm and at all times in accordance with all Applicable Laws.

15.7.4 **Return of Confidential Information**.

(a) Following expiry or any early termination of this Agreement, the Party that has Confidential Information of the other Party shall to the extent reasonably

possible destroy (at such Party's written request) all such Confidential Information in its possession as of the effective date of expiration or termination, with the exception of one copy of such Confidential Information, which may be retained by the legal department of the Party that received such Confidential Information solely for purposes of ensuring compliance with confidentiality obligations, provided that each Party may retain and continue to use such Confidential Information of the other Party to the extent necessary to exercise any surviving rights, licenses or obligations under this Agreement or any obligation under Applicable Laws. For clarity, the Party owning any Confidential Information shall at all times be entitled to fully use its Confidential Information (but not the Confidential Information of the other Party) for any purpose.

(b) Following termination of any Exclusive License, the Party that has any Confidential Information of the other Party which is subject to such Exclusive License (and which is not required for any ongoing rights or obligations under this Agreement) shall to the extent reasonably possible destroy (at such Party's written request) or put beyond use all such Confidential Information in its possession as of the effective date of termination (with the exception of one copy of such Confidential Information, which may be retained by the legal department of the Party that received such Confidential Information solely for purposes of ensuring compliance with confidentiality obligations), provided that each Party may retain and continue to use such Confidential Information of the other Party to the extent necessary to exercise any surviving rights, licenses or obligations under this Agreement or any obligation under Applicable Laws. For clarity, the Party owning any Confidential Information previously subject to any Exclusive License shall be entitled to fully use its Confidential Information (but not the Confidential Information of the other Party) for any purpose.

(c) This clause shall not require return or destruction of any Confidential Information which is held on back-up servers or archive systems, provided such back-ups have been made as part of the routine business of a Party and such back-ups are not accessible other than by members of the IT team at such Party. Any Confidential Information retained by a Party (but belonging to the other Party) will continue to be subject to the confidentiality provisions of this Agreement.

(d) For clarity, ownership of Confidential Information shall be determined in accordance with the definition of Confidential Information in Clause 11.1.

15.7.5 **Inventory at Termination**. Upon termination of this Agreement or any Exclusive License, and [***] such termination, Adaptimmune shall have the right to sell or otherwise dispose of all inventory of Products in all countries then in its stock and to continue to treat patients (including to manufacture and supply Products for such patients) who are enrolled in any Clinical Trials for any Product or who have consented to be enrolled in (or are already enrolled in) any screening protocol for any Clinical Trial for any Product prior to termination of this Agreement or such Exclusive License. Any sales of inventory of Products will remain subject to payment of Royalty under Clause 8.4, and any other applicable provisions of this Agreement. To the extent any continuing requirement to supply Product exists after such termination, the Parties may mutually agree that Adaptimmune can continue to supply to fulfil any such continuing supply requirement.

15.8 **Survival**. In addition to any provisions specified in this Agreement as surviving under the applicable circumstances, the following provisions shall survive: Articles 9 (with respect to any payments accruing prior to the date of such termination but not paid as of such time), 11, 13 (with respect to any claims arising from events occurring prior to the date of such termination), 14, 15, 16, 17, 18, and 19 and Clauses 3.6.2, 6.7, 8.4 (with respect to royalties accruing prior to the date of such termination but not paid as of such time), 10.1, 10.2.3 (which shall apply to all Joint Foreground IP after such termination), 12.4, 14.1-14.3 (with respect to any claims arising from events occurring prior to the date of such termination) and 14.5. In addition to those provisions specifically referenced in this Clause 15.8, those provisions which by their

nature are intended to survive, as well as any other provisions necessary to interpret or implement any other surviving provisions (including, to the extent applicable, the definitions in Article 1), shall survive.

16. DISPUTE RESOLUTION

16.1 **Disputes**. Adaptimmune and Alpine recognize that a dispute, controversy or claim of any nature whatsoever arising out of or relating to this Agreement, or the breach, termination or invalidity thereof (each, a "**Dispute**"), may from time to time arise during the Term. Unless otherwise specifically recited in this Agreement (for example in relation to decision making of the JSC or JPT), such Disputes between Adaptimmune and Alpine will be resolved as set out in this Article 16. In the event of the occurrence of such a Dispute, the Parties shall first refer such Dispute to their respective Alliance Managers for attempted resolution by such Alliance Managers within thirty (30) days after such referral. If such Dispute is not resolved within such thirty (30) day period, each of Adaptimmune or Alpine may, by written notice to the other Party, have such Dispute referred to their respective officers designated below, or their respective designees, for attempted resolution within thirty (30) days after such notice is received. Such designated officers are as follows:

[***]

[***]

In the event the designated officers or their respective designees are not able to resolve such Dispute within thirty (30) days of such other Party's receipt of such written notice, then subject to Clause 16.3, either Party may initiate the dispute resolution procedures set forth in Clause 16.2.

16.2 **Arbitration**.

16.2.1 **Rules**. Except as otherwise expressly provided in this Agreement (including under Clause 16.3 with respect to Patent-related matters), the Parties agree that any Dispute not resolved internally by the Parties pursuant to Clause 16.1 shall be resolved through binding arbitration conducted by the International Chamber of Commerce in accordance with the then prevailing Rules of Arbitration of the International Chamber of Commerce (the "**Rules**"), except as specifically modified in this Agreement, applying the substantive law specified in Clause 19.1.

16.2.2 **Arbitrators; Location**. Each Party shall select one (1) arbitrator, and the two (2) arbitrators so selected shall choose a third arbitrator. All three (3) arbitrators shall serve as independent arbitrators and have at least ten (10) years of (a) dispute resolution experience (including judicial experience) and/or (b) legal or business experience in the biotech or pharmaceutical industry. In any event, at least one (1) arbitrator shall satisfy the foregoing experience requirement under Clause 16.2.2(b). If a Party fails to nominate its arbitrator, or if the Parties' arbitrators cannot agree on the third arbitrator, the necessary appointments shall be made in accordance with the Rules. Once appointed by a Party, such Party shall have no ex parte communication with its appointed arbitrator. The seat, or legal place, of the arbitration proceedings shall be New York, New York. The arbitration proceedings and all pleadings and written evidence shall be in the English language. Any written evidence originally in another language shall be translated into English and accompanied by the original or a true copy thereof.

16.2.3 **Procedures; Awards**. Each Party agrees to use reasonable efforts to make all of its current employees available to the arbitrators, if reasonably needed, and agrees that the arbitrators may determine any person as necessary. The arbitrators shall be instructed and required to render a written, binding, nonappealable resolution and award on each issue that clearly states the basis upon which such resolution and award is made. The written resolution and award shall be delivered to the Parties as expeditiously as possible, but in no event more than ninety (90) days

after conclusion of the hearing, unless otherwise agreed by the Parties. Judgment upon such award may be entered in any competent court or application may be made to any competent court for judicial acceptance of such an award and order for enforcement. Each Party agrees that, notwithstanding any provision of Applicable Law or of this Agreement, it will not request, and the arbitrators shall have no authority to award, punitive or exemplary damages against any Party. All information disclosed and generated in the course of such arbitration proceeding shall be treated as Confidential Information by each of the Parties pursuant to the terms and conditions set forth in Article 11.

16.2.4 **Costs**. The prevailing Party, as determined by the arbitrators, shall be entitled to (a) its share of fees and expenses of the arbitrators and (b) its reasonable attorneys' fees and associated costs and expenses. In determining which Party "prevailed," the arbitrators shall consider (i) the significance, including the financial impact, of the claims prevailed upon and (ii) the scope of claims prevailed upon, in comparison to the total scope of the claims at issue. If the arbitrators determine that, given the scope of the arbitration, neither Party "prevailed," the arbitrators shall order that the Parties (1) share equally the fees and expenses of the arbitrators and (2) bear their own attorneys' fees and associated costs and expenses.

16.2.5 **Interim Equitable Relief**. Notwithstanding anything to the contrary in this Clause 16.2, in the event that a Party reasonably requires relief on a more expedited basis than would be possible pursuant to the procedure set forth in this Article 16, such Party may seek a temporary injunction or other interim equitable relief in a court of competent jurisdiction pending the ability of the arbitrators to review the decision under this Clause 16.2. Such court shall have no jurisdiction or ability to resolve Disputes beyond the specific issue of temporary injunction or other interim equitable relief.

16.2.6 **Protective Orders; Arbitrability**. At the request of either Party, the arbitrators shall enter an appropriate protective order to maintain the confidentiality of information produced or exchanged in the course of the arbitration proceedings. The arbitrators shall have the power to decide all questions of arbitrability.

16.3 **Subject Matter Exclusions**. Notwithstanding the provisions of Clause 16.2, any Dispute not resolved internally by the Parties pursuant to Clause 16.1 that involves the validity or infringement of a Patent shall be brought before an appropriate regulatory or administrative body in the country in which such Patent is granted or applied for, and the Parties hereby consent to the jurisdiction and venue of such courts and bodies.

16.4 **Continued Performance**. Provided that this Agreement has not terminated, the Parties agree to continue performing under this Agreement in accordance with its provisions, pending the final resolution of any Dispute.

17. ANTIBRIBERY

17.1 **Antibribery**.

17.1.1 "**Anticorruption Laws**" means all anticorruption and antibribery laws and regulations, including the US Foreign Corrupt Practices Act of 1977, as amended, and the United Kingdom Bribery Act 2010, as amended, and any other applicable anticorruption laws and laws for the prevention of fraud, racketeering, money laundering or terrorism.

17.1.2 "**Government Official**" means any person employed by or acting on behalf of a government, government-controlled entity or public international organization; any political party, party official or candidate; any person who holds or performs the duties of an appointment, office or position created by custom or convention; and

any person who holds himself out to be the authorised intermediary of any of the foregoing.

17.1.3 The Parties agree, on behalf of themselves and their respective officers, directors and employees, that in connection with this Agreement, it shall not directly or indirectly pay, offer or promise to pay, or authorise the payment of any money, or give, offer or promise to give, or authorise the giving of anything else of value, to (i) any Government Official in order to influence official action; (ii) any person (whether or not a Government Official) (a) to influence such person to act in breach of a duty of good faith, impartiality or trust, (b) to reward such person for acting improperly, or (c) where such person would be acting improperly by receiving the money or other thing of value; (iii) any other person while knowing or having reason to know that all or any portion of the money or other thing of value will be paid, offered, promised or given to, or will otherwise benefit a Government Official in order to influence official action for or against any party in connection with the matters that are the subject of this agreement; or (iv) any person to reward that person for acting improperly or to induce that person to act improperly.

17.1.4 The Parties agree, on behalf of themselves and their respective officers, directors and employees that work in connection with this Agreement that they shall not, directly or indirectly, solicit, receive or agree to accept any payment of money or anything else of value in violation of the Anticorruption Laws. In connection with the performance of the services hereunder, the Parties undertake to comply with the Anticorruption Laws and shall not take any action that will, or would reasonably be expected to, cause it to be in violation of any such laws to the extent applicable to either Party.

17.1.5 Each Party shall promptly provide the other Party with written notice of (i) becoming aware of any breach or violation by the relevant Party or its subcontractors or its or their respective officers, directors, employees, of any of the representation, warranty or undertaking set forth in this Clause 17.1 or (ii) upon receiving a formal notification that it is the target of a formal investigation by any governmental authority for any breach of Anticorruption Laws in connection with the performance of this Agreement.

18. DATA PROTECTION

18.1 The Parties agree to comply with all applicable national and international laws, regulations and guidelines relating to the protection and processing of personal data and person identifiable information and as further set out in Exhibit 3.

19. MISCELLANEOUS

19.1 **Applicable Law**. This Agreement (including the arbitration provisions of Article 16) shall be governed by and interpreted in accordance with the laws of New York, without reference to the principles of conflicts of laws. The United Nations Convention on Contracts for the International Sale of Goods shall not apply to the transactions contemplated by this Agreement.

19.2 **Notices**. Except as otherwise expressly provided in the Agreement, any notice required under this Agreement shall be in writing and shall specifically refer to this Agreement. Notices shall be sent via one of the following means and will be effective (a) on the date of delivery, if delivered in person; or (b) on the date of receipt, if sent by private express courier or by first class certified mail, return receipt requested. Notices shall be sent to the other Party at the addresses set forth below. Either Party may change its addresses for purposes of this Clause 19.2 by sending written notice to the other Party.

If to Alpine: [***]
[***]
[***]
[***]
[***]

If to Adaptimmune: [***]
[***]
[***]
[***]
[***]

19.3 **Assignment**. Neither Party may assign or otherwise transfer, in whole or in part, this Agreement without the prior written consent of the nonassigning Party, such approval not to be unreasonably withheld, conditioned or delayed. Notwithstanding the foregoing, either Party may assign this Agreement to (i) an Affiliate or (ii) any purchaser of all or substantially all of the assets of such Party that relate to the performance of this Agreement, or of all of its capital stock, or to any successor corporation or entity resulting from any merger, acquisition or consolidation or re-organization of such party with or into such corporation or entity, provided that the Party to which this Agreement is assigned expressly agrees in writing to assume and be bound by all obligations of the assigning Party under this Agreement. Subject to the foregoing, this Agreement will benefit and bind the Parties' successors and permitted assigns. Any assignment not in accordance with this Clause 19.3 shall be null and void. It is understood and agreed that the intellectual property rights of any Third Party that becomes an Affiliate of a Party as a result of any Change of Control of such Party and (a) existing immediately prior to the consummation of such Change of Control or (b) developed independent of this Agreement, shall not be included in the intellectual property licensed hereunder by the Party undergoing such Change of Control.

19.4 **Independent Contractors**. The Parties hereto are independent contractors and nothing contained in this Agreement shall be deemed or construed to create a partnership, joint venture, employment, franchise, agency or fiduciary relationship between the Parties.

19.5 **Entire Agreement**. Except to the extent expressly provided herein, this Agreement constitutes the entire agreement between the Parties relating to the subject matter of this Agreement and supersedes all previous oral and written communications between the Parties with respect to the subject matter of this Agreement. Each Party confirms that in entering into this Agreement, it has not relied on any representation or statement from the other Party that is not explicitly stated as a warranty or representation under this Agreement. Nothing in this Clause 19.5 shall exclude any liability for fraud or fraudulent misrepresentation or exclude any remedy for such.

19.6 **Amendment; Waiver**. Except as otherwise expressly provided herein, no alteration of or modification to this Agreement shall be effective unless made in writing and executed by an authorised representative of both Parties. No course of dealing or failing of either Party to strictly enforce any term, right or condition of this Agreement in any instance shall be construed as a general waiver or relinquishment of such term, right or condition. The observance of any provision of this Agreement may be waived (either generally or any given instance and either retroactively or prospectively) only with the written consent of the Party granting such waiver.

19.7 **Further Assurance**. Each Party shall, and shall use all Commercially Reasonable Efforts to procure that any necessary Third Party to, promptly execute and deliver such further documents and do such further acts as may be required or appropriate for the purpose of carrying out the purpose of and giving full effect to this Agreement.

19.8 **Severability**. The Parties do not intend to violate any public policy or statutory or common law. However, if any sentence, paragraph, section, clause or combination or part thereof of this Agreement is in violation of any law or is found to be otherwise unenforceable, such sentence, paragraph, section, clause or combination or part of the same shall be deleted and the remainder of this Agreement shall remain binding, provided that such deletion does not alter the basic purpose and structure of this Agreement.

19.9 **No Third-Party Rights**. The Parties do not intend that any term of this Agreement should be enforceable by any person who is not a Party.

19.10 **Interpretation**. The captions and headings to this Agreement are for convenience only, and are to be of no force or effect in construing or interpreting any of the provisions of this Agreement. Unless context otherwise clearly requires, whenever used in this Agreement, (a) the words "include" or "including" shall be construed as incorporating "but not limited to" or "without limitation"; (b) the words "hereof," "herein," "hereby" and derivative or similar words refer to this Agreement, including the Exhibits; (c) the word "law" or "laws" means any applicable, legally binding statute, ordinance, resolution, regulation, code, guideline, rule, order, decree, judgment, injunction, mandate or other legally binding requirement of a governmental authority (including a court, tribunal, agency, legislative body or other instrumentality of any (i) government or country or territory, (ii) any state, province, county, city or other political subdivision thereof, or (iii) any supranational body); (d) all references to the word "will" are interchangeable with the word "shall" and shall be understood to be imperative or mandatory in nature; (e) the singular shall include the plural and vice versa; and (f) the word "or" has the inclusive meaning represented by the phrase "and/or". All references to days, months, quarters or years are references to calendar days, calendar months, calendar quarters, or calendar years.

19.11 **Other Activities**. The Parties acknowledge that each of them may now or in the future engage in research, manufacturing, development or commercialisation activities that utilize technologies similar to or involve therapies or pharmaceutical products competitive with those contemplated by this Agreement. Neither Party shall be prevented from using any publicly available research results or other information (including any publicly available information of the other Party) to the same extent as Third Parties generally are legally permitted to do so. Each Party agrees to inform its key personnel assigned to perform activities hereunder of the limitations on use of Confidential Information contained in this Agreement, instruct such personnel to comply with such restrictions, and where appropriate, impose firewalls or other appropriate measures to minimize the potential for misuse of information. However, each Party has limited resources, and as a result it is anticipated that personnel assigned to activities hereunder may also participate in other activities that may utilize technologies similar to or involve therapies or pharmaceutical products competitive with those contemplated by this Agreement. In particular, it is anticipated that personnel in sales, marketing, clinical and regulatory functions, regardless of level, will participate in multiple programs and that management personnel will by nature of their leadership positions participate in multiple programs.

19.12 **Counterparts**. This Agreement may be executed in two or more counterparts, each of which will be deemed an original, but all of which together will constitute one and the same instrument. For purposes hereof, a facsimile copy, or email with attached pdf copy, of this Agreement, including the signature pages hereto, will be deemed to be an original.

[Signature page follows – the rest of this page intentionally left blank.]

IN WITNESS WHEREOF, duly authorised representatives of the Parties have executed this Agreement as of the Effective Date.

ADAPTIMMUNE LIMITED

By: /s/ Helen Tayton-Martin
Name: Helen Tayton-Martin
Title: CBO

AIS OPERATING CO., INC.
f/k/a Alpine Immune Sciences, Inc.

By: /s/ Paul Rickey
Name: Paul Rickey
Title: CFO

EXHIBIT 1 – Initial Research Programs

THIS PAGE AND THE FOLLOWING 12 PAGES OF THIS EXHIBIT HAVE BEEN OMITTED BECAUSE THEY ARE BOTH (I) NOT MATERIAL AND (II) WOULD BE COMPETITIVELY HARMFUL IF PUBLICLY DISCLOSED

[***]

EXHIBIT 2 – Payments

Upfront Payments

Upfront Payment for grant of option for the Initial Research Programs

- In consideration of the grant of the Option to Adaptimmune for an Exclusive License in relation to the two Initial Research Programs, Adaptimmune will pay to Alpine an upfront sum of two million US dollars (US$2,000,000).

Upfront Payments due on Acceptance of Targets for Other Research Programs

- With respect to each Other Research Program, upon Acceptance of any Other Research Target and mutual agreement by the Parties with respect to the Research Plan for such Other Research Program, Adaptimmune will pay [***].
- The maximum upfront payments applicable to Other Research Programs will be [***].

Total upfront payments

The total upfront payments payable by Adaptimmune under this Exhibit 2 will not exceed [***].

Milestones

The following Milestones shall be payable by Adaptimmune to Alpine in accordance with clause 8.3 of this Agreement.

Milestone Event	**Milestone payable for first Product developed from first Research Program to achieve such event ***	**Milestone payable for first Product developed from second and subsequent Research Programs to achieve such event**
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
Total Milestones per Research Program	[***]	[***]

- *Note – Payment of Milestones under first column of table above will only apply to the first Research Program under which a Product reaches the first Milestone Event. For example, where multiple Research Programs are ongoing at the same time, the first column of Milestones will be payable upon the achievement of the respective Milestone events by the first Research Program under which a patient is dosed with a Product from such Research Program [***]. For clarity, the relative start dates of the Research Programs are irrelevant to determining which column of Milestones is applicable to which Research Program.
- ** Note – [***]

EXHIBIT 3 – DATA PROTECTION

1.1 In this Exhibit:

(a) Adaptimmune is the Controller and Alpine is the Processor; and

(b) the types of Personal Data and categories of Data Subject which will be processed, the nature and purpose of that processing and the duration of that processing are as set out below:

(i) Personal Data capable of identifying any of Controller's employees, contractors or other individuals working for or on behalf of Controller.

(c) Data Protection Legislation in this Exhibit refers to all applicable privacy and data protection laws including the General Data Protection Legislation ((EU) 2016/679) (GDPR) and any applicable national implementing laws, regulations and secondary legislation in England and Wales relating to the processing of personal data and the privacy of electronic communications, as amended, replaced or updated from time to time, including the Privacy and Electronic Communications (EC Directive) Regulations 2003 (SI 2003/2426) (Privacy Regulations) as amended by the Privacy and Electronic Communications (EC Directive) (Amendment) Regulations 2011 (SI 2011/1208), the Privacy and Electronic Communications (EC Directive) (Amendment) Regulations 2015 (SI 2015/355) and the Privacy and Electronic Communications (EC Directive) (Amendment) Regulations 2016 (SI 2016/524).

(d) Personal Data and Data Subject shall have the meanings given to them under the Data Protection Legislation.

1.2 In relation to the processing of Personal Data, Processor shall:

(a) only process Personal Data in accordance with the Controller's written instructions from time to time (which may be specific instructions or standing instructions of general application in relation to the performance of a Research Program or this Agreement, whether set out in this Agreement or otherwise notified to the Processor, unless such processing is required by any law (other than contract law) to which the Processor is subject, in which case the Processor shall (to the extent permitted by law) inform the Controller of that legal requirement before carrying out the processing;

(b) immediately notify the Controller if it considers that the Controller's instructions are in breach of the GDPR or other EU member state laws; and

(c) keep a written record of all such processing activities.

1.3 In relation to the security and confidentiality of the Personal Data, Processor shall:

(a) ensure that it has in place appropriate technical and organisational measures to ensure a level of security for the Personal Data which is appropriate to the risks to individuals that may result from the accidental or unlawful destruction, loss, alteration, unauthorised disclosure of, or access to the Personal Data;

(b) in addition to the confidentiality obligations in Article 11 of this Agreement:

(i) ensure that only those of the Processor's personnel who need to have access to the Personal Data are granted access to such data and only for the purposes of the performance of this Agreement and all of the Processor's personnel required to access the Personal Data are informed of the confidential nature of the Personal Data, comply with the obligations set out in this Exhibit, and are bound by appropriate confidentiality obligations when accessing the Personal Data; and

(ii) not publish, disclose or divulge any of the Personal Data to any third party (including for the avoidance of doubt the Data Subject itself) unless directed to do so in writing by the Controller;

(c) not modify, amend or alter the contents of the Personal Data unless specifically authorised in writing by the Controller.

1.4 If the Processor becomes aware of a Personal Data breach, it shall notify the Controller without undue delay on becoming of aware of such a breach.

1.5 The Processor shall notify the Controller within five Business Days upon receiving the following:

(a) a request from a Data Subject to have access to that person's Personal Data; or

(b) a complaint or request relating to the Controller's obligations under the Data Protection Legislation; or

(c) any other communication relating directly or indirectly to the processing of any Personal Data in connection with this Agreement.

1.6 The Processor shall provide the Controller with full co-operation and assistance in order to enable the Controller to comply with its obligations under the Data Protection Legislation in relation to:

(a) the Controller's obligations in relation to responding to Data Subject requests;

(b) the security of the Personal Data;

(c) notifying Personal Data breaches to the relevant supervisory authority;

(d) communicating personal data breaches to the Data Subject; and

(e) impact assessments and related consultations with supervisory authorities or regulators.

1.7 The Processor shall:

(a) make available to the Controller all information that the Controller requests from time to time to enable the Controller to verify that the Processor is in compliance with its obligations in this Exhibit; and

(b) permit the Controller or its external advisers to inspect and audit the Processor’s data processing activities and those of its agents, subsidiaries and Subcontractors (to the extent the Processor is reasonably able to procure such third-party access).

1.8 The Processor shall not engage or authorise a subcontractor to process the Personal Data unless:

(i) it has obtained the prior written consent of the Controller (which may be granted or withheld in the Controller's sole discretion) before transferring the Personal Data to any Subcontractors in connection with the provision of the Services; and

(ii) the Subcontractor has either entered into a direct contract with the Controller or a contract with the Processor which incorporates the provisions equivalent to those in this agreement in relation to confidentiality, data protection and security

1.9 In relation to transfers of Personal Data to areas outside the European Economic Area (EEA) in addition to initial transfer of Personal Data from Controller to Processor:

(a) the Processor shall not transfer any Personal Data outside the EEA without the Controller's prior written consent; and

(b) if the Controller consents to any transfers pursuant to preceding clause, the Processor shall ensure that the following conditions are met in relation to such transfers:

(i) the Processor complies with its obligations under the Data Protection Legislation by ensuring that there is an adequate level of protection to any Personal Data that is transferred (including as relevant model clauses or adoption of Privacy Shield as appropriate);

(ii) that there are appropriate safeguards in place in relation to that transfer;

(iii) that Data Subjects have enforceable rights and effective legal remedies; and

(iv) that the Processor shall comply with any other reasonable instructions as notified to it by the Controller in relation to such transfers.

1.10 The Controller acknowledges that the Processor is reliant on the Controller alone for direction as to the extent the Processor is entitled to use and process the Personal Data. The Processor shall be entitled to relief from liability in circumstances where a Data Subject makes a claim or complaint with regards to the Processor's actions to the extent that such actions directly result from instructions received from the Controller.

1.11 On the expiry or termination of this Agreement, the Processor shall notify the Controller of the Personal Data that it holds. Promptly following such expiry or termination, and unless otherwise instructed in writing by Controller or continued storage is required by the Processor to comply with Applicable Laws, the Processor shall securely and permanently destroy all copies of Personal Data in its possession or control (other than any copy transferred to the Controller in accordance with Controller's request).

1.12 The Processor shall, at all times during and after the term of this Agreement, indemnify the Controller and keep the Controller indemnified against all losses, damages, costs or expenses and other liabilities (including legal fees) incurred by, awarded against or agreed to be paid by

the Controller arising from any breach of the Processor's obligations under this Exhibit except and to the extent that such liabilities have resulted directly from the Controller's instructions.

EXHIBIT 4 – GOVERNANCE

1. Joint Steering Committee.

1 . 1 **Formation and Composition**. As soon as reasonably possible and in any event within thirty (30) days after the Effective Date, Adaptimmune and Alpine shall establish a joint steering committee (the "**JSC**") to monitor and coordinate the communication and activities of both Parties under this Agreement. The JSC shall be composed of at least three (3) but no more than four (4) representatives designated by each Party and in each case an equal number of representatives from each Party. Representatives must be appropriate for the tasks then being undertaken and the stage of development or commercialisation applicable, in terms of their seniority, decision-making authority, availability, function in their respective organizations, training and experience. Each Party may replace its JSC representatives from time to time upon written notice to the other Party; provided, however, if a Party's JSC representative is unable to attend a JSC meeting, such Party may designate an alternate to attend such JSC meeting by providing notification in writing to the other Party's Alliance Manager and following provision of such written notification the alternate will be entitled to perform the functions of such JSC representative at such JSC meeting. The Alliance Managers may attend meetings of the JSC but shall have no right to vote on any decisions of the JSC.

1.2 **JSC Responsibilities**. In addition to its overall responsibility for monitoring the activities of the Parties under this Agreement, the JSC shall, in particular:

(a) work to resolve, through good faith discussions, any dispute, controversy or claim between the Parties arising during the performance of any Research Program and related to the matters under the authority of the JSC;

(b) review any Targets proposed by Adaptimmune for a new Research Program pursuant to Clause 3.1.3;

(c) review and approve any material amendments to any Research Program or Research Plan proposed by the JPT;

(d) review and approve any criteria (and amendments to such criteria) for the research and preclinical development of any Product under any Research Program including criteria required for any Product to proceed to the next phase of development under any Research Program;

(e) perform such other functions as may be agreed to by the Parties in writing, or as specified in this Agreement.

1 . 3 **Decision making for JSC**. Each Party will discuss and attempt to resolve any potential or evolving disagreement through its respective Alliance Managers and/or the JPT before it is brought before the JSC for resolution. With respect to the responsibilities of the JSC, each Party shall have one vote on all matters brought before the JSC. The JSC shall operate as to matters within its responsibility by unanimous vote. Each Party shall make decisions in good faith and shall not take any decisions which would unreasonably delay the performance of any Research Program. If the JSC is unable to achieve a unanimous vote within thirty (30) days of any matter being brought before the JSC and such matter relates to any Research Program or

any Product (including progression of any Product through the Research Program and in to Clinical Trials), then such matter may be referred to the President of Research at Adaptimmune and [***], President and Head of R&D, a t Alpine for resolution. If the executives are unable to resolve such matter within thirty (30) days following such matter bring brought forth thereto, [***]

1.4 Any JSC decisions, any decisions of the Party's senior managers and Adaptimmune's final decision-making authority under Paragraph 1.3 above are subject to the following: (i) neither the JSC, the senior managers nor Adaptimmune shall have the unilateral or overriding authority to amend or modify, or waive a Party's own compliance with, this Agreement including in relation to the scope or terms of any license to Intellectual Property Rights; and (ii) neither the JSC, the senior managers nor Adaptimmune will have the unilateral or overriding authority to amend any Research Program in a way which would materially increase the cost for the other Party or materially increase the resources required from the other Party.

2. Joint Project Team.

2.1 **Formation and Composition**. As soon as reasonably possible and in any event within thirty (30) days after the Effective Date, Adaptimmune and Alpine shall establish a joint project team (the "**JPT**") to monitor and coordinate the communication and activities of both Parties under all Research Programs. The JPT shall be composed of at least two (2) but no more than three (3) representatives designated by each Party and in each case an equal number of representatives from each Party. Representatives must be appropriate for the tasks then being undertaken and the applicable stage of research, in terms of their seniority, decision-making authority, availability, function in their respective organisations, training and experience. Each Party may replace its JPT representatives from time to time upon written notice to the Alliance Manager of the other Party; provided, however, if a Party's JPT representative is unable to attend a JPT meeting, such Party may designate an alternate to attend such JPT meeting by providing notification in writing to the other Party's Alliance Manager and following provision of such written notification the alternate will be entitled to perform the functions of such JPT representative at such JPT meeting. The Alliance Managers may attend meetings of the JPT but shall have no right to vote on any decisions of the JPT.

2.2 **JPT Responsibilities for Research Program**. The JPT shall have overall responsibility for monitoring the activities during each Research Program. The JPT shall, in particular:

(a) work to resolve, through good faith discussions, any dispute, controversy or claim related to the matters under the authority of the JPT;

(b) recommend to the JSC any material changes to any Research Program, including any amendments to any Research Plan;

(c) monitor performance of each Research Program; and

(d) review any data arising from any Research Program.

2.3 **JPT Decision Making**. With respect to the responsibilities of the JPT, each Party shall have one vote on all matters brought before the JPT and the JPT shall operate by unanimous vote. If the JPT is unable to achieve a unanimous vote within thirty (30) days of any matter being

brought before the JPT, then such matter may be referred in writing to the JSC at either Party's discretion. Each Party shall make decisions within the JPT in good faith and on a timely basis; provided that any JPT decisions shall be subject to the conditions applied to JSC decisions, as set forth in Paragraph 1.3 above.

2.4 **Ad-hoc Committees**. The JSC or JPT, as appropriate, may also authorise the setting up of subcommittees in relation to particular or specific aspects of any Research Program or other performance of this Agreement. Such subcommittees shall act in the same way as the JPT and regularly report in to the JPT.

3. Meetings.

3.0 **JSC Meetings**. The JSC shall hold meetings in English at such frequency as determined by the JSC members, but at least once every [***]. Such JSC meetings may be conducted in person, via teleconference or otherwise, in each case as agreed by the JSC. The in-person JSC meetings shall alternate between Adaptimmune's facilities in Abingdon, Oxfordshire, England and at Alpine's facilities in Seattle, Washington, USA.

3.1 **JPT Meetings**. The JPT shall meet once every calendar month at Adaptimmune's facilities in Abingdon, Oxfordshire, England, or at Alpine's facilities in Seattle, Washington, USA, or via teleconference or otherwise, in each case as agreed by the JPT. Where possible, meetings will be held by telephone conference. Where necessary, for example to resolve any dispute or to agree upon changes to any Research Program, as applicable, the JPT shall meet more frequently.

3.2 **Meeting Agendas and Minutes**. Not later than [***] after each of the JSC or JPT as applicable, are formed, the respective committees shall each hold an organizational meeting by videoconference or teleconference to establish their respective operating procedures, including establishment of agendas, and preparation and approvals of minutes. The Parties shall alternate responsibility for taking the meeting minutes; provided that Alpine shall be responsible for taking the meeting minutes at the first meeting of each committee or team. Meeting minutes shall be sent to both Parties promptly (and in any event within fourteen (14) days) after a meeting for review, comment and approval by each Party. Where minutes are not approved by both Parties, the dispute shall be resolved at the next committee or team meeting. A decision that is made at any meeting shall be recorded in meeting minutes.

3.3 **General.** Employees of each Party, other than its nominated committee or team representatives, may attend meetings of the JSC and JPT as nonvoting participants with fifteen (15) days' prior written notice to the JSC and JPT members, as applicable, of the other Party. Each Party shall be responsible for all of its own expenses of participating in the JSC or JPT. In addition each Party may nominate the same individuals as representatives on multiple committees.

4. Dissolution.

4.1 **Dissolution of JSC**. The JSC shall dissolve on termination of this Agreement or completion of all Research Programs, or as mutually agreed to by the Parties.

4.2 **Dissolution of JPT**. The JPT shall automatically dissolve on Completion of all Research Programs or, if earlier, termination of this Agreement or all Research Programs, or as mutually agreed by the Parties.

4.3 **Dissolution of Ad-hoc subcommittees**. Each Ad-hoc subcommittee will be deemed dissolved by the Parties on completion of the relevant activity in relation to which the subcommittee was set up, or as mutually agreed by the Parties.

Exhibit 5 – Press Release

Adaptimmune and Alpine Immune Sciences Announce Collaboration and License Agreement to Develop Next Generation SPEAR T-Cell Products

- Adaptimmune to license Alpine's Secreted and Transmembrane Immunomodulatory Protein technology for use with SPEAR T-cells to enhance antitumor responses -

May 14, 2019, Adaptimmune Therapeutics plc, Philadelphia, PA, and Oxfordshire, UK (Nasdaq:ADAP), a leader in T-cell therapy to treat cancer, and Alpine Immune Sciences, Inc., Seattle, WA, (NASDAQ:ALPN), a leading immunotherapy company focused on developing treatments for autoimmune diseases and cancer, today announced a collaboration and license agreement to develop next-generation SPEAR T-cell products which incorporate Alpine's secreted and transmembrane immunomodulatory protein (termed SIP™ and TIP™) technology. This collaboration will further enhance Adaptimmune's efforts to design and develop next-generation SPEAR T-cell therapies.

"SPEAR T-cell therapies have demonstrated clinical promise for the treatment of solid tumors. Based on knowledge emerging from translational research of resistance mechanisms, we will start our first next-gen clinical study with ADP-A2M4 CD8 in the second half of 2019," said Rafael Amado, Adaptimmune's President of R&D. "We are very excited to begin this collaboration with Alpine which complements our research on next generation SPEAR T-cells. We believe that Alpine's platform technology could engage further rapid and flexible immunomodulatory mechanisms, which would enable the development of future next-generation SPEAR T-cells with enhanced antitumor potential."

"Our directed evolution platform has successfully generated many unique, multi-functional protein domains designed to favorably modulate the tumor microenvironment via validated immune targets," said Stanford Peng, MD PhD, Alpine's President and Head of Research & Development. "We look forward to working with Adaptimmune to develop next-generation SPEAR T-cell therapies to achieve improved clinical outcomes."

Alpine and Adaptimmune will collaborate on a specified number of programs to develop SIP and TIP candidates with tailored affinities and modulatory activities that may enhance the anti-tumor responses seen with Adaptimmune's SPEAR T-cells.

For each program, Adaptimmune has an option to take a worldwide exclusive license for development and commercialization of SPEAR T-cell products incorporating the developed SIP or TIP candidate for the treatment of cancer.

Under the terms of the collaboration agreement, Adaptimmune will provide an upfront payment and research funding for ongoing programs. In addition, Alpine may be eligible for downstream development and commercialization milestones up to $288M, if all pre-specified milestones for each program are achieved.

Alpine will receive low-single digit royalties on worldwide net sales of the applicable products.

About Adaptimmune
Adaptimmune is a clinical-stage biopharmaceutical company focused on the development of novel cancer immunotherapy products for cancer patients. The Company's unique SPEAR (Specific Peptide Enhanced Affinity Receptor) T-cell platform enables the engineering of T-cells to target and destroy

cancer across multiple solid tumors. For more information, please visit http://www.adaptimmune.com.

About Alpine Immune Sciences, Inc.
Alpine Immune Sciences, Inc. is committed to leading a new wave of functional immune therapeutics. Alpine is employing directed evolution to create potentially powerful multifunctional immunotherapies to improve patients' lives. Alpine has two lead programs. The first, ALPN-101 for autoimmune/inflammatory diseases, is a dual ICOS/CD28 antagonist, engineered to reduce pathogenic immune responses. The second, ALPN-202 for cancer, is a dual PD-L1/CTLA-4 antagonist and PD-L1-dependent CD28 costimulator intended to combine checkpoint inhibition with T cell costimulation – an approach currently absent from approved checkpoint therapies. Alpine is backed by world-class research and development capabilities, a highly-productive scientific platform, and a proven management team. For more information, visit www.alpineimmunesciences.com.

Forward-Looking Statements Adaptimmune
This release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 (PSLRA). These forward-looking statements involve certain risks and uncertainties. Such risks and uncertainties could cause our actual results to differ materially from those indicated by such forward-looking statements, and include, without limitation: the success, cost and timing of our product development activities and clinical trials and our ability to successfully advance our TCR therapeutic candidates through the regulatory and commercialization processes. For a further description of the risks and uncertainties that could cause our actual results to differ materially from those expressed in these forward-looking statements, as well as risks relating to our business in general, we refer you to our Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on May 6, 2019, and our other SEC filings. The forward-looking statements contained in this press release speak only as of the date the statements were made and we do not undertake any obligation to update such forward-looking statements to reflect subsequent events or circumstances.

Forward-Looking Statements Alpine
This release contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, Section 21E of the Securities Exchange Act of 1934 and the Private Securities Litigation Reform Act of 1995. These forward-looking statements are not based on historical fact and include statements regarding our platform technology and potential therapies, the potential future development plans of our and our collaborators' product candidates and our and our collaborators' ability to successfully develop and achieve milestones in development programs. Forward-looking statements generally include statements that are predictive in nature and depend upon or refer to future events or conditions, and include words such as "may," "will," "should," "would," "expect," "plan," "intend," and other similar expressions among others. These forward-looking statements are based on current assumptions that involve risks, uncertainties and other factors that may cause actual results, events or developments to be materially different from those expressed or implied by such forward-looking statements. These risks and uncertainties, many of which are beyond our control, include, but are not limited to: clinical trials may not demonstrate safety and efficacy of any of our or our collaborators' product candidates; our ongoing discovery and pre-clinical efforts may not yield additional product candidates; our discovery-stage and pre-clinical programs may not advance into the clinic or result in approved products; any of our or our collaborators' product candidates may fail in development, may not receive required regulatory approvals, or may be delayed to a point where they are not commercially viable; we may not achieve additional milestones in our proprietary or partnered programs; the impact of competition; adverse conditions in the general domestic and global economic markets; as well as the other risks identified in our filings with the Securities and Exchange Commission. These forward-looking statements speak only as of the date hereof and we undertake

no obligation to update forward-looking statements, and readers are cautioned not to place undue reliance on such forward-looking statements.

“Transmembrane Immunomodulatory Protein”, “TIP”, “Secreted Immunomodulatory Protein”, “SIP”, “Variant Ig Domain”, “vIgD”, and the Alpine logo are registered trademarks or trademarks of Alpine Immune Sciences, Inc. in various jurisdictions.

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Exhibit 6 – Alpine Patents

THIS PAGE AND THE FOLLOWING 4 PAGES OF THIS EXHIBIT HAVE BEEN OMITTED BECAUSE THEY ARE BOTH (I) NOT MATERIAL AND (II) WOULD BE COMPETITIVELY HARMFUL IF PUBLICLY DISCLOSED

[***]

Exhibit 31.1

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 1, 2019

/s/ James Noble
James Noble
Chief Executive Officer

Exhibit 31.2

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, 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 1, 2019

/s/ Adrian Rawcliffe
Adrian Rawcliffe
Chief Financial Officer

Exhibit 32.1

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, 2019, 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 1, 2019

/s/ James Noble
James Noble
Chief Executive Officer

Exhibit 32.2

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, 2019, 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 1, 2019

/s/ Adrian Rawcliffe
Adrian Rawcliffe
Chief Financial Officer