Registered number: 13027460

Achilles Therapeutics plc

Annual Report and Financial Statements for the Period Ended 31 December 2021

INTRODUCTION AND CONTENTS

Achilles Therapeutics plc (the “Company", or the “Parent Company") is a public limited company incorporated under the laws of England and Wales and is listed on the Nasdaq Global Select Market (“Nasdaq”). This section therefore covers the requirements for being a quoted company under the UK Companies Act 2006, as follows:

The "Annual Report", as mentioned throughout these UK Financial Documents, is comprised of the reports listed above including the Annual Report on Form 20-F (the "Form 20-F") filed with the United States Securities and Exchange Commission (the “SEC”) on 1 March 2022.

On 1 December 2020, the Company changed its accounting reference date from 30 November 2021 to 31 December 2021, thereby extending the reporting period by one month. Due to this change in financial year during the period, this Annual Report covers the period from incorporation on 18 November 2020 and ending on 31 December 2021.

COMPANY INFORMATION

Directors
Edwin Moses, Chair of the Board of Directors
Iraj Ali
Carsten Boess
Derek DiRocco
Michael Giordano
Julie O'Neill

Company secretary
Daniel Hood
245 Hammersmith Road
London
W6 8PW

Independent auditors
KPMG LLP
2 Forbury Place
33 Forbury Road
Reading
RG1 3AD

Registered office
245 Hammersmith Road
London
W6 8PW

Registered number
13027460

UK STATUTORY STRATEGIC REPORT

All references in this Annual Report to "Achilles," the “Company”, the “Group", "we," "us" and "our" refer to Achilles Therapeutics plc and its subsidiaries. The directors of Achilles Therapeutics plc present their UK Statutory Strategic Report (the “Strategic Report”) on the Group and the audited financial statements for the financial period ended 31 December 2021.

Principal Activity

We are a clinical stage immuno-oncology biopharmaceutical company developing transformative precision T cell therapies to treat multiple types of solid tumours. We are focused on advancing cancer therapies through our pioneering work in the field of tumour evolution and our belief that clonal neoantigens represent the most specific class of cancer cell targets. Our platform enables us to identify mutations formed early in the development of a cancer that give rise to antigens that are expressed by all of a patient’s cancer cells but are absent from healthy tissue. We refer to this novel class of solid tumour targets as clonal neoantigens. To identify clonal neoantigens in a patient, we have developed a proprietary bioinformatic platform called PELEUS. This platform employs sophisticated statistical algorithms trained on the unique tumour genetic data derived from our exclusive license to data from the TRACERx study, which aims to analyse tumour samples from more than 840 non-small cell lung cancer, or NSCLC, patients. Once we have identified the clonal neoantigens, our proprietary manufacturing process, VELOS, uses the patient’s T cells and blood-derived dendritic cells to create a clonal neoantigen-reactive T cell, or cNeT, therapy that specifically targets multiple clonal neoantigens to eradicate the tumour or tumours. We are currently conducting two open-label Phase I/IIa trials to evaluate our cNeT product candidate, ATL001, in advanced NSCLC and metastatic or recurrent melanoma and expect to report additional, interim data from these trials in the second half of 2022. We are also using our Material Acquisition Platform, or MAP, network, which consists of a network of participating medical facilities, to collect tissue samples from other tumour types, such as head and neck squamous cell carcinoma, or HNSCC, renal cell carcinoma, or RCC, triple negative breast cancer, or TNBC, and bladder cancer, to develop our PELEUS platform to identify clonal neoantigens in these tumour types. Our investigational new drug application, or IND, for HNSCC was accepted by the FDA in January 2022 using VELOS Process 1 manufacturing and we expect to make additional submissions for our other earlier stage programs in the future.

Where the requirements of the Strategic Report in accordance with the Companies Act 2006 have been met in the Form 20-F, details of this have been provided in the table below and referenced to the Form 20-F accordingly. Additional requirements which are not met by the Form 20-F have been disclosed separately at the end of the Strategic Report. The Form 20-F is attached at the end of this report, and forms part of this report by cross reference.

Required item in the UK Statutory Strategic Report	**Where information can be found in the Form 20-F**
A fair review of the Group's business	Part I, Item 4B – Business Overview – p.83 Part I, Item 5 – Operating and Financial Review and Prospects – p.124
A description of the principal risks and uncertainties	Part I, Item 3D – Risk Factors – p.9 COVID-19 – Item 3D – p.63 Brexit – Item 3D – p.82

Analysis of the development and performance of the company's business during the financial period	Part I, Item 4B – Business Overview – p.83 Part I, Item 5A – Operating Results – p.125 Part I, Item 5B – Liquidity and Capital Resources – p.134
Main trends and factors likely to affect the future development, performance and position of the company's business	Part I, Item 4B – Business Overview – p.83 Part I, Item 5A – Operating Results – p.125 Part I, Item 5B – Liquidity and Capital Resources – p.134
Information about the company's employees	Part I, Item 6D - Employees – p.148
Description of the company's strategy	Part I, Item 4B – Business Overview – p.83
Description of the company's business model	Part I, Item 4B – Business Overview – p.83 Part I, Item 5 – Operating and Financial Review and Prospects – p.124
Explanation of amounts included in the company's annual accounts	Part I, Item 5A – Operating Results – p.125 Part I, Item 5B – Liquidity and Capital Resources – p.134

Other information required within the Strategic Report which is not included in the Form 20-F

Key Performance Indicators (KPIs)

The Directors and Management regularly review the Group's total liquidity position and gross monthly cash burn as part of the management of overall liquidity, financial flexibility and capital structure. Total liquidity is the total cash at bank and gross monthly cash burn rate is defined as cash-flows before financing income.

At 31 December 2021 the total liquidity position was $266.3M (Dec 2020: $177.8M) and the average monthly cash burn was $6.0M (Dec 2020: $2.8M).

Environmental Matters

The Group leases all of its facilities and currently manufactures its own products for our clinical trials. The Group also complies with all applicable environmental laws and regulations. We take positive steps to reduce our carbon footprint, where possible. For a full report on the carbon emissions for the Company please see the Carbon Emissions section in the Directors' Report.

Social, community and human rights issues

The Group endeavours to impact positively on the community in which it operates through various charity events. The Group does not, at present, have a specific policy on human rights. However, we have several policies that promote the principles of human rights. We will respect the human rights of all our employees, including:

- the provision of a safe, clean working environment;
- ensuring employees are free from discrimination and coercion;
- not using child or forced labour; and
- respecting the rights of privacy and protecting access and use of employee personal information.

We also have a Code of Business Conduct and Ethics and a Foreign Corrupt Practices Act, Bribery Act and Anti-Corruption Policy that all employees are required to read and confirm understanding of and which provides guidance on honest and ethical conduct and fair dealing with employees.

Diversity and Equality

Appointments within the Group are made on merit according to the balance of skills and experience offered by prospective candidates. While acknowledging the benefits of diversity, individual appointments are made irrespective of personal characteristics such as race, disability, gender, sexual orientation, religion, or age.

A breakdown of employment statistics as of 31 December 2021 is as follows:

Position	Male	Female	Total
Executive Directors	1	-	1
Leadership Team	17	13	30
Other Employees	82	139	221
Total Employees	100	152	252
Non-Executive Directors	4	1	5
Total Employees and Non-Executive Directors	104	153	257

Section 172(1) Companies Act 2006

The Directors are required by law to act in good faith to promote the success of the Company for the benefit of the shareholders as a whole and are also required per Section 172(1) of the Companies Act 2006 to have regard to the following:

The likely long-term consequences of any decision

The Group will need substantial additional funding to support continuing operations and pursue a growth strategy as outlined in our Business Overview in the Form 20-F (p.83). Until such time, if ever, as we can generate substantial product revenue, we expect to finance our operations through a combination of public or private equity offerings, debt financings, governmental funding, collaborations, strategic partnerships and alliances or marketing, distribution or licensing arrangements with third parties. If we are unable to raise capital when needed in sufficient amounts or on terms acceptable to us, we would be forced to delay, reduce or eliminate our discovery and research programs or any future commercialization efforts. There can be no assurances that our current operating plan will be achieved or that additional funding will be available on terms acceptable to us, or at all.

The interests of the Company's employees

The Board maintains constructive dialogue with employees through the Company's Executive Leadership. The interests of the Company’s employees are fostered through quarterly meetings with insight from the CEO, the Leadership Team and employees as presenters, including Q&A sessions. New starters are welcomed by our VP of People & HR to help build a strong sense of connection to our Mission and Purpose. Achilles is a diverse place to work with 46 different nationalities coming together to sustain and improve our culture. The Company takes advantage of a new people management system to communicate hobbies and interests and form affinity groups off the back of this. This system encourages a culture of employee led, peer-to-peer recognition, the opportunity to share work achievements and how teams have collaborated to deliver against our Mission.

In 2021 we launched our Employee Forum. This is made up of representatives across the company who come together to share input and feedback across a range of topics from health & safety, learning and development opportunities to key business updates. We have a Social Committee who organise events and activity under the sponsorship of the Senior Leadership Team including company

picnics and Achilles sports teams. At a more structural level, we have a robust process around health & safety with a formal Committee that meets regularly, including with Senior Leadership Team members, to review resources and activities to improve upon.

Appropriate remuneration and incentive schemes are maintained to align employees' objectives with those of the Group. More broadly, in 2021 we launched our first management development programme with a focus on helping managers be the most engaging managers they can be. 100% of responders were of the belief that the programme will help contribute to their future success.

Collaboration is at the heart of Achilles culture, supported by our open plan working environment. When combined with meeting spaces this provides a flexible infrastructure that encourages daily collaboration along with the capacity for team meetings and confidential discussions. Since the COVID-19 pandemic, our open plan working environment has been repurposed with safety screens, distanced workspaces and other appropriate measures to ensure a safe working environment for our employees. Navigating the COVID-19 pandemic has been challenging for many, and we have implemented an accredited Mental Health First Aid programme with named representatives at all sites to support their colleagues. We actively encourage employees to connect and engage with our science as well as each other, and provide a Research Seminar Series hosted by prominent external technical specialists to help foster this connection.

The need to foster the Company's business relationships with suppliers and others
Refer to Part I, Item 3D - Risk Factors – p.9 of the Form 20-F. The Group regularly reviews its business relationships with suppliers and other third parties taking into consideration the long-term objectives of the Group. The Group expanded its procurement function in 2021 to help foster its relationship with suppliers and other business partners, with a focus on ongoing management of supplier relationships and related risks. The Company maintains regular dialogue, and has agreements in place, with all key suppliers. Regular service reviews are performed to ensure satisfaction of requirements and compliance with obligations from the perspective of both the supplier and Achilles.

The impact of the Company's operations on the community and the environment
As of 31 December 2021 the Group had 243 employees in the UK and 9 employees in the US and operates offices and laboratories at multiple locations. During 2021 the majority of employees in both the UK and the US predominantly worked remotely from their home locations. In order to help us understand the impact of our direct business we measure the carbon footprint of the operational activities of Achilles over which we have direct control. In future periods we will be complying with ESOS Phase 3, the Energy Savings Opportunity Scheme, to further drive this understanding.

The Group is currently undertaking clinical trials focussing on advanced cancer therapies through its pioneering work in the field of tumour evolution and the belief that clonal neoantigens represent the most specific class of cancer cell targets. Achilles believes this will result in positive impact on the community.

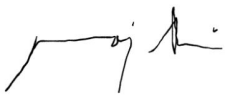
The desirability of the Company maintaining a reputation for high standards of business conduct
The Board of Directors of Achilles Therapeutics plc sets high standards for the Company's employees, officers and directors. Implicit in this philosophy is the importance of sound corporate governance. The Group operates a Code of Business Conduct and Ethics which provides mechanisms for reporting suspected violations of the Code and other policies and procedures of the Company. Employees are required to read and acknowledge this code and other policies such as our Insider Trading Policy and to follow them at all times.

The need to act fairly as between shareholders of the Company

The Board endeavours to maintain good relationships with its shareholders and treat them equally. The Board values good relations with the Company's shareholders and understands the importance of effectively communicating the Company's operational and financial performance as well as its future strategy. The Company's website provides financial information as well as historical news releases and information relating to corporate governance.

Annual and quarterly results are communicated via press releases and are filed with the U.S. Securities and Exchange Commission on a Form 20-F and Form 6-K respectively. Operational and regulatory press releases are also issued from time to time as appropriate, and corporate presentations are publicly available on the Company's website. Shareholders may also attend the Annual General Meeting where they can discuss matters with the Board.

This report was approved by the Board on 21 March 2022 and signed on its behalf.



Iraj Ali
Chief Executive Officer
21 March 2022

UK STATUTORY DIRECTORS' REPORT

The Company was incorporated on 18 November 2020 and changed its name from Achilles TX Limited to Achilles Therapeutics plc on 10 February 2021. On 1 December 2020, the Company changed its accounting reference date from 30 November 2021 to 31 December 2021, thereby extending the reporting period by one month. On 11 December 2020 the Company entered into a share for share agreement with the shareholders of Achilles Therapeutics UK Limited, pursuant to which it became the ultimate parent company of the Achilles Group. The directors present their UK Statutory Directors' Report (the "Directors' Report") on the Group for the financial period ended 31 December 2021.

Where the requirements of the Directors' Report in accordance with the Companies Act 2006 have been met in the Form 20-F, details of this have been provided in the table below and reference made to the Form 20-F accordingly. Additional requirements which are not met by the Form 20-F have been disclosed separately at the end of the Directors' Report. The Form 20-F is attached at the end of this report, and forms part of this report by cross reference.

Required item in the UK Statutory Directors' Report	**Where information can be found in the Annual Report on Form 20-F, if applicable.**
The financial risk management objectives and policies of the entity, including the policy for hedging each major type of forecasted transaction for which hedge accounting is used	Part I, Item 3D – Risk Factors – "Risks Related to our Future Cash Needs" – p.12
Credit risk	Part I, Item 8A – Consolidated Statements and Other Financial Information - Note 2 – "Concentrations of credit risk and off-balance sheet risk" – p.183
Liquidity risk	Part I, Item 5B – Liquidity and Capital Resources – p.134
Exchange rate and cash flow risk	Part I, Item 11 – Quantitative and Qualitative Disclosures About Market Risk – p.168
An indication of the Group's activities in the field of research and development	Part I, Item 4B – Business Overview – p.83 Part I, Item 5A – Operating Results – p.125 Part I, Item 5B – Liquidity and Capital Resources – p.134
Branches outside the UK	Refer to Note 4 of the Notes to the Financial Statements
Structure of the Group's capital	Refer to Note 7 of the Notes to the Financial Statements

Other information required within the Directors' Report which is not included in Form 20-F

Directors

The directors who held office during the period were as follows:

Iraj Ali (appointed 18 November 2020)
Carsten Boess (appointed 11 December 2020)
Derek DiRocco (appointed 11 December 2020)
Michael Giordano (appointed 11 December 2020)
Edwin Moses (appointed 11 December 2020)
Martin Murphy (appointed 11 December 2020, resigned 30 March 2021)
Julie O'Neill (appointed 1 May 2021)
Karl Peggs (appointed 11 December 2020, resigned 22 December 2020)
Rogier Rooswinkel (appointed 11 December 2020, resigned 28 June 2021)

Statement on dividends

The Directors do not recommend the payment of a dividend for the period ended 31 December 2021.

Directors' indemnities

The Group has made qualifying third-party indemnity provisions for the benefit of its directors which were made during the period through the directors' and officers' insurance, and which remain in force as at the date of approving the UK Statutory Directors' Report.

Political contributions

The Group has not made any political donations or incurred any political expenditure during the period.

Employee engagement

The Group is not required to report on employee engagement in the Directors' Report because there were fewer than 250 UK employees in the Group for the period ended 31 December 2021. However, the Group is committed to the continued development of employee engagement by an effective communications and consultative framework.

Business relationships

The Directors have had regard to the Company's need to foster business relationships with suppliers, customers and others. Further information is provided in the Section 172 statement set out in our Strategic Report.

Carbon Emissions

Following completion of our listing in April 2021, Achilles Therapeutics plc is required to measure and report its greenhouse gas (GHG) emissions in accordance with the provisions of the Companies Act 2006 (Strategic Report and Directors' Report) Regulations 2013.

As we were not a listed company prior to April 2021, GHG emissions have only been measured and reported since 2021, which is our baseline year for GHG reporting.

Scope	kWh	tCO2e	Total % Emissions
Estimated Scope 1 Emissions	453,379	86	30
Estimated Scope 2 Emissions	828,649	176	63
Estimated Scope 3 Emissions	13,520	19	7
Total estimated greenhouse gas emissions	1,295,548	281	100

Intensity ratio: total greenhouse gas emissions per employee on the basis of an average number of 212 employees during the year ended 31 December 2021	**1.33**

Scope 1 emissions are direct emissions produced by the burning of fuels. Scope 2 emissions are indirect emissions related to the generation of the electricity consumed and purchased by Achilles. For Achilles, Scope 3 emissions primary relate to business travel and emissions relating to the transmission and distribution of electric power.

We have used evidence and estimated derivatives derived from evidence provided by our energy supply partners and lessors to generate our disclosure of emissions for the year. These include the purchase of electricity, heat, steam or cooling directly from our energy supply partners, or through utility bills from our lessors. Standard UK Government Conversion Factors for GHG reporting were applied to estimate emissions. The Group considers that the intensity ratio of tonnes of carbon dioxide per employee is a suitable metric for its operations.

The Group introduced a Hybrid Working approach in 2021, with employees working onsite and also in their homes, which is expected to have driven a reduction in GHG emissions during the period.

Going concern

The Directors have considered the going concern status of the Group and Parent Company. Further detail on this can be found at Note 2.3 in the Notes to the Financial Statements. As of the date of this report, our Directors have a reasonable expectation that we have adequate resources to continue in business for at least 12 months from the issuance of these accounts. Accordingly, the financial statements have been prepared on the going concern basis.

Independent auditor

KPMG LLP have expressed their willingness to continue in office as Group auditors for another year. In accordance with Section 489 of the Companies Act 2006, a resolution for the re-appointment of KPMG LLP as auditor of the Company and Group is to be proposed at the forthcoming Annual General Meeting.

Future developments

Please refer to the Principal Activities section of the Strategic Report.

Events after the reporting period

On 25 February 2022 the Company paid $1.2M in exchange for one newly issued Ordinary Share of nominal value £1.00 in Achilles Therapeutics Holdings Limited, which in turn paid $1.2M for one hundred thousand newly issued Ordinary Shares of $0.00001 each in Achilles Therapeutics US, Inc..

The Directors have considered events that occurred after the reporting period and before the signing of the Annual Report and financial statements. Refer to Note 16 – Subsequent Events in the Form 20-F for further information. There were no further events between the signing of the Form 20-F and the

Annual Report and financial statements, other than those disclosed above, deemed material for further disclosure.

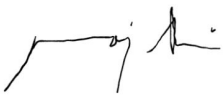
Disclosure of information to the auditor

All Directors in office at the time the report is approved confirm the following:

(i) So far as each Director is aware, there is no relevant audit information of which the Group's auditors are unaware; and

(ii) Each Director has taken all the steps that he or she ought to have taken in his or her duty as a Director in order to make himself or herself aware of any relevant audit information and to establish that the Group's auditors are aware of that information.

This report was approved by the Board on 21 March 2022 and signed on its behalf.



Iraj Ali
Chief Executive Officer
245 Hammersmith Road
London
W6 8PW

21 March 2022

ACHILLES THERAPEUTICS PLC DIRECTORS' REMUNERATION REPORT FOR THE YEAR ENDED 31 DECEMBER 2021

ANNUAL STATEMENT FROM THE CHAIR OF THE REMUNERATION COMMITTEE

Dear Shareholders,

On behalf of the Remuneration Committee (the "Committee") of Achilles Therapeutics plc (the "Company"), I am pleased to present our Directors' Remuneration Report (the "Remuneration Report") for the year ended 31 December 2021, which is the Company's first such report following its initial public offering ("IPO") in April 2021.

This Remuneration Report will, along with the Annual Report and Financial Statements, be subject to an advisory vote at the forthcoming Annual General Meeting (AGM) on 28 June 2022, with the Directors' Remuneration Policy (the "Policy") subject to a binding vote at the same meeting.

Introduction

It has been a year of continued growth and development for the Company as we have advanced our ongoing clinical trials in lung cancer and melanoma (CHIRON and THETIS respectively) and successfully developed a new, improved manufacturing process (VELOS Process 2). We also completed an IPO on Nasdaq that strengthened our balance sheet. We have increased from 159 to 252 people during the year, including growing our US operations. The majority of our staff are situated at our new 24,633 sq.ft. head office and laboratories in Hammersmith, West London, U.K., with facilities in Stevenage and the Royal Free Hospital, also both in the U.K. and a lease signed for our first site in the U.S. which will be in Philadelphia. Our commitment to manufacturing has been underlined by continued progress in developing capacity at the Catapult site in Stevenage and the commencement of design work for our own 64,181 sq.ft. site at Hayes in Middlesex, U.K..

All this very significant progress has been made while adapting to the significant challenges posed by COVID-19.

2022 will be another important year for the Company. The role of the Committee is to ensure that the Executive Directors (currently only the CEO) and senior executives at the Company are incentivised to deliver long term and sustainable growth for shareholders. The Committee aims to do this through the practical application of the Policy. The Committee also reviews and considers Non-Executive Directors as part of this policy and following a review with the Committee's compensation consultant considers that the current approach provides an appropriate level of remuneration for their services.

The Global Marketplace for Talent

Our achievements are made possible through the highly skilled and committed, international and diverse teams of people we have across our organisation. The global talent marketplace is highly competitive. The Company plans to continue to grow primarily in Europe and the U.S. over the next few years. When considering remuneration, the Committee pays close attention to the local practices where the job is based, while at the same time being cognisant of international trends and market developments.

Corporate Governance Standards

Since our listing on Nasdaq, we are subject to corporate governance standards and accompanying regulations in both the U.S. and the U.K.. We are a foreign private issuer as defined by the SEC. As such and in accordance with the Nasdaq listing requirements, we may rely on home country governance (including the Companies Act 2006) and apply certain exemptions rather than complying with Nasdaq corporate governance rules.

In considering any actions, the Committee considers the general U.K. compensation frameworks, including guidance from investor bodies and taking into consideration the principles of the U.K. Corporate Governance Code. It has worked with its compensation consultant to incorporate the relevant practices where it believes they best serve the long-term interests of shareholders.

Key decisions and activities in the year ended 31 December 2021

In the year ended 31 December 2021, the Committee has undertaken a range of activities to establish remuneration programmes and practices to position the Company as a global bio-technology company. These have included:

- Engaging an appropriately qualified expert as a compensation consultant, to support the Committee as it prepared and reviewed the Policy;
- Considering the objectives of the Annual Bonus Plan and their linkage to the Corporate Deliverables for the financial year ended 31 December 2020 for the Executive Director and the Senior Leadership Team;
- Adopting two new equity incentive plans, the 2021 Omnibus Incentive Plan and the 2021 Employee Share Purchase Plan, together with the local tax approved sub-plans that sit underneath these;
- Awarding share options under these new plans to the Executive Director, Senior Leadership Team and more widely across the Company;
- Reviewing the Company's Evergreen process in relation to the share reserve;
- Reviewing the employment contract for the CEO as sole Executive Director in the context of the Company's IPO; and
- Reviewing the reports on benchmarking and market practice prepared by our compensation consultant, and the Policy they informed, to set the pay levels for the Executive Director and Senior Leadership Team.

2021 has been a year of significant milestones for the Company. I trust that you will find the information in this report useful. There will be an opportunity to address any questions you may have at the Company's AGM and I look forward to this.

Yours faithfully,

Dr Edwin Moses
Chairman of the Remuneration Committee
21 March 2022

REMUNERATION POLICY

The information provided in this part of the Directors' Remuneration report is not subject to audit.

This part of the Remuneration Report sets out the remuneration policy for the Company's Directors and has been prepared in accordance with the Large and Medium-sized Companies and Groups (Accounts and Reports) (Amendment) Regulations 2013.

The current Directors' Remuneration Policy (the "**Policy**") will be put forward for approval by shareholders in a binding vote at the AGM on 28 June 2022. If approved, it will take effect from the date of approval and apply for a period of three years until 2025, or until a revised policy is approved by shareholders.

Key considerations when determining the Policy

The Policy was designed by the Committee with a number of specific objectives in mind. The Policy should serve to:

- attract and retain high calibre non-Executive and Executive Directors (the CEO is currently the sole Executive Director), and motivate them to focus on the delivery of the Company's strategic and business objectives;
- encourage a corporate culture that promotes the highest level of integrity, teamwork and ethical standards and rewards behaviours that are focussed on long term value creation for all stakeholders;
- be competitive against appropriate market benchmarks;
- have a strong link to performance;
- be simple and understandable, both internally and externally;
- encourage equity ownership to align Directors with the overall interests of shareholders; and
- adopt high levels of good governance and ensure that the Policy mitigates against potential reputational or behavioural risks and is affordable without overpaying for talent.

In seeking to achieve the above objectives, the Committee is mindful of the views of a broad range of stakeholders in the business and accordingly takes account of a number of factors when setting remuneration including: market conditions; pay and benefits in relevant comparator organisations; terms and conditions of employment across the Company; the Company's risk appetite; the expectations of institutional shareholders; and any specific feedback received from shareholders and other stakeholders. The Committee determined that, associated with the Company's IPO during 2021, it was appropriate to carry out a benchmarking exercise relating to the salary, bonus and option levels of Senior Management and make the necessary adjustments to ensure these remained competitive with relevant comparators.

The Policy for Executive Directors

Currently the Company has only one Executive Director, the CEO, but the Policy will apply equally to any additional Executive Directors who may be appointed in the future. The Committee annually reviews the remuneration packages to ensure they are operating effectively and in line with market practice and ensures that they do not inadvertently result in any economic, social or governance bad practice.

The total remuneration for Executive Directors is made up of the following elements:

- salary;
- benefits;
- annual bonus;
- long-term incentive awards; and
- pension.

Base Salary

Element, purpose and link to strategy	Provides market competitive fixed remuneration that reflects the responsibilities of the role undertaken, the experience of the individual and performance in the role over time. Set at a level to attract and retain employees of a sufficient calibre who can operate on a global level and in the key markets in which we operate (namely U.K., EU and the U.S.). Base salary is designed to provide an appropriate level of fixed income to avoid any over-reliance on variable pay elements that could encourage excessive risk taking.
How it operates	Salaries are normally reviewed annually, with any increases taking effect from 1 January each year. The Committee will take a number of factors into consideration when awarding any increase, including: • scope of the role and the individual's responsibilities; • the skills and experience, performance and capability of the individual; • the pay and employment conditions (including the underlying rate of inflation) in the wider workforce; • changes in the size and complexity of the Company; and • benchmark data from peer companies listed on Nasdaq and European stock exchanges.
Maximum opportunity	There is no prescribed maximum annual salary or salary increase. The Committee is informed and guided by the general increase for the broader employee population but may award a lower increase or exceed this general increase. Examples of where this award may exceed the general increase could be: an increase in the scale, scope or responsibility of the Company or the role, where benchmark data shows a market adjustment is required in order to offer a competitive base salary; where there is a need to retain key talent; or when the individual in a role has gained new experiences previously not recognised in their current base salary.
Performance-related framework	Executive Director's performance is a factor that is considered when determining any base salary increases.

Benefits

Element, purpose and link to strategy	Reasonable benefits in kind are provided to support Executive Directors in carrying out their duties and assisting with retention and recruitment.
How it operates	The Company aims to offer benefits that are in line with market practice and what is offered to the wider workforce. For Executive Directors this includes private medical insurance and life insurance. Other employment benefits may be provided from time to time and other benefits that are provided to the general workforce will be offered on broadly similar terms to Executive Directors. The Committee retains discretion to offer the following additional benefits (all with or without tax gross up): temporary living and transportation expenses, relocation assistance (in line with local norms and legislation), medical support and tax advice, including tax equalisation to allow flexibility in employing a foreign national. Any reasonable business-related expenses (including tax there-on) can be reimbursed on a gross of tax basis.
Maximum opportunity	There is no formal maximum level of benefits provided to an Executive Director as the value of each benefit is not predetermined and is typically based upon the cost to the Company of providing said benefit which will vary from year to year based on the cost from third-party providers.
Performance-related framework	None.

Pensions

Element, purpose and link to strategy	To provide a competitive and tax-efficient pension savings plan which complies with at least the minimum contribution requirements of the applicable jurisdiction.
How it operates	Executive Directors are eligible to receive employer contributions to the Company's Group Personal Pension Scheme or to a 401k plan, or a salary supplement in lieu of pension benefits, or a combination of pension contributions and salary supplement.
Maximum opportunity	The maximum contribution, cash supplement, or combination thereof payable by the Company is 10% of salary.
Performance-related framework	None.

Annual bonus

Element, purpose and link to strategy	To incentivise and reward delivery of the Company's strategy and corporate objectives on an annual basis.
How it operates	Annual bonus performance targets are set at the start of the year by the Board and performance against objectives is assessed by the Remuneration Committee after the end of the relevant financial year. Bonuses are paid in cash after the award has been approved by the

	Committee. The target bonus level for the Chief Executive Officer is 50% of base salary.
Performance-related framework	Performance measures are determined by the Committee each year and may vary to ensure that the Company's long term business strategy and shareholder value are promoted. The annual bonus will be based on strategic goals linked to the overall Company Deliverables which may include financial, strategic and personal objectives. The performance measures for the annual bonus are reviewed each year and the Committee has the discretion to vary the mix of measures or introduce new measures based on the strategy of the Company at that time. The payment of any bonus is at the discretion of the Committee who may alter the bonus outcome if it considers that the level of pay-out is inconsistent with the overall Company or individual performance.

Long Term Incentive Plan (LTIP)

Element, purpose and link to strategy	The Achilles Therapeutics 2021 Omnibus Incentive Plan (the "LTIP") is designed to incentivise the successful execution of business strategy over the longer term, to align the interests of Executive Directors and employees with long-term shareholder interests and to attract, incentivise and retain staff.
How it operates	Awards will typically be granted annually and the LTIP provides for the grant of market value options, premium and nil priced options, share appreciation rights, restricted stock units, dividend equivalents, performance awards (subject to performance conditions) and other share based awards. The Committee maintains discretion over the types and terms of equity awards and will select the most appropriate form of award each year which may be delivered via tax approved schemes in the territories in which we operate. The option awards typically vest over a period of up to four years with 25% vesting and becoming exercisable upon the first anniversary of the vesting commencement and the remaining 75% vesting and becoming exercisable in equal quarterly amounts thereafter.
Maximum opportunity	There is no maximum opportunity under the LTIP. However, the Committee will work with its compensation consultant to review the market in order to assess the position relative to appropriate comparator companies. The Committee seeks to develop equity based compensation that is competitive to a set of comparable companies with whom we may compete for executive talent.
Performance-related framework	The Committee will select the most appropriate form of LTIP for awards each year and/or each individual grant.

All employee share plans – Employee Share Purchase Plan (ESPP) (also applicable to Executive Directors)

Element, purpose and link to strategy	The Achilles Therapeutics plc 2021 Employee Share Purchase Plan (the "ESPP") is designed to encourage employee share ownership and increase alignment with shareholders in a tax efficient manner.
How it operates	The Company may, from time to time, operate tax approved share plans as sub plans of this ESPP. In the UK these would include HM Revenue and Customs approved Share Incentive Plan (SIP) and Save as You Earn (SAYE) plans. The ESPP is an Internal Revenue Services (IRS) approved plan. Executive Directors would be eligible to join these plans in line with any offer to the general population.
Maximum opportunity	The plans are subject to the prevailing limits set by the relevant local tax authority. For the ESPP, employees may contribute up to 15% of their base compensation to purchase shares up to a maximum of $25,000 worth of ordinary shares valued at the start of each purchase period under the ESPP for each calendar year in the purchase period. For the SIP employees can receive a maximum of £3,600 free shares and up to £1,800 of matching shares per tax year under HMRC guidance.
Performance-related framework	Not applicable.

The Policy for the Chairman

The Board approves fees payable to the Chairman.

The Chairman does not participate in discussions in respect of their own fees.

The Policy for Non-Executive Directors

The Chairman reviews fees annually with the CEO, seeking input and market information from the Company compensation consultant as required.

Chairman and Non-Executive Director fee

Element, purpose and link to strategy	To attract high calibre Non-Executive Directors who bring a wide range of experience and skills and who through the application of their independent judgement on a variety of business matters such as strategy, finance, management, performance and resource allocation will help advance the Company and further the interests of shareholders.
How it operates	Non-Executive Directors receive an annual fee comprising a base fee plus additional fees for extra responsibilities such as membership of a sub-committee or for Chairing said sub-committee, or for holding the role of the Chairman of the Board. Current fee levels are set out in the Non-Executive Director cash fees section of the Remuneration Report. Fees are reviewed on a periodic basis against those in comparable companies where the Company may recruit for talent. This review is in order to ensure the fees remain

	competitive and adequately reflect the time commitments and scope of the role and the overall total package to any Non-Executive Director, including Long Term Incentives separately described. Non-Executive Directors do not ordinarily participate in any pension or variable bonus plan. Travel, accommodation and other business-related expenses necessarily incurred in carrying out the role will be paid or re-imbursed by the Company including, if relevant, any gross up for tax.
Maximum opportunity	There is no prescribed maximum annual fee or fee increase. The general increase for the broader employee population and market information from compensation consultants is considered. Actual fee levels are disclosed in the Annual Remuneration Report for the relevant financial year.
Performance-related framework	None.

Chairman and Non-Executive Director Equity Incentives

Element, purpose and link to strategy	To facilitate share ownership by Non-Executive Directors in the Company in order to further align their interests with those of shareholders.
How it operates	The LTIP provides for the grant of market value options, premium and nil priced options, share appreciation rights, restricted stock unit awards, dividend equivalents, performance awards (subject to performance conditions) and other share based awards. No performance awards (subject to performance conditions) are intended to be issued to Non-Executive Directors. Non-Executive Directors usually receive share based awards annually as part of their remuneration which are subject to a vesting schedule. Under normal circumstances the annual awards will usually vest upon the first anniversary of the date of grant or the next AGM, whichever is sooner.
Maximum opportunity	There is no maximum number of equity incentive awards that may be awarded to individuals each year. However, when reviewing award levels, account is taken of market movements in equity incentive awards, Board committee responsibilities, ongoing time commitments and the general environment.
Performance-related framework	Not applicable.

Notes to the Policy Table
Legacy arrangements

For the duration of this Policy, the Company will honour any commitments made in respect of current or former Directors before the date on which either: a) the Policy becomes effective; or b) an individual becomes a Director, even where not consistent with the Policy set out in this report or prevailing at the time such commitment is fulfilled. For the avoidance of doubt, all outstanding historic equity related awards that were granted in connection with, or prior to, listing remain eligible to vest based on their original terms.

Performance conditions

The choice of annual bonus performance metrics reflects the Committee's belief that any incentive remuneration should be tied to the delivery of strategic objectives across the full spectrum of accountabilities for any Executive Director. The Committee has retained flexibility on the specific measures which will be used to ensure that any measures are fully aligned with the strategic imperatives at the time they are set. The Committee will review the calibration of targets annually to ensure they remain sufficiently challenging taking into account the Company's strategic objectives and the interests of shareholders.

The targets for the bonus scheme for the coming year will be set out in general terms and subject to limitations due to commercial sensitivity. The full details will be disclosed when they are in the public domain and are no longer considered commercially sensitive.

Malus provisions

Malus and clawback provisions will apply in respect of the operation of the annual bonus plan for the 2021 performance year onwards and for any equity allocation post January 2022.

The circumstances when the Company may apply malus provisions include the discovery of a material misstatement of financial results, a miscalculation or error in assessing the performance conditions applying to the award, or in the event of serious misconduct committed by an Executive Director.

Director shareholding requirements

The Company does not have a formal policy on Executive or Non-Executive Director shareholding.

Remuneration Committee discretions

The Committee operates under the powers it has been delegated by the Board. In addition, it complies with rules that are either subject to shareholder approval or by approval from the Board. These rules provide the Committee with certain discretion which serves to ensure that the implementation of the Policy is fair, both to individual Executive Directors and to the shareholders. To maintain an efficient administrative process, the Committee retains the following discretion relating to remuneration:

- the eligibility to participate in the plans;
- the size of awards and payments;
- the timing of grant awards and/or payments;
- determining the choice (and adjustment) of performance measures and targets for each incentive plan in accordance with the policy set out above and the rules of each plan;
- discretion to override formulaic outcomes of incentive schemes upwards as well as downwards;
- determining whether the 'malus or clawback' shall be applied to any award in the relevant circumstances and, if so, the extent to which they should be applied; and
- the annual review of performance objectives for the annual bonus plan.

In certain exceptional circumstances, such as a material acquisition/divestment of a Group business or a change in the broader business environment, which mean the original performance conditions are no longer appropriate, the Committee may adjust the objectives, alter weightings, or set different

measures as necessary, to ensure the conditions achieve their original purpose and are not materially less difficult to satisfy.

Shareholder views

The Board is committed to dialogue with shareholders and intends to engage directly with them and their representative bodies when considering any significant change to our remuneration arrangements. The Committee will consider shareholder feedback received following the AGM as well as any additional feedback and guidance received from time to time and use this to inform future practices going forward. Assisted by its compensation consultant, the Committee actively monitors developments in the expectations of institutional investors and their representative bodies.

Employment conditions

The Committee is kept abreast of conditions and market movements regularly throughout the year in relation to Company employees. Although the Committee does not formally consult with employees directly, it will consider pay conditions throughout the Group when making decisions on Executive Directors' remuneration. The same broad principles apply to the Policy both for Executive Directors and the wider employee population with a greater emphasis on variable pay for Executive Directors.

Differences in remuneration policy between Executive Directors and other employees

The overall approach to reward for employees across the workforce is a key reference point when considering and setting the remuneration of Executive Directors. When under review, the Committee pays close attention to pay and employment conditions across the wider workforce.

The key difference between the remuneration of Executive Directors and that of our other employees is that at senior levels, remuneration is increasingly long term and 'at risk' with an emphasis on performance-related pay linked to business performance and share based remuneration. This ensures that remuneration at senior levels will increase or decrease in line with business performance and provides clear alignment between the interests of Executive Directors and shareholders.

The Policy for Executive Directors is designed to support the business needs of the Company. It promotes long term success and encourages the attraction, retention and incentivisation of Executive Directors who are of a high calibre. The Committee is satisfied that the Policy supports the Company's strategy, drives shareholder value and is appropriate in the balance of fixed and variable remuneration. As a high proportion of an Executive Director's reward is delivered through equity-based instruments, the alignment with the interests of shareholders is strong.

Remuneration on recruitment

The remuneration package for any new Executive Director will be determined by the Committee in accordance with the terms of the Policy at the time of appointment (including salary, benefits, annual bonus, long-term incentive awards and pension). It is recognised that in order to attract and recruit talented individuals the Policy needs to allow sufficient flexibility with respect to remuneration on recruitment. The following policies apply to the remuneration on recruitment of new Executive Directors:

***Salary*:** Base salary will be determined based on the responsibilities of the role, experience of the individual and current market rates. It may be considered necessary to appoint a new Executive Director below market rates (e.g. to reflect limited Board experience). In such circumstances, phased increases above those of the wider workforce may be required over an appropriate time period, to bring the salary to the desired market level, subject to the continued development in the role.

***Annual bonus*:** The ongoing annual bonus will be in line with that outlined in the policy table for existing Executive Directors, pro-rated to reflect the period of service. Depending on the timing or nature of an appointment it may be necessary to set different initial performance measures and targets for the first year of appointment.

***Long-term incentive awards*:** Awards are granted in line with the policy outlined for existing Executive Directors. An award may be made shortly following an appointment. For internal appointments, existing awards will continue on their original terms.

All Employee Share Plans: New Executive Directors will be eligible for the relevant all employee share plan operating in the territory where they are appointed.

***Benefits**:* Benefits provided should be in line with those of existing Executive Directors. For external and internal appointments, where required to meet business needs, reasonable relocation support will be provided. In addition, if it becomes necessary to appoint a new Executive Director from outside the UK, additional benefits may be provided to reflect local market norms or legislation.

Pension: A company contribution or cash supplement up to the maximum as outlined for existing Executive Directors.

Sign-on payments and buy-out awards: To enable the recruitment of high calibre talent, the Committee may offer additional cash and/or share-based remuneration to take account of or compensate for remuneration that the Executive Director is required to relinquish when leaving a former employer. The Committee will seek to structure any such replacement awards in line with market practice and aim to be no more generous overall in terms of quantum or vesting than the award to be forfeited from the previous employer, taking into account the timing, form and performance requirements of the awards forgone. Where appropriate, any long-term incentive awards will be granted under the LTIP, however, the Committee will have the discretion to make awards under any relevant exemptions in the SEC Rules.

For an internal Executive Director appointment, any variable pay element awarded in respect of the prior role will be allowed to pay out according to its terms. In addition, any other contractual remuneration obligations existing prior to appointment may continue.

The fees for any new Chairman and non-Executive Director appointments will be set in accordance with the prevailing policy and at a level that is consistent with those of the existing Chairman and non-Executive Directors.

Directors Service Contracts

The Directors' service contracts and letters of appointment are kept for inspection at the Company's registered office.

All Directors are subject to re-election annually at the AGM.

Policy for payments on loss of office

The Company’s policy on remuneration for Executive Directors who leave the Company is documented in their service contract. The sole current Executive Director, the CEO, is employed under a contract with a notice period of six months from either the Executive or the Company.

The Committee will exercise its discretion when determining amounts to be paid to leavers taking into account the facts and circumstances of each case, the individual circumstances including reason for termination, individual performance, contractual obligations, potential claims the Executive Director might have against the Company and the terms of any equity plans in which the Executive Director may participate.

Details of the elements under consideration are laid out below:

Termination by notice from the Company: up to six months' notice, or if the Service Contract differs, what is documented as the contractual obligation under the Service Contract. The Committee has the discretion to make a payment in lieu of notice for base salary, pension and other benefits that would otherwise have been paid during the notice period.

Annual bonus: there is no automatic contractual entitlement to bonus or pro-rata bonus on termination, although this may be considered at the discretion of the Committee.

Long-term incentives: whether any long-term incentive awards would vest and be exercisable upon loss of office would be subject to the relevant plan rules under which such award was granted. The Committee retains discretion to determine the extent to which the award will vest, taking into consideration the circumstances. Unvested awards normally lapse, although the Committee retains the power to determine, in accordance with the "good leaver" provisions of the relevant plan rules, what proportion of unvested awards will be retained and what proportion will lapse. In determining this, the Committee will give consideration to the reason for leaving, the extent of achievement of performance objectives at the date of leaving and may decide to pro-rate awards.

All Employee Share Plans: will be treated in line with the plan rules in force at the time with the Executive Director to be treated no differently than any other employee.

Change of Control: on a change of control, all unvested pre-IPO awards vest in line with the Vesting Agreement entered into at IPO. For any post-IPO award, unless the parties to the relevant sale event provide for the assumption, continuation or substitution of awards, accelerated vesting will occur and awards become fully vested and/or exercisable.

Additional payments: The Committee reserves the right to make payments it considers reasonable under a settlement agreement, including payments or reimbursement of reasonable legal and professional fees, untaken holiday and any payment for the settlement of claims against the Company in the UK or other jurisdictions. Outplacement or career transition fees may also be provided.

ANNUAL REPORT ON REMUNERATION

The information provided in this part of the Directors' Remuneration report is subject to audit where indicated.

This part of the report has been prepared in accordance with Part 3 of The Large and Medium-sized Companies and Groups (Accounts and Reports) (Amendment) Regulations 2013. Since the Company is not FTSE-listed, it is under no obligation to comply with the UK Corporate Governance Code, but best practice and good governance have been considered when preparing this report. The Annual Report on Remuneration and the Annual Statement by the Chair will be put to a single advisory shareholder vote at the AGM on 28 June 2022.

Composition of the Board

The dates of appointment of each of the Non-Executive Directors serving at 31 December 2021 are summarised in the table below. Dates prior to our incorporation in November 2020 as Achilles Therapeutics TX Limited (now known as Achilles Therapeutics plc) are for Non-Executive Directors who served on the Board of our predecessor company, Achilles Therapeutics Limited (now known as Achilles Therapeutics UK Limited).

Non-Executive Directors	Date of contract or date of appointment (to predecessor company if before incorporation)
Carsten Boess	01/04/2020
Derek DiRocco	02/09/2019
Michael Giordano	01/09/2018
Edwin Moses	01/12/2018
Julie O'Neill	01/05/2021

Remuneration Committee

The current members of the Committee are Carsten Boess, Michael Giordano and Edwin Moses. All members have continued to serve until the date of this Annual Report on Remuneration.

Members of management are invited to attend meetings where appropriate as are compensation consultants. The VP People & HR is the secretary to the Committee. Attendees are not involved in any decisions and are not present for any discussions regarding their own remuneration.

No conflicts of interest have arisen during the period and none of the members of the Committee has any personal financial interest in the matters discussed, other than as shareholders. The fees of the Non-Executive Directors are reviewed by the Chairman annually with the CEO, seeking input and market information from the Company compensation consultant as required. The meetings attendance of Directors since IPO is disclosed below.

Meetings attendance (since Listing)	Attendance
Carsten Boess	4 of 4
Michael Giordano	4 of 4
Edwin Moses	4 of 4

Independent advisors

The Committee received advice from the executive compensation practice at PricewaterhouseCoopers ("PwC"). Since the IPO PwC has assisted with peer-group benchmarking of Director and Senior Management remuneration, the drafting of policies for Executive and Non-Executive Directors and wider remuneration practice advice. The Committee is satisfied that PwC provide independent and objective advice, as PwC is a leading global professional services firm and the Committee confirm no conflicts of interest before each meeting. During the period since listing, fees charged by PwC for advice provided to the Committee for 2021 amounted to $104,000 (excluding VAT).

Activity in the period

Activity for the period has been disclosed in the Annual Statement from the Chair of the Remuneration Committee.

Single total figure of remuneration of each Director (audited)

The table below provides a breakdown of the various elements of Director's pay for the period ended 31 December 2021, following 6 April 2021 when Achilles Therapeutics plc completed the IPO. Only 2021 data is disclosed. The below table has been presented in USD which is the presentational currency of the reporting entity:

	Salary and fees ($000)	Benefits [3] ($000)	Bonus [4] ($000)	Share-based payments [5] ($000)	Pension [6] ($000)	Total ($000)	Total fixed ($000)	Total variable ($000)
Executive Directors								
Iraj Ali	299	2	154	928	18	1,401	317	1,084
Non-Executive Directors								
Carsten Boess	70	-	-	90	-	160	70	90
Derek DiRocco	55	-	-	40	-	95	55	40
Michael Giordano	69	-	-	132	-	201	69	132
Edwin Moses	108	-	-	262	-	370	108	262
Julie O'Neill [7]	49	-	-	40	-	89	49	40
Rogier Rooswinkel [8]	-	-	-	-	-	-	-	-
Total	650	2	154	1,492	18	2,316	668	1,648

1. For the period ended 31 December 2021, remuneration was set and paid in pounds sterling. For the purpose of this table, payments made in pounds sterling have been translated into U.S dollars based on a U.S dollar/ pound rate at 31 December 2021 of $1.3497 to £1.00.
2. All amounts are pro-rata since completion of the IPO on 6 April 2021 unless otherwise disclosed.
3. Iraj Ali is the only director to receive benefits from the Company. Benefits received in the period include health and life insurance.
4. Bonus disclosed is for the 2021 financial year and was approved by the Remuneration Committee of the Board in February 2022.
5. All options are subject to service rather than performance conditions. The exercise price for Share Options issued to Directors on June 28th was set by the Board at $15.28 which was a premium to the market price at that time. Share-based payment expense is inclusive of amounts related to shares issued on completion of the IPO on 6 April 2021.
6. Pension equates to 6% of base salary.
7. Appointed 1 May 2021.
8. Resigned 28 June 2021.

2021 Annual Bonus (audited)

In 2021, the CEO's annual bonus was based on strategic objectives aligned to company deliverables and personal performance. The overall bonus outcome resulted in a pay-out of 38% of base salary for the fiscal year ended 31 December 2021.

The table below sets forth the 2021 annual base salaries, target annual cash bonus, and the 2021 annual cash bonus earned by the CEO.

Executive Director	Base Salary	Target Annual Cash Bonus (% of salary)	Cash payment (% of salary)	Cash outcome
Iraj Ali	$ 404,919	50	38	$ 153,869

LONG TERM INCENTIVE AWARDS DURING THE FINANCIAL YEAR

Awards granted in the year since listing on 6 April 2021 (audited)

The Executive Directors may be granted long term incentive awards at the discretion of the Committee.

The exercise price for Share Options issued to Directors on 28 June 2021 was set by the Board at $15.28 which was a premium to the market price at that time.

All awards are subject to a service condition and may be exercised at any time between the vesting date and the tenth anniversary of the date of grant. No performance conditions are linked to the awards. For more information on these awards, please see the table below outlining the Interests of the Directors in the Company's share options.

Awards granted in the year since listing on 6 April 2021 are set forth in the table below:

	Form of Award	Date of Grant	Shares Covered	Exercise Price	Face Value at Date of Grant	Expiry Date	Vest Terms
Executive Directors							
Iraj Ali	Share Options	28/06/2021	136,305	$15.28	$5.88	27/06/2031	(1)
Non-Executive Directors							
Carsten Boess	Share Options	28/06/2021	15,000	$15.28	$5.43	27/06/2031	(2)
Derek DiRocco	Share Options	28/06/2021	15,000	$15.28	$5.43	27/06/2031	(2)
Michael Giordano	Share Options	28/06/2021	15,000	$15.28	$5.43	27/06/2031	(2)
Edwin Moses	Share Options	28/06/2021	15,000	$15.28	$5.43	27/06/2031	(2)
Julie O'Neill	Share Options	28/06/2021	15,000	$15.28	$5.43	27/06/2031	(2)

1. The options vest over a four-year service period with 25% of the award vesting on the first anniversary of the vesting commencement date, with the balance vesting quarterly over the remaining 36 months.
2. The options fully vest on the earlier of the first anniversary of the grant date or the date of the next annual general meeting, whichever occurs first.

Payments to past Directors (audited)

No payments were made to past Directors during the financial year ending 31 December 2021.

Payments for Loss of Office (audited)

No payments were made to Directors for Loss of Office during the financial year ending 31 December 2021.

Statement of Directors' shareholding and share interests (audited)

The share interests of each Director as at 31 December 2021 (together with interests held by his or her connected persons) are set out in the table below. Where a Director has left in the period since listing their position at the date of leaving has been stated.

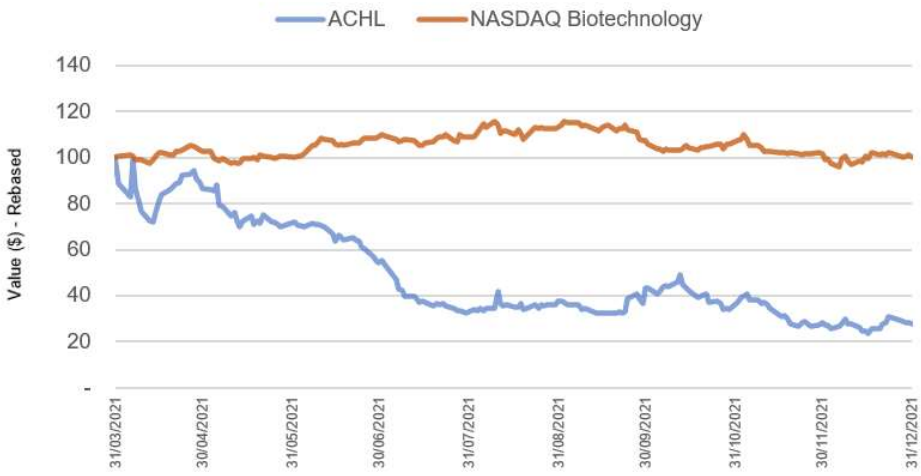
The Company does not operate any formal shareholding guidelines for Directors' shareholding requirements.

	Shares		Share options		
	Beneficially owned shares at 31 December 2021	Unvested at 31 December 2021	Total share options at 31 December 2021	Unvested without performance conditions	Vested but unexercised
Executive Directors					
Iraj Ali	844,631	386,872	136,305	136,305	-
Non-Executive Directors					
Edwin Moses	226,250	102,426	15,000	15,000	-
Carsten Boess	-	-	95,686	66,535	29,151
Derek DiRocco	-	-	15,000	15,000	-
Michael Giordano	46,663	12,248	129,711	77,380	52,331
Julie O'Neill	-	-	15,000	15,000	-

Rogier Rooswinkel held no share interests at the date of his resignation on 28 June 2021 and is therefore not included in the above table.

Total Shareholder Return

The chart below shows the Company's Total Shareholder Return (TSR) performance compared with that of the NASDAQ Biotechnology Index over the period from the date of the Company's listing on Nasdaq to 31 December 2021. The NASDAQ Biotechnology Index has been selected as an appropriate comparator as it is the index of which the Company is a constituent. TSR is defined as the return on investment obtained from holding a company's shares over a period. It includes dividends paid, the change in the capital value of the shares and any other payments made to or by shareholders within the period.



This graph shows the value, at 31 December 2021, of $100 invested in the Company on 31 March 2021 at the IPO price of $18, compared with the value of $100 invested in the NASDAQ Biotechnology Index.

Percentage change in remuneration of the Chief Executive Officer

As this is the first period reported since listing there has been no change in remuneration of the CEO. It is therefore not possible to provide meaningful comparative data. However, full disclosure of the year-on-year movement will be provided in future remuneration reports.

Annual percentage change in director and employee remuneration

As noted above, because 2021 is the first year that the Company has prepared a Remuneration Report, the remuneration history prior to 2021 is not being disclosed. Full disclosure of the percentage changes as required will be provided in future remuneration reports.

As this is the first year of the first remuneration policy, there are no deviations from the procedure for the implementation of the Policy.

Relative importance of spend on pay

The table below illustrates the Company's expenditure on pay by the Company and its direct and indirect subsidiaries for the year ended 31 December. Given that the Group remains in the early phases of its business life cycle, the comparator chosen to reflect the relative importance of the Group's spend on pay is the Group's research and development expenses as shown in its consolidated income statement disclosed on p.177 in the Form 20-F. Given this is the first period reported since listing, it is not possible to provide meaningful comparative data. Dividend distribution comparators have not been included as the Company has no history of such transactions.

Group	2021	% change
Research and development expenses ($'000)	42,224	N/A
Total group employee pay expenditure ($'000)	24,213	N/A

Total employee pay expenditure in the table above is inclusive of cash payments for salaries and wages, as well as employer benefits and tax costs.

STATEMENT OF IMPLEMENTATION OF REMUNERATION POLICY IN 2022

Annual base salary

The percentage salary increase for the CEO was set by the Remuneration Committee in line with the Directors Remuneration Policy and in light of the market information reviewed at the time. Payment will be made in pounds sterling and has been translated into U.S dollars based on a U.S dollar/ pound rate at 31 December 2021 of $1.3497 to £1.00.

	2021	2022	% change
Iraj Ali, Chief Executive Officer	$404,919	$445,411	10%

Benefits and pension

In 2022, the CEO will be eligible for the same benefits (such as health insurance) as provided to all employees in the jurisdiction in which they reside. Pension contributions for Executive Directors are up to 10% of base salary or a salary supplement in lieu of pension benefits, or a combination of pension contributions and salary supplement.

Bonus

The target bonus for the CEO for the 2022 performance year will be 50% of base salary. The performance objectives for the CEO against which the Committee will determine the annual bonus were approved by the Remuneration Committee of the Board in February 2022.

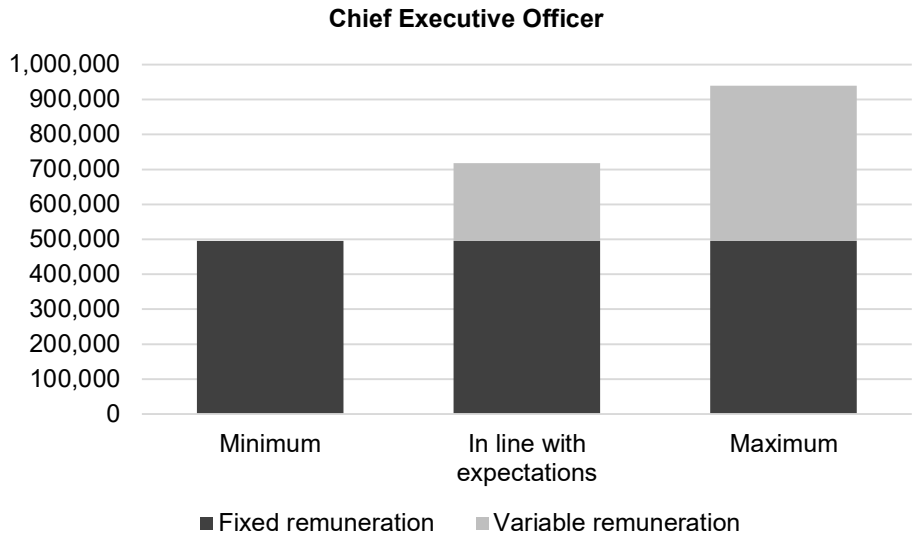
Specific targets are commercially sensitive and therefore are not disclosed in advance. However, full details of the targets and performance against them will be disclosed when they are no longer considered commercially sensitive.

Share Option Incentive Plan

On 2 February 2022, the CEO was granted 196,512 share options in the Company at a strike price of $3.62 per share, based on the closing price of the Company's ADSs on the Nasdaq Global Select Market on the grant date. The share options will expire 10 years from the date of grant. The option awards vest over a period of four years with 25% vesting and becoming exercisable upon the first anniversary of the vesting commencement date and the remaining 75% vesting and becoming exercisable in equal quarterly amounts thereafter.

Remuneration scenarios for the Chief Executive Officer

The charts below show an estimate of the 2022 remuneration package for the CEO under three assumed performance scenarios and these scenarios are based upon the remuneration policy set out above.



1. Minimum scenario comprises fixed pay only, which is made up of $445,411, benefits values based on benefits provided in 2021, and pension contribution of up to 10% of salary.
2. Target scenario comprises fixed pay as set out above, and bonus pay-outs assuming on-target performance of 50%, as set out in the policy.
3. Maximum scenario comprises fixed pay as set out above, and 200% of target bonus pay-out for 2022.

The variable remuneration in the chart above includes only annual bonus opportunity. The Chief Executive Officer will additionally receive equity incentive awards, in the form of options. The maximum and target value of any equity awards under the plan is not defined, and, therefore, the awards cannot be valued nor included in the charts. Consequently, no share price growth has been factored into the chart.

Non-Executive Directors' Fees for 2022

Non-Executive Directors are eligible to receive the following cash compensation annually:

	2022 Fee ($'000)
Base fee:	
Board Chair	61
Board Member	74
Additional fees:	
Audit Committee Chair	13
Audit Committee Member	4
Remuneration Committee Chair	13
Remuneration Committee Member	4
Nominating Committee Chair	7
Nominating Committee Member	4
R&D Committee Chair	13
R&D Committee Member	4

The disclosed fees and annual equity award are subject to review as per the Directors' Remuneration Policy.

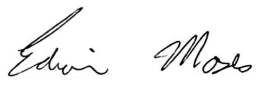
On each date of the Company's AGM following the completion of the IPO, each continuing non-employee member of the Board of Directors receives an annual equity award of 15,000 share options for Board membership. This award shall vest in full upon the earlier of the first anniversary of the date of grant or the date of the next AGM, provided that all vesting shall cease if the director resigns from the Board of Directors or otherwise ceases to serve as a director, unless the Board of Directors determines that the circumstances warrant continuation of vesting.

Each Non-Executive Director will also be entitled to reimbursement of reasonable expenses and reimbursement of fees for tax advice associated with completion of international tax returns due to their role as an Achilles Therapeutics plc Non-Executive Director.

Statement of Voting Results

As this is the first year of the Policy there is no Statement of Voting Results to report to date. The Policy will be put forward for approval by shareholders in a binding vote at the AGM on 28 June 2022. If approved, it will take effect from the date of approval and apply for a period of three years until 2025, or until a revised policy is approved by shareholders.

This report was approved by the Board on 21 March 2022 and signed on its behalf.



Dr Edwin Moses
Chair of the Remuneration Committee
21 March 2022

STATEMENT OF DIRECTORS' RESPONSIBILITIES IN RESPECT OF THE ANNUAL REPORT AND THE FINANCIAL STATEMENTS

The Directors are responsible for preparing the Annual Report and the financial statements in accordance with applicable law and regulations.

Company law requires the Directors to prepare financial statements for each financial period. Under that law they have elected to prepare the Group financial statements in accordance with US GAAP and the Parent Company financial statements in accordance with United Kingdom Generally Accepted Accounting Practice (United Kingdom Accounting Standards, comprising FRS 102 "The Financial Reporting Standard applicable in the UK and Republic of Ireland", and applicable law).

Under company law the Directors must not approve the financial statements unless they are satisfied that they give a true and fair view of the state of affairs of the Group and Parent Company and of the profit or loss of the Group for that period. In preparing the financial statements, the Directors are required to:

- select suitable accounting policies and then apply them consistently;
- make judgements and estimates that are reasonable and prudent;
- state whether applicable accounting principles generally accepted in the United States of America (US GAAP) have been followed for the Group financial statements and United Kingdom Accounting Standards, comprising FRS 102, have been followed for the Parent Company financial statements, subject to any material departures disclosed and explained in the financial statements;
- assess the Group and Parent Company’s ability to continue as a going concern, disclosing, as applicable, matters related to going concern; and
- use the going concern basis of accounting unless they either intend to liquidate the Group or the Parent Company or to cease operations, or have no realistic alternative but to do so.

The Directors are responsible for keeping adequate accounting records that are sufficient to show and explain the Group and Parent Company’s transactions and disclose with reasonable accuracy at any time the financial position of the Group and Parent Company and enable them to ensure that the financial statements and Directors’ Remuneration Report comply with the Companies Act 2006. They are responsible for such internal control as they determine is necessary to enable the preparation of financial statements that are free from material misstatement, whether due to fraud or error, and have general responsibility for taking such steps as are reasonably open to them to safeguard the assets of the Group and to prevent and detect fraud and other irregularities.

The directors are responsible for the maintenance and integrity of the Company's website. Legislation in the United Kingdom governing the preparation and dissemination of financial statements may differ from legislation in other jurisdictions.

INDEPENDENT AUDITOR'S REPORT TO THE MEMBERS OF ACHILLES THERAPEUTICS PLC

1 Our opinion is unmodified

We have audited the financial statements of Achilles Therapeutics Plc ("the Company") for the period ended 31 December 2021 which comprise the Consolidated Statement of Operations and Comprehensive Loss, Consolidated Balance Sheet, Consolidated Statement of Shareholders' Equity, Consolidated Statements of Cash Flows, and the related notes included on Form 20-F. In addition, it includes notes on page 52 and the Company Balance Sheet, and Company Statement of Changes in Equity and the related notes, including the accounting policies in note 2.

In our opinion:

- the financial statements give a true and fair view of the state of the Group's and of the Parent Company's affairs as at 31 December 2021 and of the Group's loss for the year then ended;
- the Group financial statements have been properly prepared in accordance with accounting principles generally accepted in the United States of America ("U.S. GAAP");
- the Parent Company financial statements have been properly prepared in accordance with UK accounting standards, including FRS 102 *The Financial Reporting Standard applicable in the UK and Republic of Ireland*; and
- the financial statements have been prepared in accordance with the requirements of the Companies Act 2006.

Basis for opinion

We conducted our audit in accordance with International Standards on Auditing (UK) ("ISAs (UK)") and applicable law. Our responsibilities are described below. We have fulfilled our ethical responsibilities under, and are independent of the Group in accordance with, UK ethical requirements including the FRC Ethical Standard as applied to listed entities. We believe that the audit evidence we have obtained is a sufficient and appropriate basis for our opinion.

Overview

Materiality	Group Financial statements as a whole: $751k, 1% of total expenses
	Company's Financial statement as a whole: $281k, 2.7% of total expenses
Coverage	100% of group total expenses
Key audit matters	Measurement of lease liabilities – Evaluation of discount rate
	Recoverability of parent Company's investment in and amount due from subsidiaries

2 Key audit matters: our assessment of risks of material misstatement

Key audit matters are those matters that, in our professional judgement, were of most significance in the audit of the financial statements and include the most significant assessed risks of material misstatement (whether or not due to fraud) identified by us, including those which had the greatest effect on: the overall audit strategy; the allocation of resources in the audit; and directing the efforts of the engagement team. These matters were addressed in the context of our audit of the financial statements as a whole, and in forming our opinion thereon, and we do not provide a separate opinion on these matters. In arriving at our audit opinion above, the key audit matters, in decreasing order of audit significance, were as follows:

	The risk	Our response
Measurement of lease liabilities- Evaluation of discount rate **Lease liability Current - $4.5m** **(2020: $3.7m)** **Non-current – $7.8m** **(2020: $12.3m)** Refer to page 186 of attached 20-F (accounting policy)	**Subjective estimate** The Group measures its lease liabilities based on present value of minimum lease payments over the remaining lease terms, discounted using an incremental borrowing rate. The incremental borrowing rate is a key assumption in the measurement of the lease liability. Due to the fact that the company has no external borrowing, significant judgement is required to determine the appropriate incremental borrowing rate. The incremental borrowing rate was developed using collateralised borrowing rates from third party financial institutions, adjusted for company and market specific risk factors. The evaluation of the appropriateness of the incremental borrowing rate involves a high degree of judgement which necessitated us devoting significant time and effort in this area and we have accordingly determined it to be a key audit matter.	**Our procedures included:** We performed the tests below rather than seeking to rely on any of the group's controls because the nature of the balance is such that we would expect to obtain audit evidence primarily through the detailed procedures described. **Methodology choice:** We evaluated the methodology of determination of the incremental borrowing rate by conducting a detailed assessment of the accounting policy papers that set out the group' interpretation of the accounting standards requirements, key assumptions and calculations made in determining the incremental borrowing rate used. **Benchmarking:** We compared the key inputs used in the incremental borrowing rate calculation in the context of external data of other companies in a similar industry and similar stage of development. The key inputs include: term of the lease geographical location of the lease borrowing rate We evaluated the group's incremental borrowing rate by comparing it to a borrowing rate of comparable companies. **Sensitivity analysis**: We performed sensitivity analysis by comparing the measurement of lease liabilities using group's incremental borrowing rate to that of the independently developed range noted above based on comparable companies.

Recoverability of Parent Company's investment in subsidiaries ($203.4m) and amounts owed by subsidiaries ($2.9m) Refer to note 4	**Low risk, high value** The carrying amount of the Parent Company's investment in subsidiaries represents 57% of Company's total assets. Its recoverability is not at a high risk of significant misstatements or subject to significant judgement. However, due to its materiality in the context of Parent Company financial statements, this is considered to be the area that had the greatest effect on our overall Parent Company audit.	**Our procedures included:** We performed the tests below rather than seeking to rely on any of the group's controls because the nature of the balance is such that we would expect to obtain audit evidence primarily through the detailed procedures described. **Test of detail**: We compared the aggregate of the carrying amount of the investments and amount owed by group entities to the market capitalisation as at 31 December 2021, which is an approximation of the minimum recoverable amount of the aggregation of the investment and amounts owed by group entities, to assess whether it was in excess of the aggregate carrying amount.

3 Our application of materiality and an overview of the scope of our audit

Materiality for the group financial statements as a whole was set at $751k (2020: $381k), determined with reference to a benchmark of total expenses of $75.1m (2020: $38.1m) of which it represents 1% (2020: 1%). The benchmark is consistent with prior year.

Materiality for the Parent Company financial statements as a whole was set at $281k, determined with reference to a benchmark of total expenses of $10.4m, of which it represents 2.7%.

In line with our audit methodology, our procedures on individual account balances and disclosures were performed to a lower threshold, performance materiality, so as to reduce to an acceptable level the risk that individually immaterial misstatements in individual account balances add up to a material amount across the financial statements as a whole.

Performance materiality was set at 75% (2020: 65%) of materiality for the financial statements as a whole, which equates to $563k (2020: $247k) for the group and $210k for the Parent Company. We have revised our performance materiality from 65% to 75%, as the audit progressed. We applied this percentage in our determination of performance materiality by considering a number of factors and concluded the aggregation risk was low and therefore a higher percentage was more appropriate.

We agreed to report to the Audit Committee any corrected or uncorrected identified misstatements exceeding $37k (2020: $19k) for the Group and $14k for the Parent Company, in addition to other identified misstatements that warranted reporting on qualitative grounds.

The Group team performed the audit of the Group as if it was a single aggregated set of financial information.

The audit was performed using the materiality and performance materiality levels set out above.

4 Going concern

The directors have prepared the financial statements on the going concern basis as they do not intend to liquidate the Group or the Company or to cease their operations, and as they have concluded that the Group's and the Company's financial position means that this is realistic. They have also concluded that there are no material uncertainties that could have cast significant doubt over their ability to continue as a going concern for at least a year from the date of approval of the financial statements ("the going concern period").

We used our knowledge of the Group and the Company, its industry, and the general economic environment to identify the inherent risks to its business model and analysed how those risks might affect the Group's and Company's financial resources or ability to continue operations over the going concern period. The risks that we considered most likely to adversely affect the Group's available financial resources over this period were:

- Underperformance against plan;
- Progress and alignment of dosing patients;
- Delays in cash inflows; and
- Impact of COVID-19.

We considered whether these risks could plausibly affect the liquidity in the going concern period by comparing severe but plausible downside scenarios that could arise from these risks individually and collectively against the level of available financial resources indicated by the Group's financial forecasts.

We considered whether the going concern disclosure in note 2.3 to the financial statements gives a full and accurate description of the Directors' assessment of going concern, including the identified risk and related sensitivities. We assessed the completeness of the going concern disclosure.

Our conclusions based on this work:

- we consider that the directors' use of the going concern basis of accounting in the preparation of the financial statements is appropriate;
- we have not identified, and concur with the directors' assessment that there is not, a material uncertainty related to events or conditions that, individually or collectively, may cast significant doubt on the Group's or Company's ability to continue as a going concern for the going concern period; and
- we found the going concern disclosure in note 2.3 to be acceptable.

However, as we cannot predict all future events or conditions and as subsequent events may result in outcomes that are inconsistent with judgements that were reasonable at the time they were made, the above conclusions are not a guarantee that the Group or the Company will continue in operation.

5 Fraud and breaches of laws and regulations – ability to detect

Identifying and responding to risks of material misstatement due to fraud
To identify risks of material misstatement due to fraud ("fraud risks") we assessed events or conditions that could indicate an incentive or pressure to commit fraud or provide an opportunity to commit fraud. Our risk assessment procedures included:

- Enquiring of directors, the audit committee, and inspection of policy documentation as to the Group's high-level policies and procedures to prevent and detect fraud as well as whether they have knowledge of any actual, suspected or alleged fraud.

- Reading Board of Directors, Audit Committee, Research and development committee and remuneration committee meeting minutes.
- Considering remuneration incentive schemes and performance targets of management personnel and directors.
- Using analytical procedures to identify any unusual or unexpected relationships.

We communicated identified fraud risks throughout the audit team and remained alert to any indications of fraud throughout the audit.

As required by auditing standards, and taking into account our overall knowledge of the control environment, we perform procedures to address the risk of management override of controls, in particular the risk that Group management may be in a position to make inappropriate accounting entries and the risk of bias in accounting estimates and judgements such as those used in determination of incremental borrowing rate. On this audit we do not believe there is a fraud risk related to revenue recognition because the group is in the pre-commercialization stage and no revenues are earned from trading.

We did not identify any additional fraud risks.

In determining the audit procedures, we took into account the results of our evaluation and testing of the operating effectiveness of some of the Group-wide fraud risk management controls.

We also performed procedures including:
- Identifying journal entries to test for all full scope components based on risk criteria and comparing the identified entries to supporting documentation. These included entries posted to certain account or pairings or non-related accounts.
- Evaluated the business purpose of significant unusual transactions.
- Assessing whether the judgements made in making accounting estimates are indicative of a potential bias.

Identifying and responding to risks of material misstatement related to compliance with laws and regulations

We identified areas of laws and regulations that could reasonably be expected to have a material effect on the financial statements from our general commercial and sector experience, through discussion with the directors and other management (as required by auditing standards), and from inspection of the Group's regulatory and legal correspondence and discussed with the policies and procedures regarding compliance with laws and regulations.

We communicated identified laws and regulations throughout our team and remained alert to any indications of non-compliance throughout the audit.

The potential effect of these laws and regulations on the financial statements varies considerably.

Firstly, the Group is subject to laws and regulations that directly affect the financial statements including financial reporting legislation (including related companies' legislation), distributable profits legislation, and taxation legislation, and we assessed the extent of compliance with these laws and regulations as part of our procedures on the related financial statement items.

Secondly, the Group is subject to many other laws and regulations where the consequences of non-compliance could have a material effect on amounts or disclosures in the financial statements, for instance through the imposition of fines or litigation or the loss of the Group's license to operate.

We identified the following areas as those most likely to have such an effect: health and safety, anti-bribery, employment law, human medicines regulations, regulatory capital and liquidity, and certain aspects of company legislation recognising the financial and regulated nature of the Group's activities and its legal form. Auditing standards limit the required audit procedures to identify non-compliance with these laws and regulations to enquiry of the directors and other management and inspection of regulatory and legal correspondence, if any. Therefore if a breach of operational regulations is not disclosed to us or evident from relevant correspondence, an audit will not detect that breach.

Context of the ability of the audit to detect fraud or breaches of law or regulation
Owing to the inherent limitations of an audit, there is an unavoidable risk that we may not have detected some material misstatements in the financial statements, even though we have properly planned and performed our audit in accordance with auditing standards. For example, the further removed non-compliance with laws and regulations is from the events and transactions reflected in the financial statements, the less likely the inherently limited procedures required by auditing standards would identify it.

In addition, as with any audit, there remained a higher risk of non-detection of fraud, as these may involve collusion, forgery, intentional omissions, misrepresentations, or the override of internal controls. Our audit procedures are designed to detect material misstatement. We are not responsible for preventing non-compliance or fraud and cannot be expected to detect non-compliance with all laws and regulations.

6 We have nothing to report on the other information in the Annual Report and Financial Statements

The directors are responsible for the other information presented in the Annual Report together with the financial statements. Our opinion on the financial statements does not cover the other information and, accordingly, we do not express an audit opinion or, except as explicitly stated below, any form of assurance conclusion thereon.

Our responsibility is to read the other information and, in doing so, consider whether, based on our financial statements audit work, the information therein is materially misstated or inconsistent with the financial statements or our audit knowledge. Based solely on that work we have not identified material misstatements in the other information.

Strategic report and directors' report
Based solely on our work on the other information:
- we have not identified material misstatements in the strategic report and the directors' report;
- in our opinion the information given in those reports for the financial year is consistent with the financial statements; and
- in our opinion those reports have been prepared in accordance with the Companies Act 2006.

Directors' remuneration report
In our opinion the part of the Directors' Remuneration Report to be audited has been properly prepared in accordance with the Companies Act 2006.

7 We have nothing to report on the other matters on which we are required to report by exception

Under the Companies Act 2006, we are required to report to you if, in our opinion:
- adequate accounting records have not been kept by the Parent Company, or returns adequate for our audit have not been received from branches not visited by us; or

- the Parent Company financial statements are not in agreement with the accounting records and returns; or
- certain disclosures of directors' remuneration specified by law are not made; or
- we have not received all the information and explanations we require for our audit.

We have nothing to report in these respects.

8 Respective responsibilities

Directors' responsibilities
As explained more fully in their statement set out on page 32, the directors are responsible for: the preparation of the financial statements including being satisfied that they give a true and fair view; such internal control as they determine is necessary to enable the preparation of financial statements that are free from material misstatement, whether due to fraud or error; assessing the Group and Parent Company's ability to continue as a going concern, disclosing, as applicable, matters related to going concern; and using the going concern basis of accounting unless they either intend to liquidate the Group or the Parent Company or to cease operations, or have no realistic alternative but to do so.

Auditor's responsibilities
Our objectives are to obtain reasonable assurance about whether the financial statements as a whole are free from material misstatement, whether due to fraud or error, and to issue our opinion in an auditor's report. Reasonable assurance is a high level of assurance, but does not guarantee that an audit conducted in accordance with ISAs (UK) will always detect a material misstatement when it exists. Misstatements can arise from fraud or error and are considered material if, individually or in aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of the financial statements.

A fuller description of our responsibilities is provided on the FRC's website at www.frc.org.uk/auditorsresponsibilities.

9 The purpose of our audit work and to whom we owe our responsibilities

This report is made solely to the Company's members, as a body, in accordance with Chapter 3 of Part 16 of the Companies Act 2006. Our audit work has been undertaken so that we might state to the Company's members those matters we are required to state to them in an auditor's report and for no other purpose. To the fullest extent permitted by law, we do not accept or assume responsibility to anyone other than the Company and the Company's members, as a body, for our audit work, for this report, or for the opinions we have formed.

22 March 2022

Shirley Rogan **(Senior Statutory Auditor)**
for and on behalf of KPMG LLP, Statutory Auditor
Chartered Accountants
2 Forbury Place,
33 Forbury Road
Reading
United Kingdom
RG1 3AD

ACHILLES THERAPEUTICS PLC

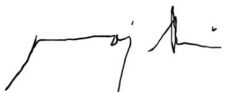
COMPANY BALANCE SHEET AS AT 31 DECEMBER 2021

	Notes		2021 $'000
Non-current assets			
Investment in subsidiaries	4		203,423
			203,423
Current assets			
Debtors	5	4,802	
Cash and cash equivalents		149,625	
		154,427	
Current liabilities			
Creditors - amounts falling due within one year	6		(922)
			(922)
Net current assets			**153,505**
Total assets less liabilities			**356,928**
Capital and reserves			
Called up share capital	7		178
Share premium			160,611
Profit and loss account			190,560
Other reserves			5,579
Equity attributable to the parent's shareholders			**356,928**

The notes on pages 42 to 51 form an integral part of these financial statements.

The Parent Company has elected to take the exemption under section 408 of the Companies Act 2006 from presenting the Parent Company statement of comprehensive income. The Parent Company loss for the period ended 31 December 2021 was $6,396,475.

The financial statements were approved by the Board of Directors on 21 March 2022 and were signed on its behalf by:



Iraj Ali
Chief Executive Officer
21 March 2022

Registered number: 13027460

ACHILLES THERAPEUTICS PLC

COMPANY STATEMENT OF CHANGES IN EQUITY FOR THE PERIOD ENDED 31 DECEMBER 2021

	Called up Share Capital ($)	Share Premium ($)	Capital Redemption Reserve ($)	Share Based Payment Reserve ($)	Other comprehensive income ($)	Profit and loss account ($)	Total Equity ($)
At 18 November 2020 (incorporation)	2	-	-	-	-	-	2
Issue of shares in consideration for the transfer of Achilles Therapeutics UK Limited on 11 December 2020	197,121,358	-	-	-	-	-	197,121,358
Capital reduction	(196,957,092)	-	-	-	-	196,957,092	-
IPO Issuance of 9,750,000 shares	13,547	175,486,453	-	-	-	-	175,500,000
Underwriter and issuance Costs	-	(14,875,338)	-	-	-	-	(14,875,338)
Equity-settled share-based payment transactions	-	-	-	1,861,641	-	-	1,861,641
Equity-settled share-based payment transactions in subsidiaries	-	-	-	5,570,966	-	-	5,570,966
Repurchase and cancellation of deferred shares	(145)	-	145	-	-	-	-
Loss for the period	-	-	-	-	-	(6,396,475)	(6,396,475)
Other Comprehensive loss	-	-	-	-	(1,853,743)	-	(1,853,743)
At 31 December 2021	**177,670**	**160,611,115**	**145**	**7,432,607**	**(1,853,743)**	**190,560,617**	**356,928,411**

The notes on pages 42 to 51 form an integral part of these financial statements.

ACHILLES THERAPEUTICS PLC

NOTES TO THE FINANCIAL STATEMENTS FOR THE PERIOD ENDED 31 DECEMBER 2021

1. Company Information

Achilles Therapeutics plc (the "Company" or the "Parent Company", formerly Achilles TX Limited) is a public limited company limited by shares and is incorporated and registered in England and Wales. The registered number is 13027460 and the registered address is 245 Hammersmith Road, London, W6 8PW. The nature of the Company's operations is to act as the holding and financing company for its subsidiary entities, which together form the Achilles Therapeutics Group (the "Group"). The business of the Group is research and development in the field of biopharmaceuticals.

Achilles Therapeutics plc was originally incorporated under the name Achilles TX Limited before being renamed Achilles Therapeutics plc as part of our corporate reorganisation. Achilles Therapeutics Holdings Limited is a direct subsidiary of the Company as of 31 December 2021, and Achilles Therapeutics UK Limited and Achilles Therapeutics US, Inc. are indirect subsidiaries. Together, these Companies form the Achilles Therapeutics Group.

The Company was incorporated on 18 November 2020. Achilles Therapeutics Holdings Limited was incorporated as a direct subsidiary of the Company on 20 November 2020. The corporate reorganisation and initial public offering, or IPO, took place in several steps which were completed on 6 April 2021.

- **Exchange of Achilles Therapeutics UK Limited Shares for Achilles TX Limited Shares**: In December 2020 all shareholders of Achilles Therapeutics UK Limited (except for the holders of deferred shares) exchanged each of the shares held by them for shares of Achilles TX Limited to result in them holding the same number and class of newly issued shares of £1.20 nominal value of Achilles TX Limited and, as a result, Achilles TX Limited became the sole shareholder of Achilles Therapeutics UK Limited.
- **Reduction of the share capital of Achilles TX Limited:** Achilles TX Limited reduced its share capital by way of a reduction of the nominal value of each share in the capital of Achilles TX Limited from £1.20 to £0.001 in order to satisfy the net asset test requirement in section 92 of the Companies Act 2006 for re-registration as a public limited company and to create distributable reserves.
- **Re-registration of Achilles TX Limited as Achilles Therapeutics plc:** In February 2021, Achilles TX Limited was re-registered as a public limited company pursuant to section 92 of the U.K. Companies Act 2006 and renamed Achilles Therapeutics plc. The Company adopted new Articles of Association appropriate for a public limited company.

On 6 April 2021, the Company completed the IPO. In the IPO, the Company sold an aggregate of 9,750,000 American Depository Shares ("ADSs") representing the same number of ordinary shares, at a public offering price of $18.00 per ADS. Net proceeds were $160.6 million, after deducting underwriting discounts and commissions and other offering expenses. Upon IPO, the Company adopted new Articles of Association suitable for a listed public limited company.

At the Company's AGM held on 28 June 2021, the shareholders approved, among other matters, a minor amendment to the Company's Articles of Association.

2. Accounting Policies

2.1 Basis of preparation

These company financial statements have been prepared in accordance with applicable United Kingdom Accounting Standards, including Financial Reporting Standard 102 'The Financial Reporting Standard applicable in the United Kingdom and Republic of Ireland' ("FRS 102") and the Companies Act 2006. There were no material departures from that standard.

The functional currency of the Company is British Pound Sterling ("GBP") given the underlying accounting records are recorded in GBP and this is the currency of the Company's primary operations. The presentation currency of these company financial statements is American Dollars ("USD") for consistency with the Group financial presentation. All amounts in the financial statements are presented in USD thousands unless otherwise stated. The financial statements are prepared under the historical cost convention.

The Parent Company is included in the consolidated financial statements and is considered to be a qualifying entity under FRS 102 paragraphs 1.8 to 1.12. The Company has taken advantage of the exemption of section 408 of the Companies Act from disclosing its individual profit and loss account. The following further exemptions available under FRS 102 in respect of certain disclosures for the Parent Company financial statements have been applied:

- No separate Parent Company Cash Flow Statement with related notes is included;
- Key Management Personnel compensation has not been included a second time;
- Certain disclosures required by FRS 102.26 Share Based Payments; and
- Certain disclosures required by FRS 102.11 Basic Financial Instruments and FRS 102.12 Other Financial Instrument Issues in respect of financial instruments not falling within the fair value accounting rules of Paragraph 36(4) of Schedule 1.

The financial statements have been prepared on a going concern basis. See note 2.3 for further detail. The Directors have considered the appropriateness of the going concern basis in the Directors' Report.

The preparation of financial statements in conformity with FRS 102 requires the use of certain accounting estimates. It also requires management to exercise its judgment in the process of applying the Company's accounting policies. The areas involving a higher degree of judgement or complexity, or areas where assumptions and estimates are significant to the financial statements are disclosed in the "Critical Accounting Judgements and Estimates" Section.

2.2 Basis of consolidation

The consolidated financial statements include the financial statements of the Parent Company and all its subsidiary undertakings. A subsidiary is an entity that is controlled by the parent. The results of subsidiary undertakings are included in the consolidated profit and loss account from the date that control commences until the date that control ceases. All intercompany transactions, balances, income and expenses are eliminated on consolidation.

The consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("U.S. GAAP"), as permitted by Statutory Instrument 2015 No. 1675, "The Accounting Standards (Prescribed Bodies) (United States of America

and Japan) Regulations 2015" and in accordance with the UK Companies Act 2006. Refer to the attached Form 20-F for these financial statements.

2.3 Going concern

The Company reported Cash and cash equivalents of $149.6M and net current assets of $153.5M as at 31 December 2021, with a loss for the period ended 31 December 2021 of $6.4M. The Group reported Cash and cash equivalents of $266.3M and net current assets of $265.6M as at 31 December 2021, with a net loss for the year ended 31 December 2021 of $61.1M. The Group has historically been loss making and anticipates that it will continue to incur losses for the foreseeable future and had an accumulated deficit of $119.1M as of 31 December 2021. The Group expects to continue to incur operating losses and negative cash outflows until such time as it generates a level of revenue that is sufficient to support its cost structure.

The spread of COVID-19 has impacted the global economy and has impacted the Group’s operations, including the interruption of preclinical and clinical trial activities and potential interruption to supply chains. The Group has maintained operations at its GMP manufacturing and research and development sites through 2021 to date. The Group continues to assess the impact COVID-19 may have on its ability to advance the development of drug candidates or to raise financing to support the development of drug candidates, but no assurances can be given that this analysis will enable it to avoid part or all of any impact from the spread of COVID-19 or its consequences, including downturns in business sentiment generally or in its sector in particular.

The Directors have reviewed the financial projections of the Company for the twelve months subsequent to the date of issuance of these financial statements including consideration of severe but plausible scenarios that may affect the Company in that period. These show that the Company will be able to pay (or otherwise discharge) its debts as they fall due immediately following the date of signing of the financial statements and for the period considered by the forecast.

Accordingly, the financial statements have been prepared on a basis that assumes the Group and the Parent Company will continue as a going concern and which contemplates the realisation of assets and settlement of liabilities and commitments as they fall due in the ordinary course of business for at least 12 months from the date of issuance of the financial statements.

2.4 Foreign currencies

Transactions in foreign currencies are recorded at the rate ruling at the date of the transaction. Monetary assets and liabilities denominated in foreign currencies are translated into the functional currency at the rates of exchange ruling at the balance sheet date. Non-monetary items that are measured in terms of historical cost in a foreign currency are translated using the exchange rate at the date of the transaction. All differences are taken to the profit and loss account in the period in which they arise.

Assets and liabilities are translated to the Company's presentational currency, US dollars, at foreign exchange rates in effect at the balance sheet date. Equity transactions are translated at the prevailing rate at the date of transaction. Profit and loss items are translated at an average rate for the financial period where this rate approximates to the foreign exchange rates in effect at the date of the transactions. Exchange differences arising from this translation are reported as an item of other comprehensive income and accumulated in the Other comprehensive income reserve.

2.5 Share capital

Ordinary shares, class A non-voting ordinary shares and deferred shares are classified as equity. Incremental costs directly attributable to the issue of new ordinary shares, preference shares or options are shown in equity as a deduction, net of tax, from the proceeds.

2.6 Investments

The investment in subsidiaries is measured at historic cost less any accumulated impairment losses. The cost is measured as the nominal value of the shares issued for the acquisition.

A provision is made for any impairment in value. When performing this impairment assessment, the Directors consider whether any events or circumstances have occurred which indicate that the carrying value of the investment in the subsidiary may not be recoverable. If such circumstances exist, a full impairment review is undertaken to establish whether the carrying amount exceeds the higher of net realisable value or value in use. If this is the case, an impairment charge is recorded to reduce the carrying value of the related investment.

2.7 Cash and cash equivalents

Cash and cash equivalents comprise cash, money market funds and short-term deposits. The Company considers all highly liquid investments that have maturities of three months or less when acquired to be cash equivalents. The carrying amount of these assets is approximately equal to their fair value.

2.8 Debtors

Short term debtors are measured at transaction price plus attributable transaction costs, less any impairment.

2.9 Payables

Short term trade creditors are measured at transaction price less attributable transaction costs.

2.10 Share-based payments

Prior to the share for share exchange agreement on 11 December 2020 the awards of share options and other equity-based awards to employees in the Achilles Group were granted in Achilles Therapeutics UK Limited. Following the share for share exchange agreement Achilles Therapeutics plc became the parent company of the Achilles Group and share options and other equity-based awards were granted in Achilles Therapeutics plc.

The share-based expense for equity awards is based on the grant date fair value of the award, which may include share options and restricted Ordinary Shares. For equity awards that vest based on a service condition, the share-based compensation expense is recognised on a straight-line basis over the requisite service period. The total amount to be expensed over the vesting year is determined by reference to the fair value of the options granted and assumptions about the number of options that are expected to vest. The Group has estimated expected forfeiture rates for share options based on historic employee data and this has been considered in the expense for the period. For equity awards with performance conditions, the Company recognises share-based compensation expense using a straight-line basis over the requisite service period when the achievement of a performance-based milestone is probable, based on the relative satisfaction of the performance condition as of the

reporting date. The Company uses the fair value of its Ordinary Shares to determine the fair value of employee shares awarded to employees and directors.

There have been no performance conditions attached to the share options granted by the Company to date. The fair value of each share option grant is estimated on the date of grant using the Black-Scholes option pricing model, which uses our ordinary shares, the expected term of our share options, the risk-free interest rate for a period that approximates the expected term of our share options and our expected dividend yield.

If any of the assumptions used in the Black-Scholes model change significantly, share-based compensation for future awards may differ materially compared with the awards granted previously.

The financial effect of awards by the Parent Company of share options and other equity-based awards to the employees of subsidiary undertakings are recognised by the Parent Company in its individual financial statements. In particular, the Parent Company initially records a debit to the investment value of the subsidiary holding entity, Achilles Therapeutics Holdings Limited, with a corresponding credit to the Share Compensation Reserve. Achilles Therapeutics Holdings Limited records a debit to the investment value of the subsidiary entity of the relevant employee, with a corresponding credit to the Share Compensation Reserve. The expense associated with the subsidiary's equity-based awards is recognised in profit and loss for the subsidiary undertaking.

For full share-based payments disclosures, please refer to p.192 of the attached Form 20-F in the consolidated financial statements presented with these Parent Company financial statements.

2.11 Financial Instruments

The Company only enters into basic financial instruments transactions which result in the recognition of financial assets and liabilities like trade and other debtors and creditors.

Financial assets that are measured at cost and amortised cost are assessed at the end of each reporting period for objective evidence of impairment. If objective evidence of impairment is found, an impairment loss is charged to the profit and loss account. For financial assets measured at amortised cost, the impairment loss is measured as the difference between an asset's carrying amount and the present value of estimated cash flows discounted at the asset's original effective interest rate. If a financial asset has a variable interest rate, the discount rate for measuring any impairment loss is the current effective interest rate determined under the contract.

For financial assets measured at cost less impairment, the impairment loss is measured as the difference between an asset's carrying amount and best estimate, which is an approximation of the amount that the Company would receive for the asset if it were to be sold at the balance sheet date.

3. Critical judgements and key sources of estimation uncertainty in applying the Company's accounting policies

In the application of the Company's accounting policies, which are described above, the Directors are required to make judgements, estimates and assumptions about the carrying amounts of assets and liabilities that are not readily apparent from other sources. The estimates and associated assumptions are based on historical experience and other factors that are considered to be relevant. Actual results may differ from these estimates. The estimates and underlying assumptions are reviewed on an

ongoing basis. Revisions to accounting estimates are recognised in the period in which the estimate is revised if the revision affects only that period or in the period of the revision and future periods if the revision affects both current and future periods.

The following are the critical judgements that the Directors have made in the process of applying the Company's accounting policies and that have the most significant effect on the amounts recognised in the financial statements.

Fair value of share-based compensation

The determination of share-based compensation expense requires numerous estimates and judgements. The estimated fair value of the share awards has been determined by a Committee of the Board as of the date of each Ordinary Share/option grant, with input from a third-party expert.

Investment in subsidiary

Management perform an annual assessment of the investment held in Achilles Therapeutics Holdings Limited by the Company. The valuation of the subsidiary is derived from publicly available information, being the market capitalisation of the group, as at the year end date, given that the future value of the group is expected to be generated from the products and treatments which are being developed by the subsidiary companies. On the balance sheet date, where the market capitalisation of the group as a whole falls below the carrying value of the investment, management will perform a fair value less cost to sell calculation and then consider whether an impairment of the investment is required, and if so, will write down the cost of the investment to its recoverable amount, with an associated impairment charge recognised in the Parent Company profit and loss account. In the event the Group’s market capitalisation increases and the reasons for any impairment loss have ceased to apply, an impairment loss may be reversed in a subsequent period in the Parent Company profit and loss account, to the extent that the carrying value would have been determined had no impairment loss been recognised for the investment in prior periods.

4. Investments

Company	**2021 ($’000)**
On incorporation	-
Arising on group re-organisation	197,121
Share-based payments associated with subsidiary employees	5,571
Impairment in subsidiary	(1,970)
Effect of foreign currency translation	2,701
	203,423

On 20 November 2020 the Company incorporated a new private limited company, Achilles Therapeutics Holdings Limited, issuing a single Ordinary Share with a nominal value of £1.00, with the subscription price paid in cash.

On 11 December 2020 the Company entered into a share for share agreement with the shareholders of Achilles Therapeutics UK Limited, under which it acquired 100% of the issued share capital of Achilles Therapeutics UK Limited.

On 26 February 2021, the Company entered into a share for share agreement with the shareholders of Achilles Therapeutics Holdings Limited, under which it exchanged its investment in Achilles

Therapeutics UK Limited for two newly issued Ordinary Shares of nominal value £1.00 each in Achilles Therapeutics Holdings Limited.

The Company has disclosed the amount arising on group re-organisation as the total amount arising at incorporation of Achilles Therapeutics Holdings Limited and the subsequent acquisition of Achilles Therapeutics UK Limited. Subsequent increases in value to the investment in Achilles Therapeutics UK Limited, and subsequently Achilles Therapeutics Holdings Limited, are as a result of share-based payment awards issued in subsidiary entities, in line with the accounting policy outlined at Note 2.10.

The Parent Company performed an impairment analysis on a fair value less cost to sell basis, whereby the Parent Company used the market capitalisation of the Group as the approximate fair value and the cost to sell and control premium were deemed to be negligible. The carrying value of the investment exceeded the fair value less cost to sell of the investment as at 31 December 2021, and the Parent Company concluded that the investment was impaired by $2.0 million. If the market capitalisation of the group increases subsequent to the year end, then all or a portion of this impairment charge could be reversed in future years.

The Group's market capitalisation was derived from a closing share price of $5.01 at the balance sheet date. The market capitalisation of the group, and therefore the investment in subsidiary asset, is sensitive to share price volatility. The impact of a +/- 1% movement in share price on the investment in subsidiary asset vs the closing share price of $5.01 is approximately +/- $2.0m with any additional impairment being recognised through the profit and loss. Were the share price to rise subsequent to the year end, the impairment loss may only be reversed to the extent that the carrying value would have been determined had no impairment loss been recognised in prior periods.

Assets and liabilities are translated to the Company's presentational currency, US dollars, at foreign exchange rates in effect at the balance sheet date. Equity transactions are translated at the prevailing rate at the date of transaction. The loss on impairment has been translated at the average exchange rate for the period. The difference arising on this translation is disclosed above.

Subsidiary undertakings

Name of undertaking	**Class of shareholding**	**% Holding**	**Principal Activity**
Direct			
Achilles Therapeutics Holdings Limited	Ordinary	100%	Holding Company
Indirect			
Achilles Therapeutics UK Limited	Ordinary	100%	Research and development and corporate services
Achilles Therapeutics US, Inc.	Ordinary	100%	Research and development and corporate services

Achilles Therapeutics UK Limited and Achilles Therapeutics US, Inc. are subsidiaries of Achilles Therapeutics Holdings Limited. The following table outlines the country of incorporation and registered office of each of the subsidiary undertakings:

Company	Registered Office
Achilles Therapeutics Holdings Limited	245 Hammersmith Road, London, W6 8PW
Achilles Therapeutics UK Limited	245 Hammersmith Road, London, W6 8PW
Achilles Therapeutics US, Inc.	1209 Orange Street, in the City of Wilmington, County of New Castle, 19801 United States of America

5. Debtors

Company	2021 ($'000)
Amounts owed by group undertakings	2,867
Other Debtors	467
Prepayments	1,468
	4,802

Amounts due from subsidiary undertakings are unsecured, interest free, have no fixed date of repayment and are repayable on demand.

6. Creditors

Company	2021 ($'000)
Amounts owed to group undertakings	126
Accruals	730
Trade creditors	66
	922

Amounts owed to subsidiary undertakings are unsecured, interest free, have no fixed date of repayment and are repayable on demand.

7. Share Capital

Company	Nominal value	Number of shares	2021 ($'000)
Allotted, called up and fully paid:			
Ordinary Shares	£0.001	38,987,122	53
Class A non-voting shares	£0.001	1,616,367	2
Deferred share created on IPO	£92,451.851	1	123
		40,603,490	178

The company was incorporated on 18 November 2020, with share capital of one ordinary share of £1.20 issued to Iraj Ali.

On 11 December 2020 all shareholders of Achilles Therapeutics UK Limited (except for the holders of deferred shares) exchanged each of the shares held by them for shares of Achilles Therapeutics plc to result in them holding the same number and class of newly issued shares of £1.20 nominal value of Achilles Therapeutics plc. This resulted in 123,414,397 newly issued ordinary and preferred shares of £1.20 being created in the Company, in addition to the ordinary share created on incorporation.

Achilles Therapeutics plc subsequently reduced its share capital by way of a reduction of the nominal value of each share in the capital of Achilles Therapeutics plc from £1.20 to £0.001 in order to satisfy the net asset test requirement in section 92 of the Companies Act 2006 for re-registration as a public limited company and to create distributable reserves. Following the transfer, and therefore as of 22 December 2020, the issued share capital of the Company comprised 123,414,398 ordinary and preferred shares of £0.001.

On 6 April 2021, the Company effected a one-for-0.2526 (rounded to four decimal places) reverse share split of its issued and outstanding ordinary shares except for N ordinary shares and a proportional adjustment to the existing conversion ratios for each class of the Company's convertible preferred shares, and a one-for-0.1792 (rounded to four decimal places) reverse share split of its issued and outstanding N ordinary shares. Two shareholders elected to receive a number of class A non-voting ordinary shares rather than their full entitlement of ordinary shares following the reverse share split. As part of the Company's reorganisation, 109,058 outstanding deferred shares were cancelled upon IPO, and a single deferred share with a nominal value of £92,451.851 in the capital of the Company was created.

On April 6 2021, the Company completed the IPO. In the IPO, the Company sold an aggregate of 9,750,000 ADSs representing the same number of ordinary shares, at a public offering price of $18.00 per ADS. Net proceeds were $160.6 million, after deducting underwriting discounts and commissions and other offering expenses. Upon IPO, the Company adopted new articles of association suitable for a listed public limited company. The nominal value of the issued shares was £0.001. Following this transaction, and therefore at 6 April 2021, the issued share capital of the Company comprised 40,603,489 ordinary and class A non-voting shares of £0.001 each and one deferred share of nominal value £92,451.851.

As of 31 December 2021, each beneficial owner of ordinary shares (as represented by a corresponding number of ADSs) is entitled to one vote per ordinary share and to receive dividends when and if such dividends are recommended by the board of directors and declared by the shareholders. Holders of Class A non-voting ordinary shares are not entitled to vote but rank pari passu in all other respects. The holder of the one deferred share has no right to receive any dividend or distribution in a winding up or liquidation and no right vote on shareholder matters, or receive notice of, attend, speak or vote at our general meetings or receive copies of our reports, accounts, circulars or other documents sent to our shareholders. The deferred share can be repurchased by the Company at any time for nil consideration. As of 31 December 2021, the Company has not declared any dividends.

8. Share based payment reserve

Company	**2021 ($'000)**
As at 18 November 2020	-
Issue of share-based payments	7,433
At 31 December 2021	**7,433**

The share-based payment reserve is made up of share-based payments granted by the Achilles Group.

9. Profit and loss account

Company	2021 ($'000)
As at 18 November 2020	-
Reserves created on capital reduction	196,957
Loss for the period	(6,396)
At 31 December 2021	**190,561**

10. Capital redemption reserve

Company	2021 ($'000)
As at 18 November 2020	-
Repurchase and cancellation of deferred shares	-
At 31 December 2021	-

11. Other comprehensive income

Company	2021 ($'000)
As at 18 November 2020	-
Other comprehensive loss	(1,854)
At 31 December 2021	**(1,854)**

Other comprehensive loss relates to the translation of the functional currency, GBP, to the presentational currency, USD, for the period from incorporation to 31 December 2021.

12. Related party transactions

These are disclosed on p.203 of the attached Form 20-F in the consolidated financial statements presented with these Parent Company financial statements. The Company has taken advantage of the exemption, under FRS 102 'The Financial Reporting Standard applicable in the UK and Republic of Ireland', not to disclose related party transactions with other companies that are wholly owned within the group.

13. Events after the reporting period

Refer to the Directors' Report for disclosure of events after the reporting period.

14. Ultimate parent undertaking and controlling party

Achilles Therapeutics plc is the ultimate parent and controlling party of the Achilles Group of Companies. Its registered address is 245 Hammersmith, London, W6 8PW, UK. There is no other immediate or ultimate controlling party.

UK STATUTORY DISCLOSURES RELEVANT TO THE FINANCIAL STATEMENTS OF ACHILLES THERAPEUTICS PLC

Basis of Preparation

The consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("U.S. GAAP"), as permitted by Statutory Instrument 2015 No. 1675, "The Accounting Standards (Prescribed Bodies) (United States of America and Japan) Regulations 2015" and in accordance with the UK Companies Act 2006. As a result of the corporate reorganisation described at Note 1 in the Notes to the Financial Statements, Achilles Therapeutics plc is the successor to Achilles Therapeutics UK Limited and the financial information for prior periods represents that of the consolidated results of Achilles Therapeutics UK Limited. These additional notes have been prepared to comply with the UK Companies Act 2006 requirements for Achilles Therapeutics plc and its subsidiaries as a UK consolidated group.

UK Statutory Disclosure Requirements

(i) Monthly average number of people employed:

Group	2021	2020
Research and development	176	99
Management and administration	36	19
Total employees	212	118

The monthly average number of people employed by the Parent Company in 2021 was 1.

(ii) Employee costs:

Group	2021 ($'000)	2020 ($'000)
Salaries and bonuses	19,833	9,943
Defined contribution pension contributions	1,879	974
Other benefits	439	141
Social insurance and social security costs	2,062	1,169
Total employee costs	24,213	12,227

Details of directors' remuneration, including that of the Parent Company's sole employee, are provided in the Directors' Remuneration Report on pages 13-31. Share-based payment expense in the Directors' Remuneration Report is inclusive of amounts related to shares issued on completion of the IPO on 6 April 2021. No share options were exercised by directors in the year ended 31 December 2021.

(iii) Auditor remuneration

During the period the Group obtained the following services from the Group's auditors and its associates:

Group	2021 ($'000)	2020 ($'000)
Fees payable for the audit of the Parent Company and the Group for the period ended 31 December	715	406
Fees payable for the audit of the Parent Company's subsidiaries for the period ended 31 December	83	-
Audit-related assurance services for the period ended 31 December	261	392
Total fees paid to Group's auditors	1,059	798

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

Form 20-F

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

OR

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

For the fiscal year ended December 31, 2021

OR

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

OR

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

Commission File Number: 001-40299

Achilles Therapeutics plc
(Exact name of registrant as specified in its charter)

England and Wales	2836	Not Applicable
(State or other jurisdiction of incorporation or organization)	(Primary Standard Industrial Classification Code Number)	(I.R.S. Employer Identification No.)

Daniel C.C. Hood
Chief Legal Officer and Company Secretary
245 Hammersmith Road
London W6 8PW
United Kingdom
Telephone: +44 (0)20 8154 4600
Email: legal@achillestx.com
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

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

Title of class	Trading Symbol(s)	Name of each exchange on which registered
American Depositary Shares, each representing one ordinary share, nominal value of £0.001 per share	ACHL	Nasdaq Global Select Market
Ordinary shares, nominal value £0.001 per share*		Nasdaq Global Select Market *

* Not for trading, but only in connection with the registration of the American Depositary Shares.

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

None

Securities for which there is a reporting obligation pursuant to Section 15(d) of the Act:

None

Indicate the number of outstanding shares of each of the issuer's classes of capital or common stock as of the close of the period covered by the Annual Report:

Ordinary shares, nominal value £0.001 per share: 40,603,489 as of December 31, 2021

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

Yes ☐ No ☒

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

Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed pursuant to 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 an accelerated filer, a large accelerated filer, a non-accelerated filer, or an emerging growth company. See definition of "large accelerated filer," "accelerated filer," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

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

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

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

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

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

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

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

Item 17 ☐ Item 18 ☐

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

Yes ☐ No ☒

Auditor Name: KPMG, LLC Auditor Location: Reading, United Kingdom Auditor Firm ID: 1118

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GENERAL INFORMATION

All references in this Annual Report on Form 20-F, or Annual Report, to "Achilles," "ACHL," the "company," "we," "us" and "our" refer to Achilles Therapeutics plc and its consolidated subsidiaries, except where the context otherwise requires.

We own various trademark registrations and applications, and unregistered trademarks, including ACHILLES, PELEUS, VELOS and our corporate logo. All other trade names, trademarks and service marks referred to in this Annual Report, are the property of their respective owners. Trade names, trademarks and service marks of other companies appearing in this Annual Report are the property of their respective holders. Solely for convenience, the trademarks and trade names in this Annual Report may be referred to without the ® and ™ symbols, but such references should not be construed as an indicator that their respective owners will not assert their rights thereto to the fullest extent under applicable law. We do not intend to use or display other companies' trademarks or trade names to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

Our audited consolidated financial statements were prepared in accordance with generally accepted accounting principles in the United States, or U.S. GAAP, as issued by the Financial Accounting Standards Board, or FASB. Our consolidated financial statements are presented in U.S. Dollars. All references in this Annual Report to "$" are to U.S. dollars and all references to "£" and "GBP" are to pounds sterling. Unless otherwise indicated, certain pounds sterling amounts contained in this Annual Report have been translated into U.S. dollars at the rate of $1.3497 to £1.00, on December 31, 2021, the last business day of our fiscal period ended December 31, 2021. Throughout this Annual Report, references to "ADSs" mean American Depositary Shares or ordinary shares represented by American Depositary Shares, as the case may be.

CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, that involve substantial risks and uncertainties. The forward-looking statements are contained principally in Part I, Item 4.B "Business Overview," Part I, Item 3.D. "Risk Factors," and Part I, Item 5. "Operating and Financial Review and Prospects," but are also contained elsewhere in this Annual Report. In some cases, you can identify forward-looking statements by the words "may," "might," "will," "could," "would," "should," "expect," "intend," "plan," "objective," "anticipate," "believe," "estimate," "predict," "potential," "continue" and "ongoing," or the negative of these terms, or other comparable terminology intended to identify statements about the future. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. The forward-looking statements contained in this Annual Report are based upon information available to us as of the date of this Annual Report and, while we believe we have a reasonable basis for each forward-looking statement contained this Annual Report, we caution you that these statements are based on a combination of facts and factors currently known by us and our expectations of the future, about which we cannot be certain.

By their nature, forward-looking statements involve risks and uncertainties because they relate to events, competitive dynamics and industry change, and depend on economic circumstances that may or may not occur in the future or may occur on longer or shorter timelines than anticipated. Although we believe that we have a reasonable basis for each forward-looking statement contained in this Annual Report, we caution you that forward-looking statements are not guarantees of future performance and involve known and unknown risks, uncertainties and other factors that are in some cases beyond our control. All of our forward-looking statements are subject to risks and uncertainties that may cause our actual results to differ materially from our expectations. These forward-looking statements include, without limitation, statements about the following:

- the success, cost, enrollment and timing of our clinical trials;
- the success, cost and timing of our research activities;
- the timing, scope or likelihood of regulatory filings and approvals, including timing of Investigational New Drug Application and Biologics License Application filings for our current and future programs and any future product candidates, and final U.S. Food and Drug Administration, European Medicines Agency, United Kingdom Medicines and Healthcare products Regulatory Agency or other foreign regulatory authority approval of our current programs or follow-on indications and any future product candidates;
- our ability to develop and advance additional follow-on indications as well as any future product candidates into, and successfully complete, clinical studies;
- our ability to continue to innovate, improve and develop our technology platform, including continuing to develop and improve our PELEUS bioinformatic platform and VELOS manufacturing process and to evaluate new approaches to our manufacturing process;
- our ability to expand our Material Acquisition Platform, or MAP, network to increase our network of clinical sites;
- our ability to establish future collaborations or strategic relationships or obtain additional funding;
- the rate and degree of market acceptance and clinical utility of our current and future programs and any future product candidates we may develop;
- our intellectual property position, including the scope of protection we are able to establish and maintain for intellectual property rights covering product candidates we may develop, including the validity of intellectual property rights held by third parties, and our ability not to infringe, misappropriate or otherwise violate any third-party intellectual property rights;
- regulatory developments in the United States, the United Kingdom, the European Union and other countries and regions;
- competitive companies, technologies and our industry and the success of competing therapies that are or may become available;
- our ability to attract and retain key scientific or management personnel;

- our ability to obtain funding for our operations, including funding necessary to complete further development and commercialization of our product candidates, if approved;
- the accuracy of our estimates of our future revenue, expenses, capital requirements and needs for additional financing;
- our estimates regarding the market opportunities for our current and future programs and any future product candidates;
- whether we are classified as a controlled foreign corporation and/or passive foreign investment company for current and future periods; and
- our ability to overcome the challenges posed by the ongoing COVID-19 pandemic to the conduct of our business.

In addition, even if our results, performance, financial condition and liquidity, and the development of the industry in which we operate are consistent with such forward-looking statements, they may not be predictive of results or developments in future periods. Among the factors that may result in differences are our expectations regarding risks and uncertainties related to the impact of the ongoing COVID-19 pandemic on our business, operations, strategy, goals and anticipated milestones, including our ongoing and planned research activities, ability to conduct ongoing and planned clinical trials, clinical supply of current or future drug candidates, commercial supply of current or future approved products, and launching, marketing and selling current or future approved products, and our ability to obtain and maintain requisite regulatory approvals and to enroll patients in our planned clinical trials, additional interactions with regulatory authorities and expectations regarding future regulatory filings, our reliance on collaborations with third parties, estimating the commercial potential of our development programs and other risks indicated in the risk factors included in this report and other filings with the U.S. Securities and Exchange Commission, or the SEC.

Actual results could differ materially from our forward-looking statements due to a number of factors, including the risks set forth under the section “Risk Factors” of this report and elsewhere in this Annual Report.

Any forward-looking statements that we make in this Annual Report are valid only as of the date of such statements, and we undertake no obligation to update such statements to reflect events or circumstances after the date of this Annual Report or to reflect the occurrence of unanticipated events.

SUMMARY OF THE MATERIAL AND OTHER RISKS ASSOCIATED WITH OUR BUSINESS

Below is a summary of the material risks to our business, operations and the investment in our ADSs. This summary does not address all of the risks that we face. Risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations. Additional discussion of the risks summarized in this risk factor summary, and other risks that we face, can be found below and should be carefully considered, together with other information in this Annual Report on Form 20-F in its entirety before making investment decisions regarding our ADSs.

- *Risks Related to our Financial Position and Capital Needs*
    - We have incurred significant losses since inception, and we expect to incur losses over the next several years and may not be able to achieve or sustain revenues or profitability in the future.
    - We will need substantial additional funding to achieve our goals, and a failure to raise additional capital when needed on acceptable terms, or at all, could force us to delay, reduce or eliminate our product development programs or commercialization efforts.

- *Risks Related to the Development of our Programs*
    - We are early in our development efforts. Our business is dependent on the successful development of ATL001 and future product candidates. If we are unable to advance our current programs, additional follow-on indications for ATL001 or any future product candidates into and through clinical trials, obtain marketing approval and ultimately commercialize some, any or all of the product candidates we develop, or experience significant delays in doing so, our business will be materially harmed.
    - Clinical development involves a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future clinical trial results. We may encounter substantial delays in clinical trials, or may not be able to conduct or complete clinical trials on the expected timelines, if at all. If our research activities and clinical trials are not sufficient to support regulatory development and approval of some, all or any of our programs for ATL001 or any future product candidates, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development of such program or product candidate.
    - Our business is highly dependent on the success of our product candidate, ATL001, which was developed based on our PELEUS platform and utilizing our VELOS manufacturing process. All of our future product candidates are based, or will be based, on the same technologies and the failure of ATL001 may adversely affect their development.
    - ATL001 or any of our future product candidates may cause undesirable side effects or have other properties that could halt their clinical development, prevent their regulatory approval, require expansion of the trial size, limit their commercial potential, or result in significant negative consequences. For example, in our ongoing trials, we have observed two serious adverse events that were deemed related or possibly related to ATL001.

- *Risks Related to our Approach to Product Development*
    - Our approach to the identification and manufacture of product candidates represents a novel approach to cancer treatment, which creates significant challenges for us. Generation of any cellular therapy, including our clonal neoantigen-reactive T-cell therapy, or cNeT, that specifically targets multiple clonal neoantigens to eradicate the tumor of an individual patient requires several weeks, in part reflecting the need to generate patient-specific genomic data and perform the bioinformatic analyses prior to initiation of manufacture. During the period from procurement of tumor and blood to completion of manufacturing, patients continue to receive standard of care therapies. In cases where disease progression is rapid, clinical deterioration of a patient's condition during the manufacturing period may mean that the patient is no longer able to receive our cNeT.

- *Risks Related to Manufacturing and Supply*

    - We have no experience manufacturing ATL001 at commercial scale. Manufacturing and administering ATL001 is complex and we may encounter difficulties in production, particularly with respect to scaling up our manufacturing capabilities. If we encounter such difficulties, our ability to provide supply of our cNeT for clinical trials or for commercial purposes could be delayed or stopped.
    - Our supply chain network is exposed to potentially adverse events such as physical disruptions, environmental and industrial accidents, trade restrictions, increases in the cost of raw materials or disruptions at a key supplier which could seriously harm our development efforts, increase our costs and expenses and have a material adverse effect on our business, financial condition and results of operations.
    - Cell-based therapies and biologics rely on the availability of reagents, specialized equipment, and other specialty materials, which may not be available to us on acceptable terms or at all. For some of these reagents, equipment, and materials, we rely or may rely on sole source vendors or a limited number of vendors, which could impair our ability to manufacture and supply our products.

- *Risks Related to Sales, Marketing and Competition*

    - We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

- *Risks Related to Protecting our Intellectual Property*

    - If we fail to comply with our current or future obligations in any agreements under which we may license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our current or future licensors, we could lose license rights that are important to our business.
    - If we are unable to obtain and maintain sufficient patent and other intellectual property protection for ATL001 and any future product candidates and technologies, our competitors could develop and commercialize products and technologies similar or equivalent to ours, and we may not be able to compete effectively in our market or successfully commercialize any product candidates we may develop.

- *Risks Related to our Business Operations and Growth*

    - The ongoing spread of COVID-19, and the proliferation of variants capable of escaping the coverage of available vaccines, has caused, and could continue to cause, severe disruptions in the global economy and could seriously harm our development efforts, increase our costs and expenses and have a material adverse effect on our business, financial condition and results of operations.

PART I

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

Not applicable.

Item 2. Offer Statistics and Expected Timetable.

Not applicable.

Item 3. Key Information.

A. [Reserved.]

B. Capitalization and Indebtedness.

Not applicable.

C. Reasons for the Offer and Use of Proceeds.

Not applicable.

D. Risk Factors.

Our business faces significant risks. You should carefully consider all of the information set forth in this Annual Report and in our other filings with the SEC including the following risk factors which we face and which are faced by our industry, any of which could materially adversely affect our business, financial condition, or results of operations. The risks and uncertainties summarized and described below are not intended to be exhaustive and are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business, prospects, financial condition and results of operations. This Annual Report also contains forward-looking statements that involve risks and uncertainties. Our results could materially differ from those anticipated in these forward-looking statements as a result of certain factors including the risks described below and elsewhere in this Annual Report and our other SEC filings. See also the "Statement Regarding Forward-Looking Statements" above.

RISKS RELATED TO OUR FINANCIAL POSITION AND CAPITAL NEEDS

Risks Related to our Financial Condition

We have incurred significant losses since inception, and we expect to incur losses over the next several years and may not be able to achieve or sustain revenues or profitability in the future.

Investment in biopharmaceutical product development is a highly speculative undertaking and entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate efficacy or an acceptable safety profile, gain regulatory approval and become commercially viable. We are still in the early stages of development of ATL001 for our lead indications in advanced non-small cell lung cancer, or NSCLC, metastatic or recurrent melanoma and follow–on indications including head and neck squamous cell carcinomas, or HNSCC. We have no products approved for commercial sale and have not generated any revenue from product sales to date, and we continue to, and will for the foreseeable future, incur significant research and development and other expenses related to our ongoing operations. We have financed our operations primarily through private placements of our preferred shares and our initial public offering, or IPO which we completed in April 2021.

We have incurred significant operating losses in each period since our inception in May 2016. For the years ended December 31, 2021 and 2020, we reported net losses of $61.1 million and $33.2 million, respectively. As of December 31, 2021, we had an accumulated deficit of $119.1 million. We expect to continue to incur significant losses for the foreseeable future, and we expect these losses to increase substantially in connection with our ongoing activities, particularly if and as we:

- continue to develop our pipeline of discovery programs and conduct research and clinical activities for our existing programs for advanced NSCLC, metastatic or recurrent melanoma, HNSCC and other solid tumors;
- continue to innovate, improve and develop our technology platform, including continuing to develop and improve our PELEUS bioinformatic platform and VELOS manufacturing process and to evaluate new approaches to our manufacturing process;
- expand our MAP network to increase our network of clinical sites;
- advance the development of our current programs, additional follow-on indications and any future product candidates into additional solid tumor indications;
- maintain, expand and protect our intellectual property portfolio;
- seek marketing approvals and complete any post-marketing studies, if required, for any of our product candidates that successfully complete clinical trials, if any;
- acquire or in-license additional product candidates and technologies;
- expand our infrastructure and facilities to accommodate our growing employee base and ongoing development activity;
- continue to improve our manufacturing process to create a fully closed end-to-end manufacturing process;
- expand our manufacturing infrastructure and facilities to support the manufacture of larger quantities of our product candidates for clinical development and potential commercialization globally;
- establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval;
- add operational, financial and management information systems and personnel, including personnel to support our research and development programs and any future commercialization efforts; and
- incur additional legal, accounting and other expenses in operating our business, including the costs associated with operating as a public company.

Because of the numerous risks and uncertainties associated with biopharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses we will incur or when, if ever, we will be able to achieve profitability. Even if we succeed in commercializing one or more product candidates, we will continue to incur substantial research and development and other expenditures to develop and market additional programs and product candidates and we may never generate revenue that is significant or large enough to achieve profitability. We may also encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. Our prior losses and expected future losses have had and will continue to have an adverse effect on our shareholders' equity and working capital.

Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Accordingly, our failure to become and remain profitable would decrease the value of the company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations.

We have not generated any revenue and may never be profitable.

Our ability to become profitable depends upon our ability to generate revenue. To date, we have not generated any revenue from ATL001 for any indication. We do not expect to generate significant revenue from ATL001 and any potential future product candidates unless or until we successfully complete clinical development and obtain regulatory approval of, and then successfully commercialize, such product candidates. ATL001 and any other product candidates that we develop will require additional research, clinical development, regulatory review and approval, substantial investment, access to sufficient commercial manufacturing capacity and significant marketing efforts

before we can generate any revenue from product sales. Our ability to generate revenue depends on a number of factors, including, but not limited to:

- timely completion of our research activities and clinical trials, which may be significantly slower or cost more than we currently anticipate;
- our ability to develop ATL001 for our current pipeline of indications and additional follow-on indications as well as to identify and develop potential new product candidates;
- our ability to complete IND-enabling activities, and successfully submit INDs or comparable applications for ATL001 in additional follow-on indications or any future product candidates;
- our successful initiation, enrollment in and completion of clinical trials, including our ability to generate positive data from any such clinical trials, including our ongoing Phase I/IIa clinical trials of ATL001 in advanced NSCLC and metastatic or recurrent melanoma;
- whether we are required by the U.S. Food and Drug Administration, or the FDA, the European Medicines Agency, or the EMA, or the United Kingdom Medicines and Healthcare products Regulatory Agency, or the MHRA, or similar foreign regulatory authorities to conduct additional clinical trials or other studies beyond those planned to support the approval and commercialization of ATL001 in our current indications or any follow-on indications as well as any future product candidates;
- our ability to demonstrate to the satisfaction of the FDA, the EMA, the MHRA and similar foreign regulatory authorities the safety, potency, purity, efficacy and acceptable risk to benefit profile of our current programs, additional follow-on indications for ATL001, or any future product candidates and such regulatory authorities' acceptance of our precision clonal neoantigen-reactive T cells, or cNeT, therapy-based development strategy;
- the prevalence, duration and severity of potential side effects or other safety issues experienced with our current programs, additional follow-on indications for ATL001, or future product candidates, if any;
- our ability to receive marketing approvals from the FDA, the EMA, the MHRA and similar foreign regulatory authorities;
- the willingness of physicians, operators of clinics and patients to utilize or adopt ATL001 or future product candidates, if approved, over alternative or more conventional approaches, such as standard tumor infiltrating lymphocyte, or TIL, therapy and other immuno-oncology therapies;
- the actual and perceived availability, cost, risk profile and safety and efficacy of our product candidates, if approved, relative to existing and future alternative immuno-oncology therapies and competitive product candidates and technologies;
- our ability to successfully increase our MAP network, including the acquisition, transportation, handling of, and management of other logistics relating to, patient tumor and other samples;
- our ability and the ability of third parties with whom we may contract to manufacture adequate clinical and commercial supplies of our product candidates or any future product candidates, remain in good standing with regulatory authorities and develop, validate and maintain commercially viable manufacturing processes that are compliant with current good manufacturing practices, or cGMP, requirements;
- our ability to successfully develop a commercial strategy and thereafter commercialize our current programs, additional follow-on indications for ATL001, or any future product candidates in the United States and internationally, if approved for marketing, reimbursement, sale and distribution in such countries and territories, whether alone or in collaboration with others;
- patient demand for our current programs, additional follow-on indications for ATL001, and any future product candidates, if approved;
- our ability to establish and enforce intellectual property rights; and
- our ability to maintain a continued acceptable safety profile in any approved product candidate.

Many of the factors listed above are beyond our control and could cause us to experience significant delays or prevent us from obtaining regulatory approvals or commercializing our product candidates. Even if we are able to commercialize our product candidates, we may not achieve profitability soon after generating product sales, if ever. If we are unable to generate sufficient revenue through the sale of our product candidates or any future product candidates, we may be unable to continue operations without continued funding.

Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

We are a clinical-stage company with a limited operating history. We commenced operations in May 2016, and our operations to date have been limited to organizing and staffing our company, business planning, raising capital, conducting discovery and research activities, filing patent applications, identifying potential product candidates, undertaking research activities and clinical trials and establishing our in-house manufacturing capabilities for the manufacture of initial quantities of our product candidates and component materials. Our lead programs in advanced NSCLC and metastatic or recurrent melanoma are in Phase I/IIa clinical trials, CHIRON and THETIS, respectively. We also have ongoing and planned IND-enabling activities for ATL001 in follow-on indications, such as HNSCC. We have not yet demonstrated our ability to successfully complete any clinical trials, obtain marketing approvals, manufacture a commercial-scale product or arrange for a third party to do so on our behalf, or conduct sales, marketing and distribution activities necessary for successful product commercialization. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

In addition, as an early-stage company, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will need to transition at some point from a company with a research and development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

We expect our financial condition and results of operations to continue to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

Risks Related to our Future Cash Needs

We will need substantial additional funding to achieve our goals, and a failure to raise additional capital when needed on acceptable terms, or at all, could force us to delay, reduce or eliminate our product development programs or commercialization efforts.

Since our inception, we have invested a significant portion of our efforts and financial resources in research and development activities for our PELEUS platform, our VELOS manufacturing process, development of our lead programs for ATL001 and identification and development of follow-on indications for ATL001. Clinical trials and additional research and development activities will require substantial funds to complete. We expect our expenses to increase in parallel with our ongoing activities, particularly as we continue the research and clinical development activities of our current programs, including our ongoing Phase I/IIa clinical trials of ATL001 in advanced NSCLC and metastatic or recurrent melanoma, our planned Phase I/IIa clinical trial of ATL001 in HNSCC and our ongoing and planned IND-enabling activities for ATL001 in follow-on indications, such as renal cell carcinoma, or RCC. In addition, if we obtain marketing approval for any product candidate, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. We have incurred and expect to continue to incur significant additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. Additionally, changing circumstances may cause us to consume capital significantly faster than we currently anticipate, and we may need to spend more money than currently expected because of circumstances beyond our control. We cannot be certain that additional funding will be available on acceptable terms, or at all. Until such time, if ever, as we can generate substantial product revenue, we expect to finance our operations through a combination of public or private equity offerings, debt financings, governmental funding, collaborations, strategic partnerships and alliances or marketing, distribution or licensing arrangements with third parties. If we are unable to raise capital when needed in sufficient amounts or on terms acceptable to us, we would be forced to delay, reduce or eliminate our discovery and research programs or any future commercialization efforts.

We had cash and cash equivalents of $266.3 million as of December 31, 2021. We believe that, based upon our current operating plan, our existing capital resources will be sufficient to fund our anticipated operations into the second half of 2024. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. In addition, because the design and outcome of our ongoing, planned and anticipated clinical trials are highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of any product candidate. Our future capital requirements will depend on many factors, including:

- the scope, progress, results and costs of research activities and clinical trials for our current programs, additional follow-on indications for ATL001 and any future product candidates, including any additional expenses attributable to adjusting our development plans in response to the COVID-19 pandemic;
- the continued development and expansion of our PELEUS platform;
- the continued development of and improvements to our VELOS manufacturing process;
- the extent to which we enter into collaboration arrangements with regard to product candidate development or acquire or in-license products or technologies;
- the costs, timing and outcome of regulatory review of ATL001 for our current programs and follow-on programs, and any future product candidates, including post-marketing studies that could be required by regulatory authorities;
- the costs of future commercialization activities, including product sales, marketing, manufacturing and distribution, for any product candidate for which we receive marketing approval;
- the costs of continued scale-up and automation of our VELOS manufacturing processes, including developing a fully closed end-to-end system, for later stages of development and commercialization;
- the costs of expanding our manufacturing infrastructure and facilities to support the manufacture of larger quantities of our product candidates for clinical development and potential commercialization globally;
- the costs associated with continuing to increase our MAP network;
- revenue, if any, received from commercial sales of our product candidates, should any of our product candidates receive marketing approval; and
- the costs of preparing, filing and prosecuting patent applications, obtaining, maintaining, enforcing and protecting our intellectual property rights and defending intellectual property-related claims.

Identifying additional follow-on indications for ATL001 and future product candidates and conducting research activities and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, any product candidate, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

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

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

We expect our expenses to increase in connection with our planned operations. Unless and until we can generate a substantial amount of revenue from our product candidates, we expect to finance our future cash needs through public or private equity offerings, debt financings, collaborations, licensing arrangements or other sources, or any combination of the foregoing. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans.

To the extent that we raise additional capital through the sale of ADSs, convertible securities or other equity securities, your ownership interest may be diluted, and the terms of these securities could include liquidation or other preferences and anti-dilution protections that could adversely affect your rights as a shareholder.

In addition, debt financing, if available, may result in fixed payment obligations and may involve agreements that include restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures, creating liens, redeeming shares or declaring dividends, that could adversely impact our ability to conduct our business. In addition, securing financing could require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect our management's ability to oversee the development of our current programs, additional follow-on indications for ATL001, and any future product candidates.

If we raise additional funds through collaborations, strategic alliances, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds when needed, we would be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

RISKS RELATED TO THE DEVELOPMENT OF OUR PROGRAMS

Risks Related to Research Activities and Clinical Development

We are early in our development efforts. Our business is dependent on the successful development of ATL001 and future product candidates. If we are unable to advance our current programs, additional follow-on indications for ATL001 or any future product candidates into and through clinical trials, obtain marketing approval and ultimately commercialize some, any or all of the product candidates we develop, or experience significant delays in doing so, our business will be materially harmed.

All of our programs are in early stages of development, including our clinical-stage programs for ATL001 in advanced NSCLC, metastatic or recurrent melanoma, and as such will require extensive research activities and clinical testing, as applicable. Our ability to generate product revenues, which we do not expect to occur for several years, if ever, will depend heavily on the successful development and eventual commercialization of the programs and product candidates we develop, which may never occur. Before we are able to generate any revenues from product sales, our current programs, additional follow-on indications for ATL001 or any future product candidates we develop, will require additional research activities and clinical development, management of clinical, research and manufacturing activities, marketing approval in the United States and other markets, demonstrating effectiveness to pricing and reimbursement authorities, obtaining sufficient manufacturing supply for both clinical development and commercial production, building of a commercial organization, and substantial investment and significant marketing efforts. The success of our current programs, additional follow-on indications for ATL001 or any future product candidates will depend on several factors, including the following:

- successful completion of research activities and clinical trials;
- sufficiency of our financial and other resources to complete the necessary research activities and clinical trials;
- regulatory authority acceptance of INDs, clinical trial applications or similar approaches required for us to commence our planned clinical trials or future clinical trials;
- successful patient enrollment in and completion of our ongoing and future clinical trials;
- successful data from our clinical trials that support an acceptable risk-benefit profile of our product candidates in the intended populations;
- receipt and maintenance of marketing approvals from applicable regulatory authorities;

- continued scale-up and automation of our VELOS manufacturing processes, including developing a fully closed end-to-end system, for later stages of development and commercialization;
- obtaining and maintaining patent and trade secret protection or regulatory exclusivity for our product candidates;
- establishing sales, marketing and distribution capabilities and launching commercial sales of our products, if and when approved, whether alone or in collaboration with others;
- entry into collaborations to further the development of our product candidates, if necessary;
- successfully launching commercial sales of our product candidates, if and when approved;
- acceptance of our product candidates, if and when approved, by patients, the medical community and third-party payors;
- the prevalence and severity of adverse events experienced with our product candidates;
- effectively competing with other cancer therapies;
- obtaining and maintaining healthcare coverage and adequate reimbursement from third-party payors;
- maintaining a continued acceptable safety profile of our products following approval, if any; and
- qualifying for, maintaining, enforcing and defending intellectual property rights and claims.

We do not have complete control over many of these factors, including certain aspects of clinical development and the regulatory approval process, potential threats to our intellectual property rights and the manufacturing, marketing, distribution and sales efforts of any future collaborator. If we are not successful with respect to one or more of these factors in a timely manner or at all, we could experience significant delays or be unable to successfully commercialize ATL001 and any future product candidates we develop, which would materially harm our business.

Clinical development involves a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future clinical trial results. We may encounter substantial delays in clinical trials, or may not be able to conduct or complete clinical trials on the expected timelines, if at all. If our research activities and clinical trials are not sufficient to support regulatory development and approval of some, all or any of our programs for ATL001 or any future product candidates, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development of such program or product candidate.

Before obtaining marketing approval from the FDA or other comparable foreign regulatory authorities for the sale of our product candidates, we must complete preclinical development and extensive clinical trials to demonstrate the safety, purity and potency of our product candidates. Clinical testing is expensive, time-consuming and subject to uncertainty. Clinical data are often susceptible to varying interpretations and analyses and many companies that believed their product candidates performed satisfactorily in clinical trials nonetheless failed to obtain FDA approval or approval from foreign regulatory authorities. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical development even after achieving promising results in earlier studies, and any such setbacks in our clinical development could have a material adverse effect on our business and operating results. It is impossible to predict when or if ATL001 in any of our current programs, ATL001 in any additional follow-on indications or any future product candidates will prove effective and safe in humans or will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete research activities and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical development testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. There can be no assurance that any of our current or future clinical trials will ultimately be successful or support further clinical development of any of our product candidates. There is a high failure rate for investigational drugs proceeding through clinical trials.

We may experience delays in initiating or completing research activities or clinical trials, including as a result of delays in obtaining, or failure to obtain, the FDA's clearance to initiate clinical trials under future INDs, completing ongoing research activities for our other product candidates and initiating our planned clinical trials. Additionally, we cannot be certain that clinical trials will begin on time, not require redesign, enroll an adequate number of subjects on

time, or be completed on schedule, if at all. We may experience numerous adverse or unforeseen events during, or as a result of, research activities and clinical trials that could delay or prevent our ability to receive marketing approval or commercialize ATL001 for any indication or any future product candidates, including:

- we may receive feedback from regulatory authorities that requires us to modify the design of our clinical trials;
- research activities or clinical trials of ATL001 or any future product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon our research efforts for our other product candidates;
- research activities or clinical trials of ATL001 or any future product candidates may not produce differentiated or clinically significant results across cancers and we may decide not to pursue further clinical development of such product candidates accordingly;
- the number of patients required for clinical trials of ATL001 or any future product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of our clinical trials at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements, fail to maintain adequate quality controls or be unable to provide us with sufficient product supply to conduct and complete clinical trials of ATL001 or any future product candidates in a timely manner, or at all;
- we or our investigators might have to suspend or terminate clinical trials of ATL001 or any future product candidates for various reasons, including non-compliance with regulatory requirements, a finding that our product candidates have undesirable side effects or other unexpected characteristics or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of ATL001 or any future product candidates may be greater than we anticipate;
- the quality of our product candidates or other materials necessary to conduct research activities or clinical trials of ATL001 or any future product candidates may be insufficient or inadequate, and our PELEUS platform may not be able to accurately identify clonal neoantigens that are effective to treat solid tumors;
- reports from clinical testing of other therapies may raise safety or efficacy concerns about ATL001 or any future product candidates;
- regulators may revise the requirements for approving ATL001 or any future product candidates, or such requirements may not be as we anticipate; and
- future collaborators may conduct clinical trials in ways they view as advantageous to them but that are suboptimal for us.

In addition, disruptions caused by the ongoing COVID-19 pandemic may increase the likelihood that we encounter difficulties or delays in initiating, enrolling, conducting or completing our planned and ongoing clinical trials. If we are required to conduct additional clinical trials or other testing of our current programs, additional follow-on indications for ATL001 or any future product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials or other testing, if the results of these trials or tests are not positive or are only moderately positive or if there are safety concerns, our business and results of operations may be adversely affected and we may incur significant additional costs. Additionally, as of May 26, 2021, the FDA noted it is continuing to ensure timely reviews of applications for medical products during the ongoing COVID-19 pandemic in line with its user fee performance goals. However, the FDA may not be able to continue its current pace and approval timelines could be extended, including where a pre-approval inspection or an inspection of clinical sites is required and due to the ongoing COVID-19 pandemic and travel restrictions FDA is unable to complete such required inspections during the review period. During the COVID-19 public health emergency, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the institutional review boards, or IRBs, or ethics committees of the institutions in which such clinical trials are being conducted, or by the FDA or other regulatory authorities, or suspended or terminated based on recommendations by the Independent Data and Safety Monitoring Committee, or IDSMC, if any, for such clinical trial. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory

requirements or our clinical trial 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 the product candidates, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

If we experience delays in the completion, or termination, of any clinical trial for our current programs, additional follow-on indications for ATL001 or of any future product candidates, the commercial prospects of ATL001 or our any future product candidates may be harmed, and our ability to generate revenues from ATL001 or any future product candidates will be delayed or not realized at all. In addition, any delays in completing our research activities or clinical trials may increase our costs, slow down our development and approval process and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences may significantly harm our business, financial condition and prospects. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of ATL001 or any future product candidates. If ATL001 or any future product candidates are generally observed to be ineffective, unsafe or commercially unviable, our entire pipeline may have little, if any, value, which would have a material and adverse effect on our business, financial condition, results of operations and prospects.

Our business is highly dependent on the success of our product candidate, ATL001, which was developed based on our PELEUS platform and utilizing our VELOS manufacturing process. All of our future product candidates are based, or will be based, on the same technologies and the failure of ATL001 may adversely affect their development.

A key element of our strategy is utilizing our PELEUS platform to identify clonal neoantigens that are effective in treating solid tumors coupled with using our VELOS manufacturing process to manufacture cNeT. The therapeutic discovery activities that we are conducting may not be successful in identifying clonal neoantigens and we may not be successful in manufacturing precision TIL product candidates. We currently have no products that are approved for commercial sale and may never be able to develop marketable products. We are very early in our development efforts, and we only have two clinical-stage programs, ATL001 for the treatment of advanced NSCLC and metastatic or recurrent melanoma, which are in early clinical-stage trials. In the event that our current programs for ATL001, additional follow-on indications for ATL001, such as HNSCC, or future product candidates, encounter safety or efficacy problems, developmental delays, regulatory issues, or other problems, our development plans and business related to our other current or future product candidates could be significantly harmed. A failure of ATL001 or future product candidates may affect the ability to obtain regulatory approval to continue or conduct clinical programs for our other or future product candidates.

Our research activities and clinical trials may fail to demonstrate adequately the safety, potency and purity of ATL001 or any future product candidates, which would prevent or delay development, regulatory approval and commercialization.

Before obtaining regulatory approvals for the commercial sale of any product candidate, including ATL001, we must demonstrate through lengthy, complex and expensive research activities and clinical trials that our product candidates are both safe and effective for use in each target indication. Research activities and 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 processes, and, because ATL001 is in an early stage of development, there is a high risk of failure and we may never succeed in developing marketable products.

Any clinical trials that we may conduct may not demonstrate the safety, potency, purity and efficacy necessary to obtain regulatory approval to market our product candidates. If the results of our ongoing or future clinical trials are inconclusive with respect to the safety, potency, purity and efficacy of our product candidates, if we do not meet the clinical endpoints with statistical and clinically meaningful significance, or if there are safety concerns associated with our product candidates, we may be prevented or delayed in obtaining marketing approval for such product candidates. In some instances, there can be significant variability in safety, potency or purity results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in

protocols, manufacturing variances in our VELOS manufacturing process, differences in the size and type of the patient populations, changes in and adherence to the clinical trial protocols and the rate of dropout among clinical trial participants.

Additionally, our currently ongoing Phase I/IIa clinical trials are and any additional clinical trials that we may conduct may be open-label in study design and may be conducted at a limited number of clinical sites on a limited number of patients. An "open-label" clinical trial is one where both the patient and investigator know whether the patient is receiving the investigational product candidate or either an existing approved drug or placebo. Most typically, open-label clinical trials test only the investigational product candidate and sometimes may do so at different dose levels. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect, as patients in open-label clinical trials are aware when they are receiving treatment. Open-label clinical trials may be subject to a "patient bias" where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. In addition, open-label clinical trials may be subject to an "investigator bias" where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. The results from an open-label trial may not be predictive of future clinical trial results with any of our product candidates for which we include an open-label clinical trial when studied in a controlled environment with a placebo or active control.

ATL001 or any of our future product candidates may cause undesirable side effects or have other properties that could halt their clinical development, prevent their regulatory approval, require expansion of the trial size, limit their commercial potential, or result in significant negative consequences.

Undesirable side effects caused by our product candidates could cause us or regulatory authorities, including IRBs, to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA, the EMA, the MHRA or other comparable foreign regulatory authorities. For example, in our ongoing trials, two patients were considered by the investigator to have experienced immune effector cell-associated neurotoxicity syndrome, or ICANS. The investigator deemed the first serious adverse event to be related to ATL001. This patient was treated with dexamethasone and tocilizumab and their acute condition improved. However, the nature of this therapeutic intervention would be expected to suppress the expansion and persistence of the infused ATL001. Subsequent to this, the patient was admitted to hospice, and subsequently died, due to cancer disease progression. The second patient experienced neurological symptoms that worsened 109 days after administration of ATL001. The event was deemed a possible ICANS event, though the clinical presentation was very atypical for this. The patient also continued to experience disease progression and was ultimately put on end of life care and medical treatment was ceased. The case was reviewed by the IDSMC, including additional data from the post-mortem and translational science outputs related to cNet engraftment and cytokine release, with the final conclusion that the event was unlikely related to the treatment with ATL001. While we have not seen additional instances of ICANS in our trials, patients may experience future serious adverse events which could halt the trials. The FDA or comparable foreign regulatory authorities, or IRBs and other reviewing entities, may also require, or we may voluntarily develop, strategies for managing adverse events during clinical development, which could include restrictions on our enrollment criteria, the use of stopping criteria, adjustments to a study's design, reconsent of enrolled patients, or the monitoring of safety data by a data monitoring committee, among other strategies. FDA, the EMA, the MHRA or a comparable foreign regulatory authority requests for additional data or information could also result in substantial delays in the approval of our current product candidate and any future product candidates. Further, clinical trials by their nature utilize a sample of the potential patient population. With a limited number of subjects, rare and severe side effects of our product candidates may only be uncovered with a significantly larger number of patients exposed to the product candidate. Additionally, results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics, which may stem from our therapies specifically or may be due to an illness from which the clinical trial subject is suffering. If we do observe severe side effects in our clinical trials, our ongoing clinical trials may be halted or put on clinical hold prior to completion if there is an unacceptable safety risk for patients.

If unacceptable toxicities arise in the development of ATL001 or any future product candidates, we could suspend or terminate our clinical trials or the FDA, the EMA, the MHRA or comparable foreign regulatory authorities, or local regulatory authorities such as IRBs or ethics committees, could order us to cease clinical trials. Competent national health authorities, such as the FDA or foreign equivalents, could also deny approval of our product candidates for any or all targeted indications. Even if the side effects presented do not preclude the product from obtaining or maintaining marketing approval, treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete the clinical trial or result in potential product liability claims. We expect to have to train medical personnel using our product candidates to understand the adverse events associated with our treatment approach for both our planned clinical trials and upon any commercialization of any product candidates, if approved. Inadequate training in recognizing or managing the potential side effects of ATL001 or any future product candidates could result in patient harm, including deaths. Any of these occurrences may significantly harm our reputation, business, financial condition and prospects.

Interim, "topline," and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose preliminary or topline data from our clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, topline data should be viewed with caution until the final data are available. From time to time, we may also disclose interim data from our clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available or as patients from our clinical trials continue other treatments for their disease. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects. Further, disclosure of interim data by us or by our competitors could result in volatility in the price of our ADSs.

If the interim, topline, or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition. In addition, the information we choose to publicly disclose regarding a particular clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure.

If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

Identifying and qualifying patients to participate in clinical trials of ATL001 and our future product candidates is critical to our success. The timing of completion of our clinical trials depends in part on the speed at which we can recruit patients to participate in testing ATL001 and any future product candidates, and we may experience delays in our clinical trials if we encounter difficulties in enrollment or patient retention due to other unforeseen factors, including impacts that have resulted or may result from the ongoing COVID-19 pandemic. We may not be able to initiate or continue clinical trials for ATL001 or any future product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA, the EMA, the MHRA or similar foreign regulatory authorities outside the United States. For example, the evolving COVID-19 pandemic may

continue to impact our ability to initiate clinical sites and recruit, enroll and retain patients or may divert healthcare resources away from clinical trials. The enrollment of patients further depends on many factors, including:

- the patient eligibility criteria defined in the clinical trial protocol;
- the size of the patient population required for analysis of the clinical trial's primary endpoints;
- the severity of the disease or condition under investigation;
- the proximity of patients to clinical trial sites;
- the design of the clinical trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- our ability to obtain and maintain patient consents;
- the availability of competing trials;
- our ability to procure sufficient tumor and blood samples from the patient to enable isolation of sufficient TILs and dendritic cells to manufacture a cNeT product candidate, identify clonal neoantigens and transport our cNeT product candidate to the trial site;
- our ability to monitor patients adequately during and after treatment;
- the risk that patients enrolled in clinical trials will drop out of the clinical trials before the manufacturing and infusion of ATL001 or any future product candidates or clinical trial completion; and
- factors we may not be able to control, such as current or potential pandemics that may limit patients, principal investigators or staff or clinical site availability.

In addition, our clinical trials will compete with other clinical trials for product candidates that are in the same therapeutic areas as ATL001 or any future product candidates, and this competition will reduce the number and types of patients available to us because some patients who might have opted to enroll in our clinical trials may instead opt to enroll in a clinical trial being conducted by one of our competitors. Since the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials at such clinical trial sites. Moreover, because our product candidates represent a departure from more commonly used methods for cancer treatment, potential patients and their doctors may be inclined to use conventional therapies, such as chemotherapy, rather than enroll patients in any ongoing or planned clinical trials.

Delays in completing patient enrollment may result in increased costs or may affect the timing or outcome of our ongoing and planned clinical trials, which could prevent completion or commencement of these clinical trials and adversely affect our ability to advance the development of our product candidates.

Since the number of patients that we plan to dose in our ongoing open-label Phase I/IIa clinical trials is small, the results from these clinical trials, once completed, may be less reliable than results achieved in larger clinical trials, which may hinder our efforts to obtain regulatory approval for ATL001 or any future product candidates.

In our ongoing first-in-human, open-label Phase I/IIa clinical trials of ATL001 for our two lead tumor indications, we are evaluating the safety, tolerability and clinical activity of cNeT administered intravenously in adult patients with advanced NSCLC and metastatic or recurrent melanoma.

The results of clinical trials with smaller sample sizes, such as our ongoing Phase I/IIa clinical trials, can be disproportionately influenced by various biases associated with the conduct of small clinical trials, such as the potential failure of the smaller sample size to accurately depict the features of the broader patient population, which limits the ability to generalize the results across a broader community, thus making the clinical trial results less reliable than clinical trials with a larger number of patients. As a result, there may be less certainty that such product candidate would achieve a statistically significant effect in any future clinical trials. If we conduct any future clinical trials of ATL001, we may not achieve a statistically significant result or the same level of statistical significance, if any, that we might have anticipated based on the results observed in our initial Phase I/IIa clinical trials.

We are conducting clinical trials for product candidates outside the United States, and the FDA and comparable foreign regulatory authorities may not accept data from such trials.

We have expanded our clinical operations to the United States and Europe, in addition to conducting our clinical trials in the United Kingdom. The acceptance of data from clinical trials conducted outside the United States or another jurisdiction by the FDA, the EMA, the MHRA or comparable foreign regulatory authority may be subject to certain conditions or may not be accepted at all. In cases where data from foreign clinical trials are intended to serve as the basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless: (i) the data are applicable to the U.S. population and U.S. medical practice; (ii) the trials were performed by clinical investigators of recognized competence and pursuant to good clinical practice, or GCP, regulations; and (iii) the FDA is able to validate the data from the study through an on-site inspection if necessary. In general, the patient population for any clinical trials conducted outside the United States must be representative of the population for whom we intend to label the product candidate in the United States. Additionally, the FDA's clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. Many foreign regulatory authorities have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA, the EMA, the MHRA or any comparable foreign regulatory authority will accept data from trials conducted outside of the United States or the applicable jurisdiction. If the FDA, the EMA, the MHRA or any comparable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which could be costly and time-consuming, and which may result in product candidates that we may develop not receiving approval for commercialization in the applicable jurisdiction.

Risks Related to our Approach to Product Development

Our approach to the identification and manufacture of product candidates represents a novel approach to cancer treatment, which creates significant challenges for us.

A key element of our strategy is to focus on targeting clonal neoantigens for the treatment of solid tumors, to continue innovating and developing our PELEUS platform to further improve our clonal neoantigen prediction capability and to expand our pipeline into several additional solid tumor indications. To date, there are no approved immuno-oncology therapies based on targeting clonal neoantigens and we are not aware of any clinical evidence supporting the clinical efficacy of our approach. Although our research and development efforts to date have resulted in clinical development of ATL001 in advanced NSCLC and metastatic or recurrent melanoma, and planned development in HNSCC, ATL001 may not be safe or effective as a cancer treatment, and we may not be able to identify any additional follow-on indications for ATL001, or identify and develop any other product candidates. Further, our approach to manufacturing cNeT on a per patient basis means that we may fail to isolate TILs from the tumor, be unable to generate the necessary amounts of dendritic cells, or at all, or not be able to identify clonal neoantigens. We may also be limited by the extent to which the peptides representing those neoantigens are presented by dendritic cells. There is high variability in sample collection between patients, which presents additional challenges of producing cNeT on a per patient basis. Generation of any cellular therapy, including our cNeT, to specifically target the mutations of an individual patient requires several weeks, in part reflecting the need to generate patient-specific genomic data and perform the bioinformatic analyses prior to initiation of manufacture. During the period from procurement of tumor and blood to completion of manufacturing, patients continue to receive standard of care therapies. In cases where disease progression is rapid, clinical deterioration of a patient's condition during the manufacturing period may mean that the patient is no longer able to receive our cNeT. The continued improvement of our PELEUS platform also requires continued sourcing of tumor samples from the TRACKing Cancer Evolution through Therapy study, or the TRACERx Study, and our MAP network, and any interruption or termination of these programs could adversely affect our PELEUS platform. Though we are continuing to invest in optimizing our manufacturing process, there is no guarantee that our efforts will result in a decrease of the end-to-end time for production.

Even if we are successful in expanding our pipeline of ATL001 programs and other product candidates, the follow-on programs and product candidates that we identify may not be suitable for clinical development or generate

acceptable clinical data, including as a result of being shown to have unacceptable toxicity or other characteristics that indicate that they are unlikely to be products that will receive marketing approval from the FDA, the EMA, the MHRA or other regulatory authorities or achieve market acceptance. We may face challenges in obtaining regulatory approval for ATL001 or any future product candidate, as the FDA, the EMA, the MHRA and other regulatory authorities may have limited experience with bioinformatics-based therapies for cancer treatment. If we do not successfully develop and commercialize product candidates, we will not be able to generate product revenue in the future, which likely would result in significant harm to our financial position and adversely affect our commercial value.

Moreover, physicians, hospitals and third-party payors often are slow to adopt new products, technologies and treatment practices that require additional upfront costs and training. Treatment centers may not be willing or able to devote the personnel and establish other infrastructure required for the administration of our therapies. Based on these and other factors, health systems, hospitals and payors may decide that the benefits of this new therapy do not or will not outweigh its costs.

We anticipate that ATL001 and any future product candidates may be used in combination with third-party drugs or biologics, some of which are still in development, and we have limited or no control over the supply, regulatory status, or regulatory approval of such drugs.

ATL001 and any future product candidates have the potential to be administered in combination with approved therapeutics, such as checkpoint inhibitor immunotherapies. Our ability to develop and ultimately commercialize ATL001 and any future product candidates used in combination with checkpoint inhibitor immunotherapies or other therapeutics will depend on our ability to access such therapeutics on commercially reasonable terms for the clinical trials and their availability for use with the commercialized product, if approved.

Any failure to maintain or enter into new successful commercial relationships, or the expense of purchasing checkpoint inhibitor immunotherapies or other comparable therapies in the market, may delay our development timelines, increase our costs and jeopardize our ability to develop our current product candidate and any future product candidates as commercially viable therapies. If any of these occur, our business, financial condition, results of operations, share price and prospects may be materially harmed.

Moreover, the development of product candidates for use in combination with another product or product candidate may present challenges that are not faced for single agent product candidates. We may develop ATL001 and any future product candidates for use in combination with checkpoint inhibitor immunotherapies. Both of our THETIS and CHIRON clinical trials may seek to evaluate the safety and clinical activity of ATL001 when given in combination with, pembrolizumab and nivolumab, respectively, which are approved anti-PD-1 antibody therapies. The FDA, the EMA, the MHRA or comparable foreign regulatory authorities may require us to use more complex clinical trial designs in order to evaluate the contribution of each product and product candidate to any observed effects. It is possible that the results of such trials could show that any positive previous trial results are attributable to the combination therapy and not ATL001 and any future product candidates. Moreover, following product approval, the FDA, the EMA, the MHRA or comparable foreign regulatory authorities may require that products used in conjunction with each other be cross labeled for combined use. To the extent that we do not have rights to the other product, this may require us to work with a third party to satisfy such a requirement. Moreover, developments related to the other product may impact our clinical trials for the combination as well as our commercial prospects should we receive marketing approval. Such developments may include changes to the other product's safety or efficacy profile, changes to the availability of the approved product, quality, manufacturing and supply issues, and changes to the standard of care.

In the event that any future collaborator or supplier cannot continue to supply their products on commercially reasonable terms, we would need to identify alternatives for accessing checkpoint inhibitor immunotherapies or other comparable therapies. Additionally, should the supply of product from any future collaborator or supplier be interrupted, delayed or otherwise be unavailable to use or our collaborators, our clinical collaborations may be delayed.

In the event we are unable to source an alternative supply, or are unable to do so on commercially reasonable terms, our business, financial conditions, results of operations and prospects may be materially harmed.

We may expend our limited resources to pursue a particular follow-on indication for ATL001 or other product candidate and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we must focus on a limited number of research programs and product candidates and on specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future discovery and research programs and product candidates for specific indications may not yield any commercially viable products.

RISKS RELATED TO MANUFACTURING AND SUPPLY

We have no experience manufacturing ATL001 at commercial scale. Manufacturing and administering ATL001 is complex and we may encounter difficulties in production, particularly with respect to scaling up our manufacturing capabilities. If we encounter such difficulties, our ability to provide supply of our cNeT for clinical trials or for commercial purposes could be delayed or stopped.

ATL001 is designed to be a precision T cell therapy and the process of manufacturing it is complex, highly regulated and subject to multiple risks. As a result of these complexities, the cost to manufacture precision T cell therapies is generally higher than traditional small molecule chemical compounds or antibody therapies, and the manufacturing process for precision T cell therapies is less reliable and is more difficult to reproduce. More specifically, the manufacture of ATL001 involves procuring tumor and blood from the patient from which DNA is extracted and sequenced, using this sequencing data together with our PELEUS platform to identify each patient's unique clonal neoantigens, isolating T cells and dendritic cells from tumor and blood, respectively, manufacturing clonal neoantigen peptides and loading them onto dendritic cells to activate and expand a sub-set of the T cells, and ultimately generating a product enriched for cNeT, which is then re-infused into the patient's body. Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects, and other supply disruptions. Furthermore, manufacturing poses the risk of the inconsistency in product quality, which could lead to adverse events. If microbial, viral or other contaminations are discovered in our product candidates or in the manufacturing facilities in which our product candidates are made, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination. We cannot assure you that any stability failures or other issues relating to the manufacture of our product candidates will not occur in the future.

As ATL001 or any future product candidate progresses through 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. Any such changes may result in a clinical hold and may require amendments to be made to regulatory applications which may further delay the timeframes under which modified manufacturing processes can be used for any of our product candidates. In the fourth quarter of 2021, regulatory authorities in the UK, Germany, France and Spain in respect of CHIRON and in the UK in respect of THETIS allowed for a modified VELOS manufacturing process and a switch from our original Process 1 to a higher dose Process 2. VELOS Process 2 includes an optimized cytokine cocktail throughout the manufacturing process and additional media supplements for T cell expansion following the dendritic cell-driven co-culture step. VELOS Process 2 retains an identical manufacturing timeline to Process 1. We are in discussions with the FDA on the proposed switch of manufacturing to Process 2 and may continue to enroll subjects and administer ATL001 to U.S. patients per protocol using VELOS manufacturing Process 1 until the switch to Process 2 is approved.

Developing a commercially viable process is a difficult and uncertain task, and there are risks associated with scaling to the level required for advanced clinical trials or commercialization, including, among others, increased costs,

potential problems with process scale-out, process reproducibility, stability issues, lot consistency, and timely availability of reagents or raw materials. Competitors have had difficulty reliably producing TIL therapies. If we experience similar challenges manufacturing product candidates to approved specifications, this may limit our product candidates' utilization and our ability to receive payment for these product candidates once approved. We may ultimately be unable to reduce the expenses associated with our product candidates to levels that will allow us to achieve a profitable return on investment.

We lease a warehouse in west London, where we expect to commence construction of a flexible GMP modular facility to scale our manufacturing footprint where pre-assembled, or pod, cleanrooms can be brought online in a phased approach. The modular facility will support commercial supply for the United Kingdom and European Union, and will provide optionality to support U.S. operations. While over time we plan to establish further regional manufacturing facilities, we may not be successful in scaling up our manufacturing capabilities.

Our manufacturing process needs to comply with FDA 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 ensure compliance with the FDA's cGMP regulations and guidelines. We may encounter difficulties in achieving quality control and quality assurance and may experience shortages in qualified personnel. Our facilities are subject to inspections by the FDA, the EMA, the MHRA and comparable foreign regulatory authorities to confirm compliance with applicable regulatory requirements. Any failure to follow cGMP or other regulatory requirements or delay, interruption or other issues that arise in the manufacture, fill-finish, packaging, or storage of our precision medicines as a result of our failure to comply with regulatory requirements or pass any regulatory authority inspection could significantly impair our ability to develop and commercialize ATL001 and any future product candidates, including leading to significant delays in the availability of ATL001 and any future product candidates for our clinical trials or the termination of or suspension of a clinical trial, or the delay or prevention of a filing or approval of marketing applications for ATL001 or any future product candidates. Significant non-compliance could also result in the imposition of sanctions, including warning or untitled letters, fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approvals, 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.

If we use hazardous and biological materials for manufacturing in a manner that causes injury or violates applicable law, we may be liable for damages.

Our research and development activities involve the controlled use of potentially hazardous substances, including chemical and biological materials. We are, and will in future be, subject to federal, state and local laws and regulations in the United Kingdom governing the use, manufacture, storage, handling and disposal of biological and hazardous materials. Although we believe that our procedures for using, handling, storing and disposing of these materials comply with legally prescribed standards, we cannot completely eliminate the risk of contamination or injury resulting from medical or hazardous materials. As a result of any such contamination or injury, we may incur liability or local, city, state or federal authorities may curtail the use of these materials and interrupt our business operations. In the event of an accident, we could be held liable for damages or penalized with fines, and the liability could exceed our resources. We do not have any insurance for liabilities arising from biological or hazardous materials. Compliance with applicable environmental laws and regulations is expensive, and current or future environmental regulations may impair our research, development and production efforts, which could harm our business, prospects, financial condition or results of operations.

Our supply chain network is exposed to potentially adverse events such as physical disruptions, environmental and industrial accidents, trade restrictions, increases in the cost of raw materials or disruptions at a key supplier which could seriously harm our development efforts, increase our costs and expenses and have a material adverse effect on our business, financial condition and results of operations.

Cell-based therapies and biologics rely on the availability of reagents, specialized equipment, and other specialty materials, which may not be available to us on acceptable terms or at all. For some of these reagents, equipment, and materials, we rely or may rely on sole source vendors or a limited number of vendors, which could impair our ability to manufacture and supply our products.

Our ability to successfully develop our product candidates, and to ultimately supply our commercial products in quantities sufficient to meet the market demand, depends in part on our ability to obtain the materials for these products in accordance with regulatory requirements and in sufficient quantities for preclinical and clinical testing and commercialization. We do not currently have arrangements in place for a redundant or second-source supply of certain of our product materials in the event any of our current vendors of such materials cease their operations for any reason. We are also unable to predict how changing global economic conditions or potential global health concerns such as the ongoing COVID-19 pandemic will affect our third-party vendors. Any negative impact of such matters on our third-party vendors may also have an adverse impact on our results of operations or financial condition. We are not certain that our single-source vendors will be able to meet our demand for their products, either because of the nature of our agreements with those vendors, our limited experience with those vendors or our relative importance as a customer to those vendors. It may be difficult for us to assess their ability to timely meet our demand in the future based on past performance. While our vendors have generally met our demand for their products on a timely basis in the past, they may subordinate our needs in the future to their other customers. Establishing additional or replacement vendors for the materials used in our product candidates, if required, may not be accomplished quickly. If we are able to find a replacement vendor, such replacement vendor would need to be qualified and may require additional regulatory inspection or approval, which could result in further delay. While we seek to maintain adequate inventory of the materials used in our product candidates, any interruption or delay in the supply of components or materials, or our inability to obtain such materials from alternate sources at acceptable prices in a timely manner could impede, delay, limit or prevent our development efforts, which could harm our business, results of operations, financial condition and prospects.

We plan to establish our own commercial-scale manufacturing facilities and infrastructure in lieu of relying on third parties for the manufacture of ATL001 and any future product candidates, which will be costly, time-consuming, and which may not be successful.

We are in the process of adding manufacturing capacity for our clinical trials and we plan to establish our own commercial manufacturing facility. The establishment of our own commercial manufacturing facility would be a costly and time-consuming process that we expect to require additional capital to fund and take several years before becoming operational. For example, we plan to develop a fully closed end-to-end manufacturing process, which is challenging, time-consuming and will require significant resources. We may experience unexpected delays or costs as we continue to improve our VELOS manufacturing process and may ultimately be unsuccessful in obtaining manufacturing scale capabilities. Furthermore, as we scale up the VELOS manufacturing process, we may be required to make changes to the process which can affect the composition of ATL001 and any future product candidates.

We have no experience as a company in setting up, building or managing a commercial-scale manufacturing facility, and may never be successful in developing our own commercial-scale manufacturing facility. We will need to hire additional personnel to manage our operations and facilities and develop the necessary infrastructure to continue the research and development, and eventual commercialization, if approved, of our product candidates. If we fail to recruit the required personnel and generally manage our growth effectively or fail to select the correct location, the development and production of our product candidates could be curtailed or delayed. Even if we are successful in establishing a commercial-scale manufacturing facility, our manufacturing capabilities could be affected by cost-overruns, unexpected delays, equipment failures, labor shortages, natural disasters, power failures and numerous other factors that could prevent us from realizing the intended benefits of our manufacturing strategy and have a material adverse effect on our business.

In addition, the FDA, the EMA, the MHRA and other foreign regulatory authorities may require us to submit samples of any lot of any approved product together with the protocols showing the results of applicable tests at any time.

Under some circumstances, the FDA, the EMA, the MHRA or other foreign regulatory authorities may require that we not distribute a lot until the relevant agency authorizes its release. Slight deviations in the manufacturing process, including those affecting quality attributes and stability, may result in unacceptable changes in the product that could result in lot failures or product recalls. Lot failures or product recalls could cause us to delay product launches or clinical trials, which could be costly to us and otherwise harm our business, financial condition, results of operations and prospects. Problems in our manufacturing process could restrict our ability to meet market demand for our products.

We also may encounter problems hiring and retaining the experienced scientific, quality-control and manufacturing personnel needed to operate our manufacturing processes, which could result in delays in production or difficulties in maintaining compliance with applicable regulatory requirements.

Any problems in our manufacturing process or facilities could make us a less attractive collaborator for potential partners, including larger pharmaceutical companies and academic research institutions, which could limit our access to additional attractive development programs.

RISKS RELATED TO SALES, MARKETING AND COMPETITION

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 product candidates, if approved, we may not be able to generate product revenue.

We currently have no sales, marketing or distribution capabilities and have no experience in marketing products. 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.

If we are unable or decide not to establish internal sales, marketing and distribution capabilities, we will pursue arrangements with third-party sales, marketing, and distribution collaborators regarding the sales and marketing of our products, if approved. However, there can be no assurance that we will be able to establish or maintain such arrangements on favorable terms or at all, or if we are able to do so, that these third-party arrangements will provide effective sales forces or marketing and distribution capabilities. 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 product sales may be lower than if we had commercialized our product candidates ourselves. We also face competition in our search for third parties to assist us with the sales and marketing efforts of our product candidates.

There can be no assurance that we will be able to develop in-house sales and distribution capabilities or establish or maintain relationships with third-party collaborators to commercialize any product in the United States or overseas.

Even if we obtain regulatory approval of ATL001 or any future product candidates, the products may not gain market acceptance among physicians, patients, hospitals, cancer treatment centers and others in the medical community.

The use of precision cNeT product candidates 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, even if approved by the appropriate regulatory authorities for marketing and sale. If we obtain regulatory approval for ATL001 in any of our current programs or additional follow-on indications or any future product candidates and such product candidates do not gain an adequate level of market acceptance, we could be prevented from or significantly delayed in achieving profitability. Various factors will influence whether our product candidates, if approved, are accepted in the market, including:

- the efficacy of ATL001 in the applicable indication or any future product candidates as demonstrated in clinical trials, and, if required by any applicable authority in connection with the approval for the applicable indications, the ability of ATL001 or any future product candidates to provide patients with incremental health benefits, as compared with other available therapies;
- potential product liability claims;
- the clinical indications for which ATL001 or any future product candidates are approved;
- physicians, hospitals, cancer treatment centers and patients considering ATL001 or any future product candidates as a safe and effective treatment;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the potential and perceived advantages of ATL001 or any future product candidates over alternative treatments;
- the prevalence and severity of any side effects of ATL001 or any future product candidates;
- the prevalence and severity of any side effects for other cancer immuno-therapeutics and public perception of other cancer immune-therapeutics;
- product labeling or product insert requirements of the FDA or other comparable foreign regulatory authorities;
- limitations or warnings contained in the labeling approved by the FDA or other comparable foreign regulatory authorities;
- any distribution and use restrictions imposed by the FDA or other comparable foreign regulatory authorities or to which we agree as part of a mandatory REMS or voluntary risk management plan;
- the timing of market introduction of ATL001 or any future product candidates as well as competitive products;
- the cost of treatment in relation to current and future alternative treatments;
- the need to dose our product candidates in combination with other therapeutic agents and related costs;
- the availability of adequate coverage, reimbursement and pricing by third-party payors and government authorities;
- the willingness of patients to pay out-of-pocket in the absence of coverage by third-party payors and government authorities;
- relative convenience and ease of administration, including as compared to current and future alternative treatments and competitive therapies; and
- the effectiveness of our sales and marketing efforts.

In addition, although ATL001 differs in certain ways from other cancer immuno-therapies, advanced T cell therapies and neoantigen directed cell or vaccine approaches, serious adverse events or deaths in other clinical trials involving cancer immuno-therapies, advanced T cell therapies or neoantigen directed cell or vaccine approaches, even if not ultimately attributable to our product or product candidates, could result in increased government regulation, unfavorable public perception and publicity, potential regulatory delays in the testing or approval of our product candidates, stricter labeling requirements for those product candidates that are approved, and a decrease in demand for any such product candidates.

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

The market opportunities for ATL001 or any future product candidates may be relatively small as it will be limited to those patients who are ineligible for or have failed prior treatments and our estimates of the prevalence of our target patient populations may be inaccurate.

Cancer therapies are sometimes characterized by line of therapy (first line, second line, third line, fourth line, etc.) and the FDA often approves new therapies initially only for a particular line or lines of use. When cancer is detected early enough, first line therapy is sometimes adequate to cure the cancer or prolong life without a cure. Whenever first line therapy, usually chemotherapy, antibody drugs, tumor-targeted small molecules, hormone therapy, radiation therapy,

surgery, or a combination of these, proves unsuccessful, second line therapy may be administered. Second line therapies often consist of more chemotherapy, radiation, antibody drugs, tumor-targeted small molecules, or a combination of these. Third line therapies can include chemotherapy, antibody drugs and small molecule tumor-targeted therapies, more invasive forms of surgery and new technologies. We expect to initially seek approval of ATL001 in most indications at least as a second or third line therapy, for use in patients with relapsed or refractory metastatic cancer. Subsequently, for those indications in which ATL001 proves to be sufficiently safe and beneficial, if any, we would expect to seek approval as a second line therapy and potentially as a first line therapy, but there is no guarantee that ATL001, even if approved as a second or third line of therapy for any indications, would be approved for an earlier line of therapy, and, prior to any such approvals, we may have to conduct additional clinical trials. Consequently, the potentially addressable patient population for ATL001 or any future product candidates may be extremely limited or may not be amenable to treatment with our product candidates.

Our projections of both the number of people who have the cancers we are targeting, as well as the subset of people with these cancers in a position to receive a particular line of therapy and who have the potential to benefit from treatment with ATL001 or future product candidates, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including scientific literature, commissioned reports, surveys of clinics, patient foundations or market research, and may prove to be incorrect. Further, new therapies may change the estimated incidence or prevalence of the cancers that we are targeting. Consequently, even if ATL001 or any product candidates are approved for a second or third line of therapy, the number of patients that may be eligible for treatment with our product candidates may turn out to be much lower than expected.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

The biotechnology and pharmaceutical industries utilize rapidly advancing technologies and are characterized by intense competition. While we believe that our differentiated product, scientific knowledge, platform technology and development expertise in the field of immuno-oncology therapy provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceuticals, specialty pharmaceuticals and biotechnology companies, academic institutions and government agencies, and public and private research institutes that conduct research, development, manufacturing and commercialization. Many of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, regulatory approvals and product marketing than we do. Our competitors may compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. As a result, our competitors may discover, develop, license or commercialize products before or more successfully than we do.

In addition, many of these competitors are active in seeking patent protection and licensing arrangements in anticipation of collecting royalties for use of technology that they have developed. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors, either alone or with collaborative partners, may succeed in developing, acquiring or licensing on an exclusive basis drug or biologic products that are more effective, safer, more easily commercialized or less costly than our product candidates or may develop proprietary technologies or secure patent protection that we may need for the development of our technologies and products. We believe the key competitive factors that will affect the development and commercial success of our product candidates are efficacy, safety, potency, purity, tolerability, reliability, convenience of use, price and reimbursement.

Specifically, advanced T cell therapies are under evaluation in solid tumors by multiple biotechnology and pharmaceutical companies, including Kite Pharma Inc. (a Gilead company), Iovance Biotherapeutics Inc., or Iovance, Adaptimmune Therapeutics PLC, Autolus Therapeutics PLC, Instil Bio, Inc., or Instil, PACT Pharma, Inc., Neogene Therapeutics, B.V., BioNTech SE, Turnstone Biologics Corp., Genocea Biosciences, Inc., Obsidian Therapeutics and KSQ Therapeutics, Inc. In particular, Iovance and Instil are developing standard TIL therapies for treatment of various

cancers including melanoma, which will compete directly with our product candidate, ATL001, in the relevant indications.

We anticipate that we will face intense and increasing competition as new products and therapies enter the market and advanced technologies become available. We expect any treatments that we develop and commercialize to compete on the basis of, among other things, efficacy, safety, delivery, price and the availability of reimbursement from government and other third-party payers.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive or better reimbursed than any products that we may commercialize. Our competitors also may obtain FDA, EMA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position for either the product or a specific indication before we are able to enter the market.

Even if we obtain regulatory approval of our product candidates, the availability and price of our competitors' products could limit the demand and the price we are able to charge for our product candidates, if approved. We may not be able to implement our business plan if the acceptance of our product candidates is inhibited by price competition or the reluctance of physicians to switch from existing methods of treatment to our product candidates, or if physicians switch to other new drug or biologic products or choose to reserve our product candidates for use in limited circumstances. For additional information regarding our competition, see "Item 4.B. Business Overview—Competition."

A variety of risks associated with marketing our product candidates internationally could materially adversely affect our business.

We plan to seek regulatory approval of ATL001 and any future product candidates outside of the United States and, accordingly, we expect that we will be subject to additional risks related to operating in foreign countries if we obtain the necessary approvals, including:

- differing regulatory requirements in foreign countries;
- unexpected changes in tariffs, trade barriers, price and exchange controls and other regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- difficulties staffing and managing foreign operations;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- potential liability under the Foreign Corrupt Practices Act of 1977 or comparable foreign laws and regulations;
- challenges enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war and terrorism.

These and other risks associated with international operations may materially adversely affect our ability to attain or maintain profitable operations.

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

We face an inherent risk of product liability as a result of the clinical testing of ATL001 or any future product candidates and will face an even greater risk if we commercialize any products. For example, we may be sued if a product candidate 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 product candidates. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for ATL001 or any future product candidates or products that we may develop;
- 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;
- regulatory investigation, 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 any product candidate; and
- a decline in our share price.

Failure to obtain or retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop, alone or with corporate collaborators. Although we have clinical trial insurance, our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. In the future, we may be unable to maintain this insurance coverage, or we may not be able to obtain additional or replacement coverage at a reasonable cost, if at all. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Even if our agreements with any future corporate collaborators entitle us to indemnification against losses, such indemnification may not be available or adequate should any claim arise.

RISKS RELATED TO GOVERNMENT REGULATION

Risks Related to Regulatory Review and Approval of Product Candidates

The FDA regulatory approval process is lengthy and time-consuming, and we may experience significant delays in the clinical development and regulatory approval of ATL001 and any future product candidates.

We have not previously submitted a Biologics License Application, or BLA, to the FDA or similar marketing applications to similar foreign regulatory authorities. A BLA must include extensive preclinical and clinical data and supporting information to establish the product candidate's safety, purity and potency for each desired indication. The BLA must also include significant information regarding the manufacturing controls for the product. We may also experience delays in completing planned clinical trials for a variety of reasons, including delays related to:

- the availability of financial resources to commence and complete the planned trials;

- reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- obtaining approval at each clinical trial site by an IRB or ethics committee;
- recruiting suitable patients to participate in a clinical trial;
- having patients complete a clinical trial or return for post-treatment follow-up;
- clinical trial sites deviating from trial protocol or dropping out of a trial;
- addressing any patient safety concerns that arise during the course of a trial;
- adding new clinical trial sites; or
- manufacturing sufficient quantities of qualified materials under cGMPs and including current good tissue practices requirements and applying them on a subject-by-subject basis for use in clinical trials.

Securing regulatory approval also requires the submission of information about the biologic manufacturing process and inspection of manufacturing facilities by the relevant regulatory authority. The FDA, the EMA, the MHRA or similar foreign regulatory authorities may fail to approve our manufacturing processes or facilities, whether run by us or our contract manufacturing organizations, or CMOs. In addition, if we make changes to our manufacturing process for ATL001 or any future product candidates in the future, including adding a new CMO, we may need to conduct additional research or clinical trials to bridge our modified product candidates to earlier versions.

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 ATL001 and any future product candidates.

Regulatory authorities in the United States, United Kingdom and European Union have limited experience in reviewing and approving cell therapy products, which could affect the time and data required to obtain marketing authorization of any of our product candidates.

Our future success depends in part on our successful development of viable cell therapy product candidates utilizing our PELEUS bioinformatics platform. We may experience problems or delays in developing such product candidates and any such problems or delays may result in unanticipated costs and time to develop our product candidates and/or may not be resolved in a satisfactory manner.

The regulatory approval process and clinical trial requirements for novel product candidates can be more expensive and take longer than for other, better known or more extensively studied product candidates, and we cannot predict how long it will take or how much it will cost to complete clinical developments and obtain regulatory approvals for a cell therapy product candidate in either the United States, the European Union or the United Kingdom or how long it will take to commercialize a cell therapy product candidate, if and when approved. Regulatory requirements governing cell therapy products have changed frequently and may continue to change in the future. For example, the FDA established the Office of Tissues and Advanced Therapies within its Center for Biologics Evaluation and Research, or CBER, to consolidate the review of cell therapies and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. These and other regulatory review agencies, committees and advisory groups and the requirements and guidelines they promulgate may lengthen the regulatory review process, require us to perform additional preclinical studies or clinical trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these treatment candidates or lead to significant post-approval limitations or restrictions.

A similar framework is in place in the European Union, or the EU. The European Medicines Agency, or the EMA, has a Committee for Advanced Therapies, or CAT, that is responsible for assessing the quality, safety and efficacy of advanced-therapy medicinal products. Advanced-therapy medical products include gene therapy medicines, somatic-cell therapy medicines and tissue-engineered medicines, which must be centrally authorized in the EU. The role of the CAT is to prepare a draft opinion on an application for marketing authorization for a cell therapy medicinal candidate that is submitted to the EMA. In the EU, the development and evaluation of a cell therapy medicinal product must be considered in the context of the relevant EU guidelines. The EMA may issue new guidelines concerning the

development and marketing authorization for somatic cell therapy medicinal products and require that we comply with these new guidelines. Similarly, complex regulatory environments exist in other jurisdictions in which we might consider seeking regulatory approvals for our product candidates, further complicating the regulatory landscape. As a result, the procedures and standards applied to gene therapy products and cell therapy products may be applied to any of our cell therapy or genome editing product candidates, but that remains uncertain at this point.

The clinical trial requirements of the FDA, the EMA, the MHRA and other regulatory authorities and the criteria these regulators use to evaluate the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the potential products. The regulatory approval process for product candidates such as ours can be more lengthy, rigorous and expensive than the process for other better known or more extensively studied product candidates and technologies. Since we are developing novel treatments for diseases in which there is little clinical experience with new endpoints and methodologies, there is heightened risk that the FDA, the EMA, the MHRA or comparable regulatory bodies may not consider the clinical trial endpoints to provide clinically meaningful results, and the resulting clinical data and results may be more difficult to analyze. This may be a particularly significant risk for many of the diseases for which we may develop product candidates alone or with collaborators due to small patient populations for those diseases, and designing and executing a rigorous clinical trial with appropriate statistical power is more difficult than with diseases that have larger patient populations. Regulatory agencies administering existing or future regulations or legislation may not allow production and marketing of cell therapy products in a timely manner or under technically or commercially feasible conditions.

Even if our product candidates obtain required regulatory approvals, such approvals may later be withdrawn as a result of changes in regulations or the interpretation of regulations by applicable regulatory agencies. Additionally, adverse developments in clinical trials conducted by others of cell therapy products or products created using similar technology, or adverse public perception of the field of cell therapies, may cause the FDA, the EMA, the MHRA and other regulatory bodies to revise the requirements for approval of any product candidates we may develop or limit the use of products utilizing technologies such as ours, either of which could materially harm our business.

As we advance our product candidates, we will be required to consult with various regulatory authorities, and we must comply with applicable laws, rules, and regulations, which may change from time to time including during the course of development of our product candidates. If we fail to do so, we may be required to delay or discontinue the clinical development of certain of our product candidates. These additional processes may result in a review and approval process that is longer than we otherwise would have expected. Even if we comply with applicable laws, rules, and regulations, and even if we maintain close coordination with the applicable regulatory authorities with oversight over our product candidates, our development programs may fail to succeed. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product to market would materially and adversely affect our business, financial condition, results of operations and prospects.

We may in the future seek orphan drug designation for ATL001 and any future product candidates, but we may be unable to obtain such designations or to maintain the benefits associated with orphan drug designation, including market exclusivity, which may cause our revenue, if any, to be reduced.

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition, defined as a disease or condition with a patient population of fewer than 200,000 in the United States, or a patient population of 200,000 or more in the United States when there is no reasonable expectation that the cost of developing and making available the drug or biologic in the United States will be recovered from sales in the United States for that drug or biologic. Orphan drug designation must be requested before submitting a BLA. In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. After the FDA grants orphan drug designation, the generic identity of the drug or biologic and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

If a product candidate that has orphan drug designation subsequently receives the first FDA approval for a particular active ingredient for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications, including a BLA, to market the same product for the same indication for seven years, except in limited circumstances such as a showing of clinical superiority to the product with orphan drug exclusivity or if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the product was designated. As a result, even if one of our product candidates receives orphan exclusivity, the FDA can still approve other drugs that have a different active ingredient for use in treating the same indication or disease. Furthermore, the FDA can waive orphan exclusivity if we are unable to manufacture sufficient supply of our product.

We may seek orphan drug designation for ATL001 in the indications we are currently targeting or any follow-on indications as well as for any future product candidates in additional orphan indications in which there is a plausible basis for the evaluation of these product candidates. Even if we obtain orphan drug designation, exclusive marketing rights in the United States may be limited if we seek approval for an indication broader than the orphan designated indication and may be lost if the FDA later determines that the request for designation was materially defective or if we are unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Further, even if we obtain orphan drug exclusivity for a product candidate, that exclusivity may not effectively protect the product from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve a later product for the same condition if the FDA concludes that the later product is clinically superior in that it is safer, more effective, or makes a major contribution to patient care.

On August 3, 2017, Congress passed the FDA Reauthorization Act of 2017, or FDARA. FDARA, among other things, codified the FDA's pre-existing regulatory interpretation, to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. The legislation reverses prior precedent holding that the Orphan Drug Act unambiguously requires that the FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority. Moreover, in the Consolidated Appropriations Act of 2021, Congress did not further change this interpretation when it clarified that the interpretation codified in FDARA would apply in cases where the FDA issued an orphan designation before the enactment of FDARA but where product approval came after the enactment of FDARA. The FDA may further re-evaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

A breakthrough therapy designation or accelerated approval by the FDA, even if granted for ATL001 or any of our future product candidates, may not lead to a faster development or regulatory review or approval process and it does not increase the likelihood that our product candidates will receive marketing approval.

We may seek breakthrough therapy designation for ATL001 in the indications we are currently targeting or any follow-on indications as well as for any future product candidates. A breakthrough therapy is defined as a drug or biologic that is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug, or biologic, may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Sponsors of product candidates that have been designated as breakthrough therapies are eligible to receive more intensive FDA guidance on developing an efficient drug development program, an organizational commitment involving senior managers, and eligibility for rolling review and priority review. A product candidate is eligible for Priority Review if it has the potential to provide a significant improvement in safety or effectiveness in the treatment, diagnosis or prevention of a serious disease or condition. Under priority review, the FDA must review an application in six months compared to ten months for a standard review.

Drugs and biologics designated as breakthrough therapies by the FDA may also be eligible for other expedited approval programs, including accelerated approval. A product candidate may be eligible for accelerated approval if it treats a serious or life-threatening condition, generally provides a meaningful advantage over available therapies, and demonstrates an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. As a condition of accelerated approval, the FDA may require that a sponsor of a product receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. These confirmatory trials must be completed with due diligence. In addition, the FDA generally requires, unless otherwise informed by the agency, that all advertising and promotional materials intended for dissemination or publication within 120 days of marketing approval be submitted to the agency for review during the pre-approval review period, which could adversely impact the timing of the commercial launch of the product. Even if we do receive accelerated approval, we may not experience a faster development or regulatory review or approval process, and receiving accelerated approval does not provide assurance of ultimate full FDA approval. Accelerated approval may also be withdrawn if, among other things, a confirmatory trial required to verify the predicted clinical benefit of the product fails to verify such benefit or if such trial is not conducted with due diligence.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a Breakthrough Therapy Designation for a product candidate may not result in a faster development process, review or approval compared to candidate products considered for approval under non-expedited FDA review procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that the product no longer meets the conditions for qualification. Thus, even though we intend to seek breakthrough therapy designation for certain of our current and future product candidates for the treatment of various cancers, there can be no assurance that we will receive Breakthrough Therapy Designation.

A fast track or regenerative medicine advanced therapy, or RMAT, designation by the FDA, even if granted for ATL001 or any future product candidates, may not lead to a faster development or regulatory review or approval process, and does not increase the likelihood that our product candidates will receive marketing approval.

If a drug or biologic is intended for the treatment of a serious or life-threatening disease or condition and the product candidate demonstrates the potential to address unmet medical needs for such disease or condition, the sponsor may apply for FDA Fast Track designation for a particular indication. The sponsor of a Fast Track product candidate has opportunities for more frequent interactions with the applicable FDA review team during product development and, once a BLA is submitted, the product candidate may be eligible for priority review. Fast Track designation does not, however, guarantee that the application will be designated for priority review. A Fast Track product candidate may also be eligible for rolling review, where the FDA may consider for review sections of the BLA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the BLA, the FDA agrees to accept sections of the BLA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the BLA.

A company may request RMAT designation of its product candidate, and FDA may granted such designation if the product meets the following criteria: (i) it is a cell therapy, therapeutic tissue engineering product, human cell and tissue product, or any combination product using such therapies or products, with limited exceptions; (ii) it is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition; and (iii) preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such a disease or condition. RMAT designation provides potential benefits that include more frequent meetings with FDA to discuss the development plan for the product candidate, and potential eligibility for rolling review and priority review. Products granted RMAT designation may also be eligible for accelerated approval on the basis of a surrogate or intermediate endpoint reasonably likely to predict long-term clinical benefit, or reliance upon data obtained from a meaningful number of sites, including through expansion of trials to additional sites.

The FDA has broad discretion whether or not to grant fast track or RMAT designation, so even if we believe a particular product candidate is eligible for such designations, there can be no assurance that the FDA would decide to grant it. Even if we do receive fast track or RMAT designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures, and receiving a fast track or RMAT designation does not provide assurance of ultimate FDA approval. In addition, the FDA may withdraw fast track or RMAT designation if it believes that the designation is no longer supported by data from our clinical development program.

Even if we obtain FDA, EMA or MHRA approval for ATL001 in the indications we are currently targeting or any follow-on indications or any future product candidates that we may identify and pursue in the United States, Europe or the United Kingdom, we may never obtain approval to commercialize any such product candidates outside of those jurisdictions, which would limit our ability to realize their full market potential.

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction, while a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. In order to market any products outside of the United States, we must establish and comply with numerous and varying regulatory requirements of other countries regarding safety and effectiveness. Regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval processes vary among countries and can involve additional product testing and validation and additional or different administrative review periods from those in the United States, including additional research 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 product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our products is also subject to approval.

Seeking foreign regulatory approval could result in difficulties and costs and require additional nonclinical studies or clinical trials which could be costly and time-consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our current or future product candidates in those countries. The foreign regulatory approval process may include all of the risks associated with obtaining FDA, EMA or MHRA approval. We do not have any product candidates approved for sale in any jurisdiction, including international markets, and we do not have experience in obtaining regulatory approval in international markets for our current or future product candidates. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approval in international markets is delayed, our target market will be reduced and our ability to realize the full market potential of our current or future product candidates will be harmed.

RISKS RELATED TO ONGOING REGULATORY OBLIGATIONS

Even if we receive regulatory approval of ATL001 in the indications we are currently targeting or any follow-on indications or any future product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our product candidates.

Any regulatory approvals that we receive for our product candidates will require surveillance to monitor the safety and efficacy of the product candidate. The FDA may also require a risk evaluation and mitigation strategy, or REMS, in order to approve our product candidates, which could entail requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or a comparable foreign regulatory authority approves our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export and recordkeeping for our product candidates will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMPs, good laboratory practice, or GLP, regulations and GCPs, for any clinical trials that we conduct post-approval. Manufacturers and manufacturers' facilities are also required to comply with applicable product tracking and tracing requirements. Later

discovery of previously unknown problems with our product candidates, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of our product candidates, withdrawal of the product from the market or voluntary or mandatory product recalls;
- manufacturing delays and supply disruptions where regulatory inspections identify observations of noncompliance requiring remediation;
- revisions to the labeling, including limitation on approved uses or the addition of additional warnings, contraindications or other safety information, including boxed warnings;
- imposition of a REMS which may include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools;
- requirements to conduct additional post-market clinical trials to assess the safety of the product;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or revocation of approvals;
- product seizure or detention, or refusal to permit the import or export of our product candidates; and
- injunctions or the imposition of civil or criminal penalties.

The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and generate revenue and could require us to expend significant time and resources in response and could generate negative publicity. In addition, 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 product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses.

We must comply with requirements concerning advertising and promotion for any product candidates for which we obtain marketing approval. Promotional communications with respect to therapeutics are subject to a variety of legal and regulatory restrictions and continuing review by the FDA, Department of Justice, Department of Health and Human Services' Office of Inspector General, state attorneys general, members of Congress, and the public. When the FDA or comparable foreign regulatory authorities issue regulatory approval for a product candidate, the regulatory approval is limited to those specific uses and indications for which a product is approved.

Physicians may choose to prescribe products for uses that are not described in the product's labeling and for uses that differ from those tested in clinical trials and approved by the regulatory authorities. Regulatory authorities in the United States generally do not restrict or regulate the behavior of physicians in their choice of treatment within the practice of medicine. Regulatory authorities do, however, restrict communications by biopharmaceutical companies concerning off-label use.

If ATL001 or any future product candidates are approved and we are found to have improperly promoted off-label uses of those products, we may become subject to significant liability. The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription products, if approved. In particular, while the FDA permits the dissemination of truthful and non-misleading information about an approved product, a manufacturer may not promote a product for uses that are not approved by the FDA or such other regulatory agencies, as reflected in the product's approved labeling. If such regulatory agencies find that we have promoted such off-label uses, we may become subject to significant liability. The federal government has levied large civil and criminal fines against

companies for alleged improper promotion of off-label use of their products and has enjoined several companies from engaging in off-label promotion. The FDA and other regulatory agencies have also required companies to enter into consent decrees or corporate integrity agreements, or imposed permanent injunctions under which specified promotional conduct must be changed or curtailed.

In the United States, engaging in the impermissible promotion of any products, following approval, for off-label uses can also subject us to false claim actions and other litigation under federal and state statutes. These statutes include fraud and abuse and consumer protection laws, which can lead to civil and criminal penalties and fines, agreements with governmental authorities that materially restrict the manner in which we promote or distribute therapeutic products and conduct our business. These restrictions could include corporate integrity agreements, suspension or exclusion from participation in federal and state healthcare programs, suspension and debarment from government contracts and refusal of orders under existing government contracts. False Claims Act lawsuits brought by federal and state enforcement agencies against manufacturers of drugs and biologics have increased significantly in volume and breadth, leading to several substantial civil and criminal settlements pertaining to certain sales practices and promoting off-label uses. In addition, False Claims Act lawsuits may expose manufacturers to follow-on claims by private payers based on fraudulent marketing practices. This growth in litigation has increased the risk that a biopharmaceutical company will have to defend a false claim action, pay settlement fines or restitution, as well as criminal and civil penalties, agree to comply with burdensome reporting and compliance obligations, and be excluded from Medicare, Medicaid, or other federal and state healthcare programs. If we do not lawfully promote our approved products, if any, we may become subject to such litigation and, if we do not successfully defend against such actions, those actions may have a material adverse effect on our business, financial condition, results of operations, stock price and prospects.

In the United States, the promotion of biopharmaceutical products is subject to additional FDA requirements and restrictions on promotional statements. If, after ATL001 or any of our future product candidates obtains marketing approval, the FDA determines that our promotional activities violate its regulations and policies pertaining to product promotion, it could request that we modify our promotional materials or subject us to regulatory or other enforcement actions, including issuance of warning letters or untitled letters, suspension or withdrawal of an approved product from the market, requests for recalls, payment of civil fines, disgorgement of money, imposition of operating restrictions, injunctions or criminal prosecution, and other enforcement actions. Similarly, industry codes in foreign jurisdictions may prohibit companies from engaging in certain promotional activities, and regulatory agencies in various countries may enforce violations of such codes with civil penalties. If we become subject to regulatory and enforcement actions, our business, financial condition, results of operations, stock price and prospects will be materially harmed.

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

The Affordable Care Act includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCIA, which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. Under the BPCIA, an application for a highly similar or "biosimilar" product may not be submitted to the FDA until four years following the date that the reference product was first approved by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first approved. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty.

We believe that any of our product candidates approved as a biological product under a BLA should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action

or otherwise, or that the FDA will not consider our product candidates to be reference products for competing products, potentially creating the opportunity for competition sooner than anticipated. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. 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.

The success of current programs, additional follow-on indications for ATL001 and any future product candidates, if approved, will depend significantly on our ability to obtain adequate coverage and reimbursement of, or the willingness of patients to pay for, our product candidates.

In the United States and in other countries, 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. We believe our success depends on obtaining and maintaining coverage and adequate reimbursement for our product candidates, and the extent to which patients will be willing to pay out-of-pocket for such products. The availability of insurance coverage and adequacy of reimbursement for our products by third-party payors, including government health care programs (e.g., Medicare, Medicaid, TRICARE), managed care providers, private health insurers, health maintenance organizations, and other organizations is essential for most patients to be able to afford medical services and novel pharmaceutical products such as our product candidates.

In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors and coverage and reimbursement levels for products can differ significantly from payor to payor. As a result, decisions regarding the extent of coverage and amount of reimbursement to be provided are made on a payor-by-payor basis. One payor's determination to provide coverage for a drug or biological product does not assure that other payors will also provide coverage for the same product. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own coverage and reimbursement policies. It is difficult to predict what the Centers for Medicare & Medicaid Services, or CMS, the federal agency responsible for administering the Medicare program, will decide with respect to reimbursement for fundamentally novel products such as ours.

Eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale, and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services.

Patients who are treated in-office for a medical condition generally rely on third-party payors to reimburse all or part of the costs associated with the procedure, including costs associated with products used during the procedure, and may be unwilling to undergo such procedures in the absence of such coverage and adequate reimbursement. Physicians may be unlikely to offer procedures for such treatment if they are not covered or are inadequately covered by insurance and may be unlikely to purchase and use our product candidates, if approved, for our stated indications unless coverage is provided and reimbursement is adequate. In addition, for products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs.

Reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that a product is safe, effective and medically necessary; appropriate for the specific patient; cost-effective; supported by peer-reviewed medical journals; included in clinical practice guidelines; and neither cosmetic, experimental, nor investigational. Further, increasing efforts by third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. In order to secure coverage and reimbursement for any product that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-

effectiveness of our products, in addition to the costs required to obtain FDA or comparable regulatory approvals. Additionally, we may also need to provide discounts to purchasers, private health plans or government healthcare programs. Our product candidates may, nonetheless, not be considered medically necessary or cost-effective. If third-party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover the product after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to sell its products at a profit. We expect to experience pricing pressures in connection with the sale of any of our product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional upcoming and anticipated legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products.

Foreign governments also have their own healthcare reimbursement systems, which vary significantly by country and region, and we cannot be sure that coverage and adequate reimbursement will be made available with respect to our product candidates under any foreign reimbursement system. To that end, reimbursement agencies in the United Kingdom and European Union may be more conservative than CMS. For example, a number of cancer drugs have been approved for reimbursement in the United States and have not been approved for reimbursement in the United Kingdom and/or certain European countries.

There can be no assurance that any of our product candidates, if approved for sale in the United States or in other countries, will be considered medically reasonable and necessary and/or cost-effective by third-party payors, that coverage or an adequate level of reimbursement will be available or that reimbursement policies and practices in the United States and in foreign countries where our products are sold will not adversely affect our ability to sell our product candidates profitably, even if they are approved for sale.

Healthcare legislative or regulatory reform measures may have a material adverse effect on our business and results of operations.

The United States and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system that could prevent or delay marketing approval of our product candidates or any future product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell a product for which we obtain marketing approval. Changes in applicable laws, rules, and regulations or the interpretation of existing laws, rules, and regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

Among policy makers and payors in the United States and in many foreign jurisdictions, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. For example, in March 2010, the Affordable Care Act, or ACA, was passed, which substantially changed the way healthcare is financed by both the government and private insurers, and significantly impacts the United States pharmaceutical industry. The ACA, among other things: (i) established an annual, nondeductible fee on any entity that manufactures or imports certain specified branded prescription drugs and biologic agents apportioned among these entities according to their market share in some government healthcare programs; (ii) expanded the entities eligible for discounts under the 340B drug pricing program; (iii) increased the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for most branded and generic drugs, respectively, and capped the total rebate amount for innovator drugs at 100% of the Average Manufacturer Price, or AMP; (iv) expanded the eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new eligibility categories for individuals with income at or below 133% (as calculated, it constitutes 138%) of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability; (v) addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug

Rebate Program are calculated for certain drugs and biologics that are inhaled, infused, instilled, implanted or injected; (vi) introduced a new Medicare Part D coverage gap discount program pursuant to which manufacturers must now agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D (increased from 50%, effective January 1, 2019, pursuant to the Bipartisan Budget Act of 2018); (vii) created a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and (viii) established the Center for Medicare and Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drugs.

Since the ACA was enacted, there have been numerous judicial and Congressional challenges to certain aspects of the ACA, some of which remain unresolved, as well as efforts by the current administration to repeal or replace certain aspects of the ACA. By way of example, the Tax Cuts and Jobs Act of 2017, or Tax Act, includes a provision that repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." In addition, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the ACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminates the health insurer tax. The Bipartisan Budget Act of 2018, or the BBA, among other things, amended the ACA, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." In December 2018, CMS published a new final rule permitting further collections and payments to and from certain ACA qualified health plans and health insurance issuers under the ACA risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. On April 27, 2020, the United States Supreme Court reversed a federal circuit court decision that previously upheld Congress' denial of $12 billion in "risk corridor" funding. On December 14, 2018, a Texas United States District Court Judge ruled that the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Act. Additionally, on December 18, 2019, the United States Court of Appeals for the 5th Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA without specifically ruling on the constitutionality of the ACA. It is unclear how such litigation and other efforts to repeal and replace the ACA will impact the ACA or our business, financial condition and results of operations.

Other legislative changes have been proposed and adopted since the ACA was enacted. These changes include aggregate reductions to Medicare payments to providers of 2% per fiscal year pursuant to the Budget Control Act of 2011. These reductions went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022. Then, a 1% payment reduction will occur beginning April 1, 2022 through June 30, 2022, and the 2% payment reduction will resume on July 1, 2022. The American Taxpayer Relief Act of 2012, among other things, further 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. These laws and similar future legislative initiatives may result in additional reductions in Medicare and other healthcare funding that could have an adverse effect on customers for our product candidates, if approved, and, accordingly, our financial operations.

Additionally, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products.

At a federal level, President Biden signed an Executive Order on July 9, 2021 affirming the administration's policy to (i) support legislative reforms that would lower the prices of prescription drug and biologics, including by allowing Medicare to negotiate drug prices, by imposing inflation caps, and, by supporting the development and market entry of lower-cost generic drugs and biosimilars; and (ii) support the enactment of a public health insurance option. Among other things, the Executive Order also directs HHS to provide a report on actions to combat excessive pricing of prescription drugs, enhance the domestic drug supply chain, reduce the price that the Federal government pays for drugs, and address price gouging in the industry; and directs the FDA to work with states and Indian Tribes that propose to develop section 804 Importation Programs in accordance with the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, and the FDA's implementing regulations. FDA released such implementing regulations on September 24, 2020, which went into effect on November 30, 2020, providing guidance for states to build and submit importation plans for drugs from Canada. On September 25, 2020, CMS stated drugs imported by states under this rule will not be eligible for federal rebates under Section 1927 of the Social Security Act and manufacturers would not report these drugs for "best price" or Average Manufacturer Price purposes. Since these drugs are not considered covered outpatient drugs, CMS further stated it will not publish a National Average Drug Acquisition Cost for these drugs. If implemented, importation of drugs from Canada may materially and adversely affect the price we receive for any of our product candidates. Further, on November 20, 2020 CMS issued an Interim Final Rule implementing the Most Favored Nation, or MFN, Model under which Medicare Part B reimbursement rates would have been be calculated for certain drugs and biologicals based on the lowest price drug manufacturers receive in Organization for Economic Cooperation and Development countries with a similar gross domestic product per capita. However, on December 29, 2021 CMS rescinded the Most Favored Nations rule. Additionally, on November 30, 2020, HHS published a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. Pursuant to court order, the removal and addition of the aforementioned safe harbors were delayed and recent legislation imposed a moratorium on implementation of the rule until January 1, 2026. Although a number of these and other proposed measures may require authorization through additional legislation to become effective, and the Biden administration may reverse or otherwise change these measures, both the Biden administration and Congress have indicated that they will continue to seek new legislative measures to control drug costs.

Furthermore, on July 9, 2021, President Biden issued an executive order directing the FDA to, among other things, continue to clarify and improve the approval framework for biosimilars, including the standards for interchangeability of biological products, facilitate the development and approval of biosimilar and interchangeable products, clarify existing requirements and procedures related to the review and submission of BLAs, and identify and address any efforts to impede biosimilar competition.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

We expect that these and other healthcare reform measures that may be adopted in the future may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product candidate. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our drugs, and could have a material adverse effect on our business, financial condition, and results of operations.

Our business activities are subject to the Foreign Corrupt Practices Act, or FCPA, and similar anti-bribery and anti-corruption laws.

As we engage in and expand our business activities outside of the United States, including our clinical trial efforts, we are subject to the FCPA and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which we operate. The FCPA generally prohibits offering, promising, giving, or authorizing others to give anything of value, either directly or indirectly, to a non-United States government official in order to influence official action, or otherwise obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the corporation and to devise and maintain an adequate system of internal accounting controls. Our business is heavily regulated and therefore involves significant interaction with public officials, including officials of non-United States governments. Additionally, in many other foreign jurisdictions, the healthcare providers who prescribe pharmaceuticals are employed by their government, and the purchasers of pharmaceuticals are government entities; therefore, our dealings with these prescribers and purchasers are subject to regulation under the FCPA. Recently the SEC and Department of Justice have increased their FCPA enforcement activities with respect to biotechnology and pharmaceutical companies. There is no certainty that all of our employees, agents, suppliers, manufacturers, contractors, or collaborators, or those of our affiliates, will comply with all applicable laws and regulations, particularly given the high level of complexity and variability of these laws. Violations of these laws and regulations could result in fines, criminal sanctions against us, our officers, or our employees, the closing down of facilities, including those of our suppliers and manufacturers, requirements to obtain export licenses, cessation of business activities in sanctioned countries, implementation of compliance programs, and prohibitions on the conduct of our business. Any such violations could include prohibitions on our ability to offer our products in one or more countries as well as difficulties in manufacturing or continuing to develop our products, and could materially damage our reputation, our brand, our international expansion efforts, our ability to attract and retain employees, and our business, prospects, operating results, and financial condition.

Inadequate funding for the FDA, the SEC and other government agencies, including from government shut downs, global health concerns or other disruptions to these agencies' operations, could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory and policy changes. Average review times at the FDA have fluctuated in recent years as a result. Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which could adversely affect our business. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Separately, since March 2020 when foreign and domestic inspections of facilities were largely placed on hold in response to the COVID-19 pandemic, the FDA has been working to resume routine surveillance, bioresearch monitoring and pre-approval inspections on a prioritized basis. Since April 2021, the FDA has conducted limited

inspections and employed remote interactive evaluations, using risk management methods, to meet user fee commitments and goal dates. Ongoing travel restrictions and other uncertainties continue to impact oversight operations both domestic and abroad and it is unclear when standard operational levels will resume. The FDA is continuing to complete mission-critical work, prioritize other higher-tiered inspectional needs (e.g., for-cause inspections), and carry out surveillance inspections using risk-based approaches for evaluating public health. Should FDA determine that an inspection is necessary for approval and an inspection cannot be completed during the review cycle due to restrictions on travel, and the FDA does not determine a remote interactive evaluation to be adequate, the FDA has stated that it generally intends to issue, depending on the circumstances, a complete response letter or defer action on the application until an inspection can be completed. During the COVID-19 public health emergency, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. Additionally, regulatory authorities outside the U.S. may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities. If a prolonged government shutdown or other disruption occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Future shutdowns or other disruptions could also affect other government agencies such as the SEC, which may also impact our business by delaying review of our public filings, to the extent such review is necessary, and our ability to access the public markets.

Our business operations and current and future relationships with investigators, health care professionals, consultants, third-party payors and customers may be subject, directly or indirectly, to U.S. federal and state healthcare fraud and abuse laws, false claims laws, health information privacy and security laws, other healthcare laws and regulations and other foreign privacy and security laws. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

Although we do not currently have any therapies on the market, our current and future operations may be directly, or indirectly through our relationships with investigators, health care professionals, customers and third-party payors, subject to various U.S. federal and state healthcare laws and regulations. Healthcare providers, physicians and others play a primary role in the recommendation and prescription of any therapies for which we may obtain marketing approval. These laws impact, among other things, our research activities and proposed sales, marketing and education programs and constrain our business and financial arrangements and relationships with third-party payors, healthcare professionals who participate in our clinical research program, healthcare professionals and others who recommend, purchase, or provide our approved therapies, and other parties through which we market, sell and distribute our therapies for which we obtain marketing approval. In addition, we may be subject to patient data privacy and security regulation by both the U.S. federal government and the states in which we conduct our business, along with foreign regulators (including European data protection authorities). Finally, our current and future operations are subject to additional healthcare-related statutory and regulatory requirements and enforcement by foreign regulatory authorities in jurisdictions in which we conduct our business. These laws include, but are not limited to, the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or paying any remuneration (including any kickback, bribe, or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under U.S. federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Violations are subject to significant civil and criminal fines and penalties for each violation, plus up to three times the remuneration involved, imprisonment, and exclusion from government healthcare programs. The definition of the "remuneration" under the federal Anti-Kickback Statute has been interpreted to include anything of value. Further, courts have found that if "one purpose" of remuneration is to induce referrals, the federal Anti-Kickback Statute is violated. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers, and formulary managers on the other. There are a number of statutory exceptions and regulatory safe harbors protecting some common

activities from prosecution; but the exceptions and safe harbors are drawn narrowly and require strict compliance in order to offer protection;

- the federal civil and criminal false claims laws, such as the FCA, which prohibits individuals or entities from, among other things, knowingly presenting, or causing to be presented, false or fraudulent claims for payment to, or approval by Medicare, Medicaid, or other federal healthcare programs, knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim or an obligation to pay or transmit money to the federal government, or knowingly concealing or knowingly and improperly avoiding or decreasing or concealing an obligation to pay money to the U.S. federal government.
- Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. In addition, the government may assert that a claim that includes items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act, or the FCA. The FCA also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery. When an entity is determined to have violated the FCA, the government may impose civil fines and penalties for each false claim, plus treble damages, and exclude the entity from participation in Medicare, Medicaid and other federal healthcare programs;
- the federal civil monetary penalties laws, which impose civil fines for, among other things, the offering or transfer or remuneration to a Medicare or state healthcare program beneficiary if the person knows or should know it is likely to influence the beneficiary's selection of a particular provider, practitioner, or supplier of services reimbursable by Medicare or a state health care program, unless an exception applies;
- the U.S. federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (i.e., public or private), and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements, in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity can be found guilty of violating HIPAA without actual knowledge of the statute or specific intent to violate it;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, which imposes certain obligations, with respect to safeguarding the privacy, security and transmission of individually identifiable health information without appropriate authorization by covered entities, such as health plans, healthcare clearinghouses and certain healthcare providers, as well as their business associates that perform certain services involving such individually identifiable health information. Mandatory penalties for HIPAA violations can be significant. A single breach incident can result in violations of multiple standards. If a person knowingly or intentionally obtains or discloses PHI in violation of HIPAA requirements, criminal penalties may also be imposed;
- the Federal Food, Drug and Cosmetic Act, or FDC Act, which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices;
- federal government price reporting laws, which require us to calculate and report complex pricing metrics in an accurate and timely manner to government programs;
- the U.S. federal legislation commonly referred to as Physician Payments Sunshine Act, and its implementing regulations, which requires certain manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program to report annually to the CMS information related to certain payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists, and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made during the previous year to certain non-physician providers such as physician assistants and nurse practitioners;
- analogous state laws and regulations, including the following: state anti-kickback and false claims laws, which may be broader in scope than their federal equivalents, and which may apply to our business practices, including research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines

and the relevant compliance guidance promulgated by the U.S. federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, and/or require tracking gifts and other remuneration and items of value provided to healthcare professionals and entities; state and local laws that require the registration of pharmaceutical sales representatives 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 often are not preempted by HIPAA, thus complicating compliance efforts; and

- the United Kingdom, European Union and other foreign law equivalents of each of these laws, including reporting requirements detailing interactions with and payments to healthcare providers, and privacy-related requirements in the United Kingdom, European Union and other jurisdictions.

The distribution of pharmaceutical products is subject to additional requirements and regulations, including approval, extensive record-keeping, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement bodies have recently increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. Even if precautions are taken, it is possible that governmental authorities will conclude that our business practices including compensation of physicians with stock or stock options, could, despite efforts to comply, be subject to challenge under current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion of drugs from government funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, reputational harm and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, that person or entity may be subject to significant criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs. Prohibitions or restrictions on sales or withdrawal of future marketed products could materially affect our business in an adverse way.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. The shifting compliance environment and the need to build and maintain robust and expandable systems to comply with multiple jurisdictions with different compliance or reporting requirements increases the possibility that a healthcare company may run afoul of one or more of the requirements.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

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

Failure to comply with current or future national, supranational, federal or state laws and regulations, regulatory guidance and industry standards relating to data protection, privacy and information security, including restrictive European regulations, could lead to government enforcement actions (which could include civil or criminal penalties), private litigation, and/or adverse publicity and could negatively affect our operating results and business.

We and our collaborators and third-party providers are subject to national, supranational, federal or state laws and regulations, regulatory guidance and industry standards relating to data protection, privacy and information security. This includes the EU General Data Protection Regulation, or GDPR, as well as other national data protection legislation in force in relevant EU and EEA member states (including the Data Protection Act 2018 in the United Kingdom), which governs the collection, use, storage, disclosure, transfer, or other processing of personal data (including health data processed in the context of clinical trials): (i) regarding individuals in the EU and EEA; and/or (ii) carried out in the context of the activities of our establishment in any EU and EEA member state. Following the United Kingdom's withdrawal from the EU on January 31, 2020, pursuant to the transitional arrangements agreed between the United Kingdom and the EU, the GDPR continued to have effect in English law until December 31, 2020, in the same fashion as was the case prior to that withdrawal as if the United Kingdom remained an EU member state for such purposes. The United Kingdom has implemented laws that are equivalent to the GDPR in national legislation. Since December 31, 2020, the data protection obligations of the GDPR have continued to apply to our processing of personal data in substantially unvaried form.

The GDPR is wide-ranging in scope and imposes numerous additional requirements on companies that process personal data, including imposing special requirements in respect of the processing of health and other sensitive data, requiring that consent of individuals to whom the personal data relates is obtained in certain circumstances, requiring additional disclosures to individuals regarding data processing activities, requiring that safeguards are implemented to protect the security and confidentiality of personal data, creating mandatory data breach notification requirements in certain circumstances, and requiring that certain measures (including contractual requirements) are put in place when engaging third-party processors. The GDPR defines personal data to include coded data and imposes high thresholds for informed consent and detailed notices for clinical trial subjects and investigators. The GDPR provides individuals with various rights in respect of their personal data, including rights of access, erasure, portability, rectification, restriction and objection. EU data protection authorities may impose large penalties for violations of the data protection laws, including potential fines of up to €20 million or 4% of annual global revenue, whichever is greater.

The GDPR imposes strict rules on the transfer of personal data to countries outside the EEA and Switzerland, including the United States. For example, in July 2020, the Court of Justice of the European Union limited how organizations could lawfully transfer personal data from the EEA to the United States by invalidating the EU-US Privacy Shield and imposing further restrictions on use of the standard contractual clauses, which could increase our costs and our ability to efficiently process personal data from the EEA. The United Kingdom and Switzerland have adopted similar restrictions. Since January 1, 2021, the United Kingdom is considered a third country by the EU. On June 28, 2021, the European Commission published its decision recognizing the United Kingdom as having adequate laws to the protect the rights and freedoms of data subjects such that personal data may transfer to from the EU to the United Kingdom without an approved transfer mechanism. The decision is effective for four years and its continuing effect is dependent on UK law and regulation on data privacy not diverging materially from the GDPR.

The GDPR may increase our responsibility and liability in relation to personal data that we process where such processing is subject to the GDPR. While we have taken steps to comply with the GDPR, and implementing legislation in the UK and applicable EU member states, including by seeking to establish appropriate lawful bases for the various

processing activities we carry out as a controller or joint controller, reviewing our security procedures and those of our vendors and collaborators, and entering into data processing agreements with relevant vendors and collaborators, we cannot be certain that our efforts to achieve and remain in compliance have been, and/or will continue to be, fully successful. Given the breadth and depth of changes in data protection obligations, preparing for and complying with the GDPR and similar laws, requirements are rigorous and time intensive and require significant resources and a review of our technologies, systems and practices, as well as those of any third-party collaborators, service providers, contractors or consultants that process or transfer personal data.

In the United States, numerous federal and state laws and regulations, including federal health information privacy laws, state data breach notification laws, state health information privacy laws and federal and state consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act), that govern the collection, use, disclosure and protection of health-related and other personal information could apply to our operations or the operations of our collaborators and third-party providers. For example, California enacted the California Consumer Privacy Act, or the CCPA, which became effective on January 1, 2020. The CCPA gives California residents expanded rights to access and delete their personal information, opt out of certain personal information sharing and receive detailed information about how their personal information is used. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. Additionally, the California Privacy Rights Act, or the CPRA, recently passed in California, which will amend the CCPA to impose additional data protection obligations on companies doing business in California, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It will also create a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. The majority of the provisions will go into effect on January 1, 2023, and additional compliance investment and potential business process changes may be required. In the United States, states are constantly amending existing laws, requiring attention to frequently changing regulatory requirements.

Many international laws, including the GDPR, require businesses to notify regulators and data subjects in the event of a data breach. Meanwhile, in the United States, all 50 states of the United States require businesses to provide notice to customers whose personal data has been disclosed as a result of a data breach. These laws are not consistent, and compliance in the event of a widespread data breach is costly.

In many jurisdictions, enforcement actions and consequences for non-compliance with protection, privacy and information security laws and regulations are rising. The authorities have shown a willingness to impose significant fines and issue orders preventing the processing of personal data on non-compliant businesses. Data subjects also have a private right of action, as do consumer associations, to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of applicable data protection laws. In the United States, possible consequences for non-compliance include enforcement actions in response to rules and regulations promulgated under the authority of federal agencies and state attorneys general and legislatures and consumer protection agencies. In addition, privacy advocates and industry groups have regularly proposed, and may propose in the future, self-regulatory standards that may legally or contractually apply to us. If we fail to follow these security standards, even if no customer information is compromised, we may incur significant fines or experience a significant increase in costs.

The risk of our being found in violation of these laws is increased by the fact that many of them have not been fully interpreted by applicable regulatory authorities or the courts, and their provisions are open to a variety of interpretations. Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. The shifting compliance environment and the need to build and maintain robust and expandable systems to comply with multiple jurisdictions with different compliance and/or reporting requirements increases the possibility that a healthcare company may run afoul of one or more of the requirements.

The global data protection landscape is rapidly evolving, and implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future. This evolution may create uncertainty in our business, affect our or our CROs', collaborators', service providers' and other contractors' ability to operate in certain jurisdictions or to collect, store, transfer use and share personal information, necessitate the acceptance of more onerous obligations in our contracts, result in liability or impose additional costs on us.

Failure by us or our collaborators and third-party providers to comply with data protection laws and regulations could result in government enforcement actions (which could include civil or criminal penalties), private litigation and/or adverse publicity and could negatively affect our operating results and business. Moreover, clinical trial subjects about whom we or our potential collaborators obtain information, as well as the providers who share this information with us, may contractually limit our ability to use and disclose the information. Claims that we have violated individuals' privacy rights, failed to comply with data protection laws or breached our contractual obligations, even if we are not found liable, could be expensive and time-consuming to defend, could result in adverse publicity and could have a material adverse effect on our business, financial condition, results of operations and prospects.

RISKS RELATED TO OUR INTELLECTUAL PROPERTY

Risks Related to Protecting our Intellectual Property

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

We currently are, and in the future may continue to be, party to license or collaboration agreements with third parties to advance our research or allow commercialization of ATL001 or any future product candidates. In particular, we are party to a license agreement, or the CRT Agreement, with Cancer Research Technology Limited, to obtain exclusive and non-exclusive licenses under certain patents, know-how, data, and information relating to a multi-institution study known as the TRACERx Study, focused on advanced NSCLC. We rely on this license for the development of ATL001 and may rely on it for future product candidates, and we rely on the data from TRACERx to continue to improve our PELEUS platform. The CRT Agreement and other future agreements may impose, and may continue to impose, numerous obligations, such as development, diligence, payment, commercialization, funding, milestone, royalty, sublicensing, insurance, patent prosecution, enforcement and other obligations on us and may require us to meet development timelines, or to exercise commercially reasonable efforts to develop and commercialize approved products, in order to maintain the licenses. In spite of our best efforts, our current and future licensors might conclude that we have materially breached our future license agreements and might therefore terminate the license agreements, thereby removing or limiting our ability to develop and commercialize products and technologies covered by these license agreements.

Any termination of the CRT Agreement or future licenses, or if the underlying patents or applications fail to provide the intended exclusivity, could result in the loss of significant rights and could harm our ability to commercialize ATL001 and any future product candidates and we may be required to cease our development and commercialization of certain of our product candidates. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

Disputes may also arise between us and our future licensors regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe, misappropriate or otherwise violate intellectual property rights of the licensor that are not subject to the licensing agreement;
- our right to sublicense patent and other rights to third parties under collaborative development relationships;

- our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our product candidates, and what activities satisfy those diligence obligations;
- the right to claim priority of invention of any patented technology; and
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our future licensors and us and our partners.

In addition, the agreements under which we license intellectual property or technology from third parties, and which we may continue to license in the future, are and may be complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations and prospects. Moreover, if disputes over intellectual property that we may license in the future prevent or impair our ability to maintain future licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates, which could have a material adverse effect on our business, financial conditions, results of operations and prospects.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to the protection afforded by patents we may own or in-license in the future, we seek to rely on trade secret protection, in particular in relation to our proprietary VELOS manufacturing process and PELEUS bioinformatics platform, confidentiality agreements, and license agreements to protect proprietary know-how that is not patentable, processes for which patents are difficult to enforce and any other elements of our product discovery and development processes. Although we require all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information, or technology to enter into confidentiality agreements, trade secrets can be difficult to protect and we have limited control over the protection of trade secrets used by our collaborators and suppliers. We cannot be certain that we have or will obtain these agreements in all circumstances and we cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary information.

Moreover, any of these parties might breach the agreements and intentionally or inadvertently disclose our trade secret information and we may not be able to obtain adequate remedies for such breaches. In addition, competitors may otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Furthermore, the laws of some foreign countries do not protect proprietary rights and trade secrets to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we are unable to prevent unauthorized material disclosure of our intellectual property to third parties, we will not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, financial condition, results of operations and future prospects.

Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. If we choose to go to court to stop a third party from using any of our trade secrets, we may incur substantial costs. These lawsuits may consume our time and other resources even if we are successful. Although we take steps to protect our proprietary information and trade secrets, including through contractual means with our employees and consultants, third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them from using that technology or information to compete with us.

Thus, we may not be able to meaningfully protect our trade secrets, in particular those relating to our proprietary VELOS manufacturing process or PELEUS bioinformatics platform. It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information concerning our business or financial affairs developed or made known to the individual or entity during the course of the party's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. In addition, we take other appropriate precautions, such as physical and technological security measures, to guard against misappropriation of our proprietary technology by third parties. In the case of employees, the agreements provide that all inventions conceived by the individual, and which are related to our current or planned business or research and development or made during normal working hours, on our premises or using our equipment or proprietary information, are our exclusive property. Although we require all of our employees to assign their inventions to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Third-party claims of intellectual property infringement, misappropriation or other violations may be costly and time-consuming and may prevent or delay our product discovery and development efforts.

Third parties may initiate legal proceedings alleging that we are infringing, misappropriating, or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business. Our commercial success depends upon our ability to develop or manufacture our current product candidate in the indications we are currently targeting or any follow-on indications as well as any future product candidates and use our proprietary technologies without infringing, misappropriating or otherwise violating the intellectual property rights of third parties. There is a substantial amount of litigation involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, as well as administrative proceedings for challenging patents, including derivation, interference, reexamination, *inter partes* review, and post grant review proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. We or any of our future licensors or strategic partners may be party to, exposed to, or threatened with, future adversarial proceedings or litigation by third parties having patent or other intellectual property rights alleging that our current or future product candidates and/or proprietary technologies infringe, misappropriate or otherwise violate their intellectual property rights. We cannot assure you that ATL001 or future product candidates and other technologies that we have developed, are developing or may develop in the future do not or will not infringe, misappropriate or otherwise violate existing or future patents or other intellectual property rights owned by third parties. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing our product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may give rise to claims of infringement of the patent rights of others. Moreover, it is not always clear to industry participants, including us, which patents cover various types of products or their methods of use or manufacture. Thus, because of the large number of patents issued and patent applications filed in our fields, there may be a risk that third parties may allege they have patent rights encompassing our product candidates, technologies or methods.

If a third party claims that we infringe, misappropriate or otherwise violate its intellectual property rights, we may face a number of issues, including, but not limited to:

- infringement, misappropriation and other intellectual property claims which, regardless of merit, may be expensive and time-consuming to litigate and may divert our management's attention from our core business and may impact our reputation;
- substantial damages for infringement, misappropriation or other violations, which we may have to pay if a court decides that the product candidate or technology at issue infringes, misappropriates or violates the third

party's rights, and, if the court finds that the infringement was willful, we could be ordered to pay treble damages and the patent owner's attorneys' fees;

- a court order prohibiting us from developing, manufacturing, marketing or selling our product candidates, or from using our proprietary technologies, unless the third party licenses its product rights to us, which it is not required to do, on commercially reasonable terms or at all;
- if a license is available from a third party, we may have to pay substantial royalties, upfront fees and other amounts, and/or grant cross-licenses to intellectual property rights for our products, or the license to us may be non-exclusive, which would permit third parties to use the same intellectual property to compete with us;
- redesigning our product candidates or processes so they do not infringe, misappropriate or violate third party intellectual property rights, which may not be possible or may require substantial monetary expenditures and time; and
- there could be public announcements of the results of hearings, motions or other interim proceedings or developments, and, if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our ADSs.

Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations or could otherwise have a material adverse effect on our business, results of operations, financial condition and prospects. The occurrence of any of the foregoing could have a material adverse effect on our business, financial condition, results of operations or prospects.

We may choose to challenge the patentability of claims in a third party's U.S. patent by requesting that the USPTO review the patent claims in an *ex-parte* re-exam, *inter partes* review or post-grant review proceedings. These proceedings are expensive and may consume our time or other resources. We may choose to challenge a third party's patent in patent opposition proceedings in the EPO, or other foreign patent office. The costs of these opposition proceedings could be substantial, and may consume our time or other resources. If we fail to obtain a favorable result at the USPTO, EPO or other patent office then we may be exposed to litigation by a third party alleging that the patent may be infringed by our product candidates or proprietary technologies.

Third parties may assert that we are employing their proprietary technology without authorization. Patents issued in the United States by law enjoy a presumption of validity that can be rebutted only with evidence that is "clear and convincing," a heightened standard of proof. There may be issued third-party patents of which we are currently unaware with claims to compositions, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Patent applications can take many years to issue. In addition, because some patent applications in the United States may be maintained in secrecy until the patents are issued, patent applications in the United States and many foreign jurisdictions are typically not published until 18 months after filing, and publications in the scientific literature often lag behind actual discoveries, we cannot be certain that others have not filed patent applications covering our product candidates or technology. If any such patent applications issue as patents, and if such patents have priority over our patent applications or patents we may own or in-license, we may be required to obtain rights to such patents owned by third parties which may not be available on commercially reasonable terms or at all, or may only be available on a non-exclusive basis. There may be currently pending patent applications which may later result in issued patents that our product candidates may infringe. It is also possible that patents owned by third parties of which we are aware, but which we do not believe are relevant to our product candidates or other technologies, could be found to be infringed by our product candidates or other technologies. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Moreover, we may fail to identify relevant patents or incorrectly conclude that a patent is invalid, not enforceable, exhausted, or not infringed by our activities. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of our product candidates, molecules used in or formed during the manufacturing process, or any final product itself, the holders of any such patents may be able to block our ability to commercialize the product candidate unless we obtained a license under the applicable patents, or until such patents expire or they are finally determined to be held invalid or unenforceable. Similarly, if any third-party patent were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or methods of use, including combination

therapy or patient selection methods, the holders of any such patent may be able to block our ability to develop and commercialize the product candidate unless we obtained a license or until such patent expires or is finally determined to be held invalid or unenforceable. In either case, such a license may not be available on commercially reasonable terms or at all. If we are unable to obtain a necessary license to a third-party patent on commercially reasonable terms, or at all, our ability to commercialize our product candidates may be impaired or delayed, which could in turn significantly harm our business. Even if we obtain a license, it may be nonexclusive, thereby giving our competitors access to the same technologies licensed to us. In addition, if the breadth or strength of protection provided by our patent applications or any patents we may own or in-license in the future is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Parties making claims against us may seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize our product candidates. Defense of these claims, regardless of their merit, could involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement, misappropriation or other violation against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. We cannot predict whether any such license would be available at all or whether it would be available on commercially reasonable terms. Furthermore, even in the absence of litigation, we may need or may choose to obtain licenses from third parties to advance our research or allow commercialization of our product candidates. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to further develop and commercialize our product candidates, which could harm our business significantly.

If we are unable to obtain and maintain sufficient patent and other intellectual property protection for ATL001 and any future product candidates and technologies, our competitors could develop and commercialize products and technologies similar or equivalent to ours, and we may not be able to compete effectively in our market or successfully commercialize any product candidates we may develop.

Our success depends in significant part on our ability and the ability of our current or future collaborators and licensors to obtain, maintain, enforce and defend patents and other intellectual property rights with respect to ATL001 and any future product candidates and technology and to operate our business without infringing, misappropriating, or otherwise violating the intellectual property rights of others. If we and our current or future collaborators and licensors are unable to obtain and maintain sufficient intellectual property protection for ATL001 or other future product candidates that we may identify, or if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors and other third parties could develop and commercialize product candidates similar or equivalent to ours, and our ability to successfully commercialize our product candidates and other product candidates that we may pursue may be impaired.

Further, we may not be successful in obtaining or maintain necessary rights to product components and processes for our development pipeline through acquisitions and in-licenses. Presently we have rights to certain intellectual property, through licenses from third parties and under patent applications that we own or will own, related to use of data and materials from the TRACERx study, the use of clonal neoantigens and T cells in cell therapy, certain processes and devices used in our proprietary VELOS manufacturing process, aspects of our proprietary PELEUS bioinformatics platform and ATL001. Because any future product candidates may require the use of proprietary rights held by third parties, the growth of our business will likely depend in part on our ability to acquire, in-license or use these proprietary rights.

ATL001 and any future product candidates may also require specific formulations to work effectively and efficiently and these rights may be held by others. Similarly, efficient production or delivery of our product candidates may also require specific compositions or methods, and the rights to these may be owned by third parties. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify as necessary or important to our business operations. We may fail to obtain any of these

licenses at a reasonable cost or on reasonable terms, if at all, which would harm our business. We may need to cease use of the compositions or methods covered by such third-party intellectual property rights, and may need to seek to develop alternative approaches that do not infringe on such intellectual property rights which may entail additional costs and development delays, even if we were able to develop such alternatives, which may not be feasible. Even if we are able to obtain a license, it may be nonexclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology. Moreover, the molecules that may in the future be used with our product candidates may be covered by the intellectual property rights of others.

Additionally, we sometimes collaborate with academic institutions to accelerate our research activities or development under written agreements with these institutions. In certain cases, these institutions provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to others, potentially blocking our ability to pursue our program and allowing third parties to compete with us. If we are unable to successfully obtain rights to required third-party intellectual property or to maintain the existing intellectual property rights we have, we may have to abandon development of such program and our business and financial condition could suffer.

The licensing and acquisition of third-party intellectual property rights is a competitive area, and companies, which may be more established, or have greater resources than we do, may also be pursuing strategies to license or acquire third-party intellectual property rights that we may consider necessary or attractive in order to commercialize our product candidates. More established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. There can be no assurance that we will be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding the additional product candidates that we may seek to acquire. If we are unable to successfully obtain rights to required third-party intellectual property or to maintain the existing intellectual property rights we have, we may have to abandon development of such program and our business, results of operations, financial condition and prospects could suffer.

Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other government fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process and following the issuance of a patent. While an inadvertent lapse can in some cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Noncompliance events that could result in abandonment or lapse of a patent include, but are not limited to, failure to respond to official actions or carry out the required acts within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In such an event, our competitors might be able to enter the market with similar or equivalent products or platforms, which could have a material adverse effect on our business prospects and financial condition.

If we do not obtain patent term extension and data exclusivity for ATL001 or any future product candidates we may develop, our business may be materially harmed.

Depending upon the timing, duration and specifics of any FDA marketing approval of any of our current or future product candidates we may develop, one or more U.S. patents we may own or in-license in the future may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent term extension of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. However, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is shorter than what we request, our competitors may obtain approval of competing products following expiration of any patents that issue from our patent applications, and our business, financial condition, results of operations, and prospects could be materially harmed.

Changes to patent law in the United States and in foreign jurisdictions 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 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. 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 patents that we might obtain in the future. For example, in the case *Assoc. for Molecular Pathology v. Myriad Genetics, Inc.,* the U.S. Supreme Court held that certain claims to DNA molecules are not patentable. Any adverse changes in the patent laws of other jurisdictions could have a material adverse effect on our business and financial condition. Changes in the laws and regulations governing patents in other jurisdictions could similarly have an adverse effect on our ability to obtain and effectively enforce any rights we may have in our patent applications or any patents we may own or in-license in the future.

Recent or future patent reform legislation could also increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of any patents we may own or in-license in the future. The United States has enacted and implemented wide-ranging patent reform legislation. On September 16, 2011, the Leahy-Smith America Invents Act, or America Invents Act, was signed into law, which includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art, may affect patent litigation, establish a new post-grant review system and switch the U.S. patent system from a "first-to-invent" system to a "first-to-file" system. Under a "first-to-file" system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to a patent on the invention regardless of whether another inventor had made the invention earlier. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we were the first to either: (i) file any patent application related to our product candidates or other technologies; or (ii) invent any of the inventions claimed in our patent applications or any patents we may own or in-license. These changes also allow third party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post-grant proceedings, including post-grant review, *inter partes* review, and derivation proceedings. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim,

a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. An adverse determination in any such proceeding could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. Accordingly, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of any issued patents we may own or in-license in the future, all of which could have a material adverse effect on our business and financial condition.

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

Our trademarks or trade names may be challenged, infringed, diluted, circumvented or declared generic or determined to be infringing on other marks. We intend to rely on both registration and common law protection for our trademarks. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. During the trademark registration process, we may receive Office Actions from the USPTO objecting to the registration of our trademark. Although we would be given an opportunity to respond to those objections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and/or to seek the cancellation of registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. If we are unable to obtain a registered trademark or establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected.

Numerous factors may limit any potential competitive advantage provided by our intellectual property rights.

The degree of future protection afforded by our intellectual property rights, whether owned or in-licensed, is uncertain because intellectual property rights have limitations, and may not adequately protect our business, provide a barrier to entry against our competitors or potential competitors, or permit us to maintain our competitive advantage. Moreover, if a third party has intellectual property rights that cover the practice of our technology, we may not be able to fully exercise or extract value from our intellectual property rights. The following examples are illustrative:

- patent applications that we own or may in-license in the future may not lead to issued patents;
- patents, should they issue, that we may own or in-license in the future, may not provide us with any competitive advantages, may be narrowed in scope, or may be challenged and held invalid or unenforceable;
- others may be able to develop and/or practice technology that is similar to our technology or aspects of our technology but that is not covered by the claims of any patents we may own or in-license in the future, should any patents issue;
- third parties may compete with us in jurisdictions where we do not pursue and obtain patent protection;
- we, or our future licensors or collaborators, might not have been the first to make the inventions covered by a patent application that we own or may in-license in the future;
- we, or our future licensors or collaborators, might not have been the first to file patent applications covering a particular invention;
- others may independently develop similar or alternative technologies without infringing, misappropriating or otherwise violating our intellectual property rights;
- our competitors might conduct research and development activities in the United States and other countries that provide a safe harbor from patent infringement claims for certain research and development activities, as well as in countries where we do not have patent rights, and may then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not be able to obtain and/or maintain necessary licenses on reasonable terms or at all;

- third parties may assert an ownership interest in our intellectual property and, if successful, such disputes may preclude us from exercising exclusive rights, or any rights at all, over that intellectual property;
- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such trade secrets or know-how;
- we may not be able to maintain the confidentiality of our trade secrets or other proprietary information;
- we may not develop or in-license additional proprietary technologies that are patentable; and
- the patents of others may have an adverse effect on our business.

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

Risks Related to Intellectual Property Litigation

We may be involved in lawsuits to protect or enforce our intellectual property rights, including any patents we may own or in-license in the future, which could be expensive, time-consuming and unsuccessful.

Competitors may infringe any patents we may own or in-license in the future. In addition, any patents we may own or in-license also may become involved in inventorship, priority, validity or unenforceability disputes. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. In addition, in an infringement proceeding, a court may decide that one or more of any patents we may own or in-license in the future is not valid or is unenforceable or that the other party's use of our technology that may be patented falls under the safe harbor to patent infringement under 35 U.S.C. §271(e)(1). There is also the risk that, even if the validity of these patents is upheld, the court may refuse to stop the other party from using the technology at issue on the grounds that any patents we may own or in-license in the future do not cover the technology in question or that such third party's activities do not infringe our patent applications or any patents we may own or in-license in the future. An adverse result in any litigation or defense proceedings could put one or more of any patents we may own or in-license in the future at risk of being invalidated, held unenforceable, or interpreted narrowly and could put our patent applications at risk of not issuing. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing, or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

Post-grant proceedings provoked by third parties or brought by the USPTO may be necessary to determine the validity or priority of inventions with respect to our patent applications or any patents we may own or in-license in the future. These proceedings are expensive and an unfavorable outcome could result in a loss of our current patent rights and could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. In addition to potential USPTO review proceedings, we may become a party to patent opposition proceedings in the European Patent Office, or EPO, or similar proceedings in foreign patent offices, where our foreign patents are challenged. The costs of these opposition or similar proceedings could be substantial, and may result in a loss of scope of some claims or a loss of the entire patent. An unfavorable result at the USPTO, EPO or other patent office may result in the loss of our right to exclude others from practicing one or more of our inventions in the relevant country or jurisdiction, which could have a material adverse effect on our business.

Litigation or post-grant proceedings may result in a decision adverse to our interests and, even if we are successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent misappropriation of our trade secrets or confidential information, particularly in countries where the laws may not protect those rights as fully as in the United States.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. 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 detect infringement of any patents we may own or in-license in the future. Even if we detect infringement by a third party of any patents we may own or in-license in the future, we may choose not to pursue litigation against or settlement with the third party. If we later sue such third party for patent infringement, the third party may have certain legal defenses available to it, which otherwise would not be available except for the delay between when the infringement was first detected and when the suit was brought. Such legal defenses may make it impossible for us to enforce any patents we may own or in-license against such third party.

Any issued patents we may own or in-license in the future covering ATL001 or any future product candidates could be narrowed or found invalid or unenforceable if challenged in court or before administrative bodies in the United States or abroad, including the USPTO.

If we or our future licensors or strategic partners initiate legal proceedings against a third party to enforce a patent covering ATL001 or any future product candidates, the defendant could counterclaim that the patent covering our product candidate, as applicable, is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace, and there are numerous grounds upon which a third party can assert invalidity or unenforceability of a patent. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of patentable subject matter, lack of written description, lack of novelty, obviousness, or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. 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, *inter partes* review, post grant review and equivalent proceedings in foreign jurisdictions (such as opposition proceedings). Such proceedings could result in revocation or amendment to our patent applications or any patents we may own or in-license in the future in such a way that they no longer cover our product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate or render unenforceable, any rights we may have from our patent applications or any patents we may own or in-license in the future, allow third parties to commercialize our product candidates or other technologies and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. Moreover, we may have to participate in interference proceedings declared by the USPTO to determine priority of invention or in post-grant challenge proceedings, such as oppositions in a foreign patent office, that challenge our priority of invention or other features of patentability with respect to our patent applications and any patents we may own or in-license. Such challenges may result in loss of patent rights, loss of exclusivity, or in patent claims being narrowed, invalidated, or held unenforceable, which could limit our ability to stop others from using or commercializing similar or equivalent technology and products, or limit the duration of the patent protection of our product candidates and other technologies. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we or our future licensing partners and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, or if we are otherwise unable to adequately protect our rights, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Such a loss of patent protection could have a material adverse impact on our business and our ability to commercialize or license our technology and product candidates.

Such proceedings also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us. If we are unsuccessful in any such proceeding or other priority or inventorship dispute, we may be required to obtain and maintain licenses from third parties, including parties involved in any such interference proceedings or other priority or inventorship disputes. Such licenses may not be available on commercially reasonable terms or at all, or may be non-exclusive. If we are unable to obtain and maintain such licenses, we may need to cease the development, manufacture, and commercialization of one or more of the product candidates we may develop. The loss of exclusivity or the narrowing of our patent application claims could limit our ability to stop others from using or commercializing similar or equivalent technology and products. Any of the foregoing could have a material adverse effect on our business, results of operations, financial condition and prospects.

We may be subject to claims challenging the inventorship or ownership of any intellectual property, including any patents we may own or in-license in the future.

We may be subject to claims that former employees, collaborators or other third parties have an interest in any patents we may own or in-license in the future, trade secrets, or other intellectual property as an inventor or co-inventor. For example, we may have inventorship disputes arise from conflicting obligations of employees, consultants or others who are involved in developing ATL001 or any future product candidates or other technologies. We generally enter into confidentiality and intellectual property assignment agreements with our employees, consultants, and contractors. These agreements generally provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property. However, those agreements may not be honored and may not effectively assign intellectual property rights to us. Moreover, there may be some circumstances, where we are unable to negotiate for such ownership rights. Disputes regarding ownership or inventorship of intellectual property can also arise in other contexts, such as collaborations and sponsored research. If we are subject to a dispute challenging our rights in or to patents or other intellectual property, such a dispute could be expensive and time-consuming. Litigation may be necessary to defend against these and other claims challenging inventorship of any patents we may own or in-license in the future, trade secrets or other intellectual property. If we were unsuccessful, in addition to paying monetary damages, we could lose valuable rights in intellectual property that we regard as our own, such as exclusive ownership of, or right to use, intellectual property that is important to our product candidates and other technologies. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information or alleged trade secrets of third parties or competitors or are in breach of non-competition or non-solicitation agreements with our competitors.

We have received confidential and proprietary information from third parties. In addition, as is common in the biotechnology and pharmaceutical industries, we employ individuals who were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors, in some cases until recently. We may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed confidential information or trade secrets of these third parties or our employees' former employers or our consultants' or contractors' current or former clients or customers. In addition, we may in the future be subject to claims that we caused an employee to breach the terms of his or her non-competition or non-solicitation agreement. Litigation or arbitration may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation or other legal proceedings relating to intellectual property claims and possible aftermath could result in substantial cost and be a distraction to our management and employees. Any litigation or the threat thereof may adversely affect our ability to hire employees.

A loss of key personnel or their work product could hamper or prevent our ability to commercialize product candidates, which could have an adverse effect on our business, results of operations and financial condition. In addition, there

could be public announcements of the results of hearings, motions or other interim proceedings or developments, and, if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of the ADSs. This type of litigation or proceeding could substantially increase our operating losses and reduce our resources available for development activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other intellectual property-related proceedings could adversely affect our ability to compete in the marketplace.

RISKS RELATED TO OUR RELIANCE ON THIRD PARTIES

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

We utilize and depend upon independent investigators and collaborators, such as medical institutions, CROs, CMOs, and strategic partners to conduct and support certain of our research activities and clinical trials under agreements with us.

We expect to have to continue to negotiate budgets and contracts with CROs, trial sites and CMOs and we may not be able to do so on favorable terms, which may result in delays to our development timelines and increased costs. We will rely heavily on these third parties over the course of our research activities and clinical trials, and we control only certain aspects of their activities. As a result, we will have less direct control over the conduct, timing and completion of these research activities and clinical trials and the management of data developed through research activities and clinical trials than would be the case if we were relying entirely upon our own staff. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with applicable protocol, legal and regulatory requirements 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 good clinical practices, or GCPs, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for product candidates in clinical development. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of these third parties fail to comply with applicable GCP regulations, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, such regulatory authorities will determine that any of our clinical trials comply with the GCP regulations. In addition, supplies of our product candidates used in our clinical trials must be manufactured under good manufacturing practices, or cGMP, regulations. Our failure or any failure by these third parties to comply with these regulations or to recruit 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 performing services or otherwise acting on our behalf 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, we cannot control whether or not they devote sufficient time and resources to our ongoing clinical and preclinical product candidates. 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 product 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 product candidates. As a result, our financial results and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenue could be delayed.

Switching or adding third parties to conduct our research and 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 occur, which can materially impact our ability to meet our desired clinical development timelines. If we engage directly with third-party CROs and CMOs, we may incur additional costs or experience delays. For example, in February 2022, we signed a letter of intent with a CMO, Center for Breakthrough Medicines, or CBM, to initiate the technology transfer of ATL001 with an intention to supply clinical doses to U.S. patients in 2024. If any CMO with whom we contract fails to perform its obligations, we may be forced to manufacture the materials ourselves or enter into an agreement with a different CMO, which we may not be able to do on reasonable terms, if at all. In either scenario, our clinical trials supply could be delayed significantly as we establish alternative supply sources. In some cases, the technical skills required to manufacture our product candidates may be unique or proprietary to the original CMO and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills to a back-up or alternate supplier, or we may be unable to transfer such skills at all. In addition, if we are required to change CMOs for any reason, we will be required to verify that the new CMO maintains facilities and procedures that comply with quality standards and with all applicable regulations. We will also need to verify, such as through a manufacturing comparability study, that any new manufacturing process will produce our product candidate according to the specifications previously submitted to the FDA or another regulatory authority. The delays associated with the verification of a new CMO could negatively affect our ability to develop product candidates or commercialize our products in a timely manner or within budget. Furthermore, a CMO may possess technology related to the manufacture of our product candidate that such CMO owns independently. This would increase our reliance on such CMO or require us to obtain a license from such CMO in order to have another CMO manufacture our product candidates. In addition, changes in manufacturers often involve changes in manufacturing procedures and processes, which could require that we conduct bridging studies between our prior clinical supply used in our clinical trials and that of any new manufacturer. We may be unsuccessful in demonstrating the comparability of clinical supplies which could require the conduct of additional clinical trials.

Our employees, independent contractors, consultants, commercial partners and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk of employee fraud or other illegal activity by our employees, independent contractors, consultants, commercial partners and vendors. Misconduct by these parties could include intentional, reckless and negligent conduct that fails to: comply with the regulations of the FDA and other comparable foreign regulatory bodies, provide true, complete and accurate information to the FDA and other comparable foreign regulatory bodies, comply with manufacturing standards we have established, comply with healthcare fraud and abuse laws in the United States and similar foreign fraudulent misconduct laws or report financial information or data accurately or to disclose unauthorized activities to us. If we obtain FDA approval of any of our product candidates and begin commercializing those products in the United States, our potential exposure under such laws and regulations will increase significantly, and our costs associated with compliance with such laws and regulations are also likely to increase. These laws may impact, among other things, our current activities with principal investigators and research patients, as well as proposed and future sales, marketing and education programs. In particular, the promotion, sales and marketing of healthcare items and services, as well as certain business arrangements in the healthcare industry, are subject to extensive laws designed to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, structuring and commission(s), certain customer incentive programs and other business arrangements generally.

It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent inappropriate conduct may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations.

We may form or seek additional collaborations or strategic alliances or enter into additional licensing arrangements in the future, and we may not realize the benefits of such collaborations, alliances or licensing arrangements.

We may form or seek additional strategic alliances, create joint ventures or collaborations, or enter into additional licensing arrangements with third parties that we believe will complement or augment our development and commercialization efforts with respect to our product candidates and any future product candidates that we may develop. 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 shareholders or disrupt our management and business.

In addition, we face significant competition in seeking appropriate strategic partners and the negotiation process is time-consuming and complex. Moreover, we may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for ATL001 and any future product candidates because they may be deemed to be at too early of a stage of development for collaborative effort and third parties may not view our product candidates as having the requisite potential to demonstrate safety, potency, purity and efficacy and obtain marketing approval.

Further, collaborations involving ATL001 and any future product candidates are subject to numerous risks, which may include the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to a collaboration;
- collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization of our product candidates based on clinical trial results, changes in their strategic focus due to the acquisition of competitive products, availability of funding or other external factors, such as a business combination that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial, stop a clinical trial, abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates;
- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to their marketing and distribution;
- collaborators may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability;
- disputes may arise between us and a collaborator that cause the delay or termination of the research, development or commercialization of our product candidates, or that result in costly litigation or arbitration that diverts management attention and resources;
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates; and
- collaborators may own or co-own intellectual property covering our products that results from our collaborating with them, and in such cases, we would not have the exclusive right to commercialize such intellectual property.

As a result, if we enter into additional collaboration agreements and strategic partnerships or license ATL001 or any future product candidates, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture, which could delay our timelines or otherwise adversely affect our business. We also cannot be certain that, following a strategic transaction or license, we will achieve the revenue or specific net income that justifies such transaction. Any delays in entering into new collaborations or strategic partnership agreements related to ATL001 or any future product candidates could delay the development and commercialization of our product candidates in certain geographies for certain indications, which would harm our business prospects, financial condition and results of operations.

RISKS RELATED TO EMPLOYEE MATTERS, MANAGING OUR GROWTH AND OTHER RISKS

Risks Related to our Employee Matters

We are highly dependent on our key personnel, and if we are not successful in attracting and retaining highly qualified personnel, we may not be able to successfully implement our business strategy.

Our ability to compete in the highly competitive biotechnology and pharmaceutical industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. We are highly dependent on our key management, scientific and technical personnel, many of whom have been instrumental for us and have substantial experience in our therapies and related technologies.

The loss of the services of any of our executive officers, other key employees and other scientific and medical advisors, and an inability to find suitable replacements could result in delays in product development and harm our business.

To encourage valuable employees to remain at our company, in addition to salary, bonus scheme and our benefits package, we have provided shares for some United Kingdom based employees and share options for U.S. and some United Kingdom based employees that vest over time. The value to employees of shares and 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. 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. To date this success has been geared towards building an attractive employee value proposition which puts culture at the heart of how we engage our people. This focus on soft retention elements has worked well to date and we are now exploring wider incentive mechanisms to be in-line with the market. Notwithstanding our current and future development of incentive mechanisms, we may be exposed to increases in wage inflation that have an adverse impact on our financial position and on our ability to attract, hire and retain key employees.

Risks Related to our Business Operations and Growth

Insurance policies are expensive and protect us only from some business risks, which leaves us exposed to significant uninsured liabilities.

We do not carry insurance for all categories of risk that our business may encounter. Some of the policies we currently maintain include general liability, employment practices liability, travel, property, umbrella, and directors' and officers' insurance.

Insurance coverage is becoming increasingly expensive and in the future we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. We do not carry specific biological or hazardous waste insurance coverage, and our property, casualty and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended.

We also expect that operating as a public company has made it, and will continue to make it, more difficult and more expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. As a result, it may be more difficult for us to attract and retain qualified people to serve on our board of directors, our board committees or as executive officers. We do not know, however, if we will be able to maintain existing insurance with adequate levels

of coverage. Any significant uninsured liability may require us to pay substantial amounts, which would adversely affect our cash position and results of operations.

The ongoing spread of COVID-19, and the proliferation of variants capable of escaping the coverage of available vaccines has caused, and could continue to cause, severe disruptions in the global economy and could seriously harm our development efforts, increase our costs and expenses and have a material adverse effect on our business, financial condition and results of operations.

Broad-based business or economic disruptions could adversely affect our ongoing or planned research and development activities. For example, in December 2019, an outbreak of a novel strain of coronavirus, which causes coronavirus disease, or COVID-19, was reported to have surfaced in Wuhan, China, and in March 2020, the World Health Organization declared the COVID-19 outbreak a pandemic. The pandemic and government measures taken in response have had a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred; supply chains have been disrupted; facilities and production have been suspended; and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services, such as travel, has fallen. There is a risk that government actions will not be effective at containing COVID-19 or other infectious diseases, and that government actions, including the orders and restrictions described above, that are intended to contain the spread of COVID-19 will have a devastating negative impact on the world economy at large, in which case the risks to our sales, operating results and financial condition described herein would be elevated significantly.

As a result of the COVID-19 pandemic, we have experienced and we expect to continue to experience disruptions that could severely impact our business, research and clinical trials, including:

- continued delays or difficulties in enrolling and retaining patients in our clinical trials;
- continued delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- delays in receiving authorizations from regulatory authorities to initiate our planned clinical trials;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- interruption of key clinical trial activities, such as clinical trial site data monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others or interruption of clinical trial subject visits and study procedures (such as endoscopies that are deemed non-essential), which may impact the integrity of subject data and clinical trial endpoints;
- risk that participants enrolled in our clinical trials will contract COVID-19 while the clinical trial is ongoing, which could impact the results of the clinical trial, including by increasing the number of observed adverse events;
- risk that we are unable to enroll participants in our clinical trials in adequate numbers;
- interruption or delays in the operations of the FDA or other regulatory authorities, which may impact review and approval timelines;
- interruption of, or delays in, our manufacturing supply chain, including any inability to access or run the GMP manufacturing facility at the Royal Free Hospital;
- interruptions in research activities due to restricted or limited operations at our laboratory facility;
- delays in necessary interactions with local regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government employees;
- changes in local regulations as part of a response to the COVID-19 pandemic, which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, or to discontinue such clinical trials altogether;
- limitations on employee resources that would otherwise be focused on the conduct of our research and clinical trials, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people; and
- interruption or delays to our sourced discovery and clinical activities.

Since the beginning of the COVID-19 pandemic, three vaccines for COVID-19 have received Emergency Use Authorization by the FDA and two of those later received marketing approval. Additional vaccines may be authorized or approved in the future. The resultant demand for vaccines and potential for manufacturing facilities and materials to be commandeered under the Defense Production Act of 1950, or equivalent foreign legislation, may make it more difficult to obtain materials for the products needed for our clinical trials, which could lead to delays in these trials.

The global COVID-19 pandemic continues to rapidly evolve. The extent to which COVID-19 ultimately impacts our business, results of operations and financial condition will depend on future developments, which remain highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of the disease, the evolution and proliferation of new variants, duration of the outbreak, travel restrictions, new information that may emerge concerning the severity of COVID-19 or the effectiveness of actions taken in the United States and other countries to contain the pandemic or treat its impact, among others. In addition, recurrences or additional waves of COVID-19 cases could cause other widespread or more severe impacts depending on where infection rates are highest. We cannot presently predict the scope and severity of any potential business shutdowns or disruptions, but if we or any of the third parties with whom we engage, including the suppliers, clinical trial sites, service providers, regulators and other third parties with whom we conduct business, were to experience prolonged business shutdowns or other business disruptions, our ability to conduct our business in the manner and on the timelines presently planned could be materially or negatively impacted, which could have a material adverse impact on our business, results of operations and financial condition.

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

As of December 31, 2021, we had 242 full-time employees and 10 part-time employees. As our development and commercialization plans and strategies develop, and as we transition into operating as a public company, we expect to need additional managerial, operational, sales, marketing, financial and other personnel, as well as additional facilities to expand our operations. Future growth would 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 product candidates, while complying with our contractual obligations to contractors and other third parties; and
- improving our operational, financial and management controls, reporting systems and procedures.

Our future financial performance and our ability to commercialize ATL001 and any future product candidates will depend, in part, on our ability to effectively manage any future growth, and our management may also have to divert a disproportionate amount of its attention away from day-to-day activities in order to devote a substantial amount of time to managing these growth activities.

If we are not able to effectively expand our organization by hiring new employees, consultants and/or contractors, or we are not able to effectively build out new facilities to accommodate this expansion, we may not be able to successfully implement the tasks necessary to further develop and commercialize ATL001 and any future product candidates and, accordingly, may not achieve our research, development and commercialization goals.

Risks Related to our International Operations

A variety of risks associated with operating our business internationally could materially adversely affect our business.

We plan to seek regulatory approval of ATL001 and any future product candidates outside of the United States and, accordingly, we expect that we, and any potential collaborators in those jurisdictions, will be subject to additional risks related to operating in foreign countries, including:

- differing regulatory requirements in foreign countries;
- unexpected changes in tariffs, trade barriers, price and exchange controls, and other regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration, and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- difficulties staffing and managing foreign operations;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- potential liability under the FCPA, Office of Foreign Assets Control Anti-Money Laundering Program as required by the Bank Secrecy Act and its implementing regulations, or comparable foreign laws;
- challenges enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war and terrorism.

These and other risks associated with our planned international operations may materially adversely affect our ability to attain or maintain profitable operations.

Our business is subject to economic, political, regulatory and other risks associated with international operations.

Our business is subject to risks associated with conducting business internationally. Accordingly, our future results could be harmed by a variety of factors, including the following:

- economic weakness, including inflation, political instability in particular in foreign economies and markets, and the potentially severe continued global economic impact caused by the ongoing COVID-19 pandemic;
- differing regulatory requirements for drug approvals;
- differing jurisdictions potentially presenting different issues for securing, maintaining or obtaining freedom to operate in such jurisdictions;
- potentially reduced protection for intellectual property rights;
- difficulties in compliance with different, complex and changing laws, regulations and court systems of multiple jurisdictions and compliance with a wide variety of foreign laws, treaties and regulations;
- changes in regulations and customs, tariffs and trade barriers;
- changes in currency exchange rates of the pound sterling, euro, U.S. dollar and currency controls;
- changes in a specific country's or region's political or economic environment;
- trade protection measures, import or export licensing requirements or other restrictive actions by governments;
- differing reimbursement regimes and price controls in certain international markets;
- negative consequences from changes in tax laws;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- workforce uncertainty in countries where labor unrest is more common than in the United States, United Kingdom and EU;
- difficulties associated with staffing and managing international operations, including differing labor relations;

- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war, terrorism, pandemics, or natural disasters including earthquakes, typhoons, floods and fires.

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

We are incorporated under the laws of England and Wales. Most of the members of our senior management and certain members of our board of directors are non-residents of the United States, and all or a substantial portion of our assets and the assets of such persons are located outside the United States. As a result, it may not be possible to serve process on such persons or us in the United States or to enforce judgments obtained in U.S. courts against them or us based on civil liability provisions of the U.S. federal securities laws.

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

As a result, U.S. investors may not be able to enforce against us or certain of our directors any judgments obtained in U.S. courts in civil and commercial matters, including judgments under the U.S. federal securities laws.

Fluctuations in the exchange rate between the U.S. dollar and the pound sterling may increase the risk of holding our ADSs and may materially affect our results of operations and financial condition.

Our ADSs trade on Nasdaq in U.S. dollars. Due to the international scope of our operations, our assets, earnings and cash flows are influenced by movements in exchange rates of several currencies, particularly the U.S. dollar, the pound sterling and the euro. Our reporting currency is denominated in U.S. dollars and our functional currency is the pound sterling (except that the functional currency of our U.S. subsidiaries is the U.S. dollar) and the majority of our operating expenses are paid in pound sterling. We also regularly acquire services, consumables and materials in U.S. dollars and the euro. Further potential future revenue may be derived from abroad, particularly from the United States. As a result, our business and the price of our ADSs may be affected by fluctuations in foreign exchange rates between the pound sterling and these other currencies, which may also have a significant impact on our results of operations and cash flows from period to period. Currently, we do not have any exchange rate hedging arrangements in place. See Note 2 to our annual financial statements appearing elsewhere in this Annual Report for a description of foreign exchange risks.

The possible abandonment of the euro by one or more members of the European Union, or the EU, could materially affect our business in the future. Despite measures taken by the EU to provide funding to certain EU member states in financial difficulties and by a number of European countries to stabilize their economies and reduce their debt burdens, it is possible that the euro could be abandoned in the future as a currency by countries that have adopted its use. This could lead to the re-introduction of individual currencies in one or more EU member states, or in more extreme circumstances, the dissolution of the EU. The effects on our business of a potential dissolution of the EU, the

exit of one or more EU member states from the EU or the abandonment of the euro as a currency, are impossible to predict with certainty, and any such events could have a material adverse effect on our business, financial condition and results of operations.

In addition, as a result of fluctuations in the exchange rate between the U.S. dollar and the pound sterling, the U.S. dollar equivalent of the proceeds that a holder of ADSs would receive upon the sale in the United Kingdom of any ordinary shares withdrawn from the depositary and the U.S. dollar equivalent of any cash dividends paid in pounds sterling on our ordinary shares represented by ADSs could also decline.

RISKS RELATED TO OWNERSHIP OF OUR ADSs

Certain significant shareholders own a substantial number of our ordinary shares and as a result (together with low attendance in recent shareholders meetings), may be able to exercise control over us, including the outcome of shareholder votes. These shareholders may have different interests from us or your interests.

We have a number of significant shareholders. For an overview of our current significant shareholders, please see "Item 7.A. Major Shareholders."

Currently, we are not aware that any of our existing shareholders have entered or will enter into a shareholders' agreement with respect to the exercise of their voting rights. Nevertheless, depending on the level of attendance at our general meetings of shareholders, or the General Meeting, these significant shareholders could, alone or together, have the ability to determine the outcome of decisions taken at any such General Meeting. Any such voting by these shareholders may not be in accordance with our interests or those of our other shareholders. Among other consequences, this concentration of ownership may have the effect of delaying or preventing a change in control and might therefore negatively affect the market price of our ADSs or ordinary shares.

If securities or industry analysts cease coverage of us, or publish inaccurate or unfavorable research about our business, the price of our ADSs and our trading volume could decline.

The trading market for our ADSs depends in part on the research and reports that securities or industry analysts publish about us or our business. We do not have any control over these analysts. Securities or industry analysts may elect not to provide research coverage of our ADSs, and such lack of research coverage may negatively impact the market price of our ADSs. If one or more of the analysts who cover us downgrade our ADSs or publish inaccurate or unfavorable research about our business, the price of the ADSs would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, demand for our ADSs could decrease, which might cause the price of our ADSs and trading volume to decline.

We are an emerging growth company, and we cannot be certain if the reduced reporting requirements applicable to emerging growth companies make our ADSs less attractive to investors.

In April 2012, the JOBS Act was enacted. Section 107 of the JOBS Act provides that an "emerging growth company" may take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act for complying with new or revised accounting standards. Therefore, an emerging growth company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to avail ourselves of this extended transition period and, as a result, we may adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for non-public companies instead of the dates required for other public companies. However, we may early adopt these standards.

In addition, as an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable generally to public companies. These provisions include:

- reduced "Management's discussion and analysis of financial condition and results of operations" disclosure;
- an exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting pursuant to the Sarbanes-Oxley Act; and
- an exemption from new or revised financial accounting standards until they would apply to private companies and from compliance with any new requirements adopted by the Public Company Accounting Oversight Board requiring mandatory audit firm rotation.

We may take advantage of these exemptions until we are no longer an emerging growth company. We would cease to be an emerging growth company on the date that is the earliest of: (1) the last day of the fiscal year in which we have total annual gross revenues of $1.07 billion or more; (2) December 31, 2026 ,which is the last day of our fiscal year following the fifth anniversary of the date of the completion of our initial public offering; (3) the date on which we have issued more than $1.0 billion in nonconvertible debt during the previous three years; or (4) the date on which we are deemed to be a large accelerated filer under the rules of the SEC. We may choose to take advantage of some but not all of these exemptions.

We qualify as a foreign private issuer and, as a result, are not subject to U.S. proxy rules. We are subject to reporting obligations under the Securities Exchange Act of 1934, as amended, that, to some extent, permit less detailed and frequent reporting than that of a U.S. domestic public company.

We report under the Securities Exchange Act of 1934, as amended, or the Exchange Act, as a non-U.S. company with foreign private issuer status. Because we qualify as a foreign private issuer under the Exchange Act, we are exempt from certain provisions of the Exchange Act that are applicable to U.S. domestic public companies, including: (i) the sections of the Exchange Act regulating the solicitation of proxies, consents or authorizations in respect of a security registered under the Exchange Act; (ii) the sections of the Exchange Act requiring insiders to file public reports of their share ownership and trading activities and liability for insiders who profit from trades made in a short period of time; and (iii) the rules under the Exchange Act requiring the filing with the Securities and Exchange Commission, or SEC, of quarterly reports on Form 10-Q containing unaudited financial and other specified information, or current reports on Form 8-K, upon the occurrence of specified significant events. In addition, foreign private issuers are not required to file their Annual Report on Form 20-F until 120 days after the end of each fiscal year, while U.S. domestic issuers that are accelerated filers are required to file their Annual Report on Form 10-K within 75 days after the end of each fiscal year. Foreign private issuers are also exempt from the Regulation Fair Disclosure, aimed at preventing issuers from making selective disclosures of material information. As a result of the above, you may not have the same protections afforded to shareholders of companies that are not foreign private issuers, some investors may find our ADSs less attractive, and there may be a less active trading market for our ADSs.

As a foreign private issuer and as permitted by the listing requirements of Nasdaq, we rely on certain home country governance practices rather than the corporate governance requirements of Nasdaq.

We are entitled to rely on a provision in Nasdaq's corporate governance rules that allows us to follow English corporate law and the United Kingdom Companies Act 2006, or the Companies Act 2006, with regard to certain aspects of corporate governance, known as home country governance practices. Following our home country governance practices allows us to follow English corporate law and the Companies Act 2006 with regard to certain corporate governance matters as opposed to the requirements that would otherwise apply to U.S. companies listed on Nasdaq and may provide less protection to our shareholders than what is accorded to investors under the Nasdaq rules applicable to domestic U.S. issuers.

As a foreign private issuer, we are exempt from the rules and regulations under the Exchange Act related to the furnishing and content of proxy statements. Our officers, directors and principal shareholders are also exempt from the reporting and short-swing profit recovery provisions contained in Section 16 of the Exchange Act. In addition, we

are not required under the Exchange Act to file reports and financial statements with the SEC as frequently or as promptly as U.S. domestic companies whose securities are registered under the Exchange Act and we are exempt from filing quarterly reports with the SEC under the Exchange Act. Moreover, we are not required to comply with Regulation Fair Disclosure, which restricts the selective disclosure of material information. These exemptions and leniencies reduce the frequency and scope of information and protections to which you may otherwise have been eligible in relation to a U.S. domestic issuer.

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

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

While we currently qualify as a foreign private issuer, the determination of foreign private issuer status is made annually on the last business day of an issuer's most recently completed second fiscal quarter and, accordingly, the next determination will be made with respect to us on June 30, 2022.

In the future, we would lose our foreign private issuer status if we to fail to meet the requirements necessary to maintain our foreign private issuer status as of the relevant determination date. For example, if more than 50% of our securities are held by U.S. residents and more than 50% of the members of our executive committee or members of our board of directors are residents or citizens of the United States, we could lose our foreign private issuer status.

The regulatory and compliance costs to us under U.S. securities laws as a U.S. domestic issuer may be significantly more than costs we incur as a foreign private issuer. If we are not a foreign private issuer, we will be required to file periodic reports and registration statements on U.S. domestic issuer forms with the SEC, which are more detailed and extensive in certain respects than the forms available to a foreign private issuer. In addition, we may lose our ability to rely upon exemptions from certain corporate governance requirements on U.S. stock exchanges that are available to foreign private issuers such as the ones described above and exemptions from procedural requirements related to the solicitation of proxies.

We have and will continue to incur significant costs as a result of operating as a company listed in the U.S., and our board of directors have been and will continue to be required to devote substantial time to new compliance initiatives and corporate governance practices.

As a company listed in the U.S., and particularly after we no longer qualify as an emerging growth company, we have and will continue to incur significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of Nasdaq, and other applicable securities rules and regulations impose various requirements on foreign reporting public companies, including the establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our board of directors, management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations increase our legal and financial compliance costs and make some activities more time-consuming and costly. For example, these rules and regulations have made it more expensive for us to obtain director and officer liability insurance, which in turn could make it more difficult for us to attract and retain qualified members of our board of directors.

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

Pursuant to Section 404 of the Sarbanes-Oxley Act, or Section 404, we are required to furnish a report by our board of directors on our internal control over financial reporting. However, while we remain an emerging growth company, we are not required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we engage in a process to document and evaluate our internal controls over financial reporting, which is both costly and challenging. In this regard, we have needed to and will need to continue to dedicate internal resources, engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that in the future we will not be able to conclude, within the prescribed timeframe, that our internal controls over financial reporting are effective as required by Section 404. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

You may not receive distributions on our ordinary shares represented by our ADSs or any value for them if it is illegal or impractical to make them available to holders of ADSs.

The depositary for our ADSs has agreed to pay to you the cash dividends or other distributions it or the custodian receives on our ordinary shares or other deposited securities after deducting its fees and expenses. You would receive these distributions in proportion to the number of our ordinary shares your ADSs represent. However, in accordance with the limitations set forth in the deposit agreement, it may be unlawful or impractical to make a distribution available to holders of ADSs. We have no obligation to take any other action to permit distribution on the ADSs, ordinary shares, rights or anything else to holders of our ADSs. This means that you may not receive the distributions we make on our ordinary shares or any value from them if it is unlawful or impractical to make them available to you. These restrictions may have an adverse effect on the value of your ADSs.

We have not paid, and do not intend to pay, dividends on our ADSs, so any future returns will be limited to the value of our ordinary shares.

We currently anticipate that we will retain future earnings for the development, operation, and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. In addition, we may enter into agreements that prohibit us from paying cash dividends without prior written consent from our contracting parties, or which include other terms prohibiting or limiting the amount of dividends that may be declared or paid on the ADSs. Furthermore, under the Companies Act 2006, a company's accumulated realized profits, so far as not previously utilized by distribution or capitalization, must exceed its accumulated realized losses so far as not previously written off in a reduction or reorganization of capital duly made (on a non-consolidated basis), before dividends can be paid. In the future, were our dividend policy to change, a dividend or distribution may still be restricted from being declared and paid. For these reasons, any return to shareholders may therefore be limited to the appreciation of their shares, which may never occur.

Holders of our ADSs do not have the same voting rights as the holders of our ordinary shares, and may not receive voting materials or any other documents that would need to be provided to our shareholders pursuant to English corporate law, including the Companies Act 2006, in time to be able to exercise their right to vote.

Except as described elsewhere in this Annual Report and the deposit agreement, holders of our ADSs are not able to exercise voting rights attaching to the ordinary shares represented by our ADSs. The deposit agreement provides that, upon receipt of notice of any meeting of holders of our ordinary shares, the depositary will fix a record date for the

determination of ADS holders who shall be entitled to give instructions for the exercise of voting rights. Upon our request, the depositary shall distribute to the holders as of the record date: (i) the notice of the meeting or solicitation of consent or proxy sent by us; and (ii) a statement as to the manner in which instructions may be given by the holders. We cannot guarantee that ADS holders will receive the voting materials in time to ensure that they can instruct the depositary to vote the ordinary shares underlying their ADSs.

Otherwise, ADS holders are not able to exercise their right to vote, unless they cancel the ADSs and withdraw the ordinary shares underlying the ADSs they hold. However, ADS holders may not know about the meeting far enough in advance to cancel the ADSs and withdraw those ordinary shares. In addition, the depositary and its agents are not responsible for failing to carry out voting instructions or for the manner of carrying out voting instructions. As a result, ADS holders may not be able to exercise their right to vote, and there may be nothing they can do if the ordinary shares underlying their ADSs are not voted as they requested or if their shares cannot be voted.

Holders of ADSs may not be able to participate in equity offerings we may conduct from time to time.

Certain shareholders and holders of ADSs, including those in the United States, may, even in the case where preferential subscription rights have not been cancelled or limited, not be entitled to exercise such rights, unless the offering is registered or the ordinary shares are qualified for sale under the relevant regulatory framework. As a result, there is the risk that investors may suffer dilution of their holdings should they not be permitted to participate in preference right equity or other offerings that we may conduct in the future.

Holders of ADSs may be subject to limitations on the transfer of their ADSs and the withdrawal of the underlying ordinary shares.

ADSs are transferable on the books of the depositary. However, the depositary may close its books at any time or from time to time when it deems expedient in connection with the performance of its duties. The depositary may refuse to deliver, transfer or register transfers of ADSs generally when our books or the books of the depositary are closed, or at any time if we or the depositary think it is advisable to do so because of any requirement of law, government or governmental body, or under any provision of the deposit agreement, or for any other reason, subject to the right of ADS holders to cancel their ADSs and withdraw the underlying ordinary shares. Temporary delays in the cancellation of your ADSs and withdrawal of the underlying ordinary shares may arise because the depositary has closed its transfer books or we have closed our transfer books, the transfer of ordinary shares is blocked to permit voting at a shareholders meeting or we are paying a dividend on our ordinary shares. In addition, ADS holders may not be able to cancel their ADSs and withdraw the underlying ordinary shares when they owe money for fees, taxes and similar charges and when it is necessary to prohibit withdrawals in order to comply with any laws or governmental regulations that apply to ADSs or to the withdrawal of ordinary shares or other deposited securities. See “Item 12.D. American Depositary Shares.”

ADS holders may not be entitled to a jury trial with respect to claims arising under the deposit agreement, which could result in less favorable outcomes to the plaintiff(s) in any such action.

The deposit agreement governing our ADSs representing our ordinary shares provides that, to the fullest extent permitted by law, owners and holders of ADSs irrevocably waive the right to a jury trial of any claim they may have against us or the depositary arising out of or relating to our ADSs or the deposit agreement.

If this jury trial waiver provision is not permitted by applicable law, an action could proceed under the terms of the deposit agreement with a jury trial. If we or the depositary opposed a jury trial demand based on the waiver, the court would determine whether the waiver was enforceable based on the facts and circumstances of that case in accordance with the applicable state and federal law. To our knowledge, the enforceability of a contractual pre-dispute jury trial waiver in connection with claims arising under the federal securities laws has not been finally adjudicated by the United States Supreme Court. However, we believe that a contractual pre-dispute jury trial waiver provision is generally enforceable, including under the laws of the State of New York, which govern the deposit agreement, by a

federal or state court in the City of New York, which has non-exclusive jurisdiction over matters arising under the deposit agreement. In determining whether to enforce a contractual pre-dispute jury trial waiver provision, courts will generally consider whether a party knowingly, intelligently and voluntarily waived the right to a jury trial. We believe that this is the case with respect to the deposit agreement and the ADSs. Any person or entity purchasing or otherwise acquiring any of the ADSs, whether by transfer, sale, operation of law or otherwise, shall be deemed to have notice of and have irrevocably agreed and consented to these provisions.

If you or any other holders or beneficial owners of ADSs bring a claim against us or the depositary in connection with matters arising under the deposit agreement or the ADSs, including claims under federal securities laws, you or such other holder or beneficial owner may not be entitled to a jury trial with respect to such claims, which may have the effect of limiting and discouraging lawsuits against us and/or the depositary. If a lawsuit is brought against us and/or the depositary under the deposit agreement, it may be heard only by a judge or justice of the applicable trial court, which would be conducted according to different civil procedures and may result in different outcomes than a trial by jury would have had, including results that could be less favorable to the plaintiff(s) in any such action, depending on, among other things, the nature of the claims, the judge or justice hearing such claims, and the venue of the hearing.

No condition, stipulation or provision of the deposit agreement or ADSs serves as a waiver by any holder or beneficial owner of ADSs or by us or the depositary of compliance with U.S. federal securities laws and the rules and regulations promulgated thereunder.

ADS holders have limited choice of forum, which could limit your ability to obtain a favorable judicial forum for complaints against us, the depositary or our respective directors, officers or employees.

The deposit agreement governing the ADSs provides that: (i) the deposit agreement and the ADSs will be interpreted in accordance with the laws of the State of New York; and (ii) as an owner of ADSs, you irrevocably agree that any legal action arising out of the deposit agreement and the ADSs involving us or the depositary may only be instituted in a state or federal court in the city of New York. Any person or entity purchasing or otherwise acquiring any ADSs, whether by transfer, sale, operation of law or otherwise, shall be deemed to have notice of and have irrevocably agreed and consented to these provisions. This choice of forum provision may increase your cost and limit your ability to bring a claim in a judicial forum that you find favorable for disputes with us, the depositary or our and the depositary's respective directors, officers or employees, which may discourage such lawsuits against us, the depositary and our and the depositary's respective directors, officers or employees. However, it is possible that a court could find such choice of forum provisions to be inapplicable or unenforceable. The enforceability of similar choice of forum provisions has been challenged in legal proceedings.

To the extent that any such claims may be based upon federal law claims, Section 27 of the Exchange Act creates exclusive federal jurisdiction over all suits brought to enforce any duty or liability created by the Exchange Act or the rules and regulations thereunder. Furthermore, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all suits brought to enforce any duty or liability created by the Securities Act or the rules and regulations thereunder. Accordingly, actions by our ADS holders to enforce any duty or liability created by the Exchange Act, the Securities Act or the respective rules and regulations thereunder must be brought in a federal court in the city of New York. Our ADS holders will not be deemed to have waived our compliance with the federal securities laws and the regulations promulgated thereunder.

As an English public limited company, certain capital structure decisions require shareholder approval, which may limit our flexibility to manage our capital structure.

English law provides that a board of directors may only allot shares (or grant rights to subscribe for or to convert any security into shares) with the prior authorization of shareholders, either pursuant to an ordinary resolution or as set out in the articles of association adopted from time to time with the approval of our shareholders. This authorization must state the aggregate nominal amount of shares that it covers, can be valid up to a maximum period of five years and can be varied, renewed or revoked by shareholders. Such authority from our shareholders to allot additional shares for

a period of five years from March 15, 2021 was included in the ordinary resolution passed by our shareholders on March 15, 2021, which authorization will need to be renewed upon expiration (i.e., at least every five years) but may be sought more frequently for additional five-year terms (or any shorter period).

English law also generally provides shareholders with preemptive rights when new shares are issued for cash. However, it is possible for the Articles, or for shareholders to pass a special resolution at a general meeting, being a resolution passed by at least 75% of the votes cast, to disapply preemptive rights. Such a disapplication of preemptive rights may be for a maximum period of up to five years from the date of adoption of the Articles, if the disapplication is contained in the Articles, but not longer than the duration of the authority to allot shares to which this disapplication relates or from the date of the shareholder special resolution, if the disapplication is by shareholder special resolution. In either case, this disapplication would need to be renewed by our shareholders upon its expiration (i.e., at least every five years). Such authority from our shareholders to disapply preemptive rights for a period of five years was included in the special resolution passed by our shareholders on March 15, 2021, which disapplication will need to be renewed upon expiration (i.e., at least every five years) to remain effective, but may be sought more frequently for additional five-year terms (or any shorter period).

English law also generally prohibits a public company from repurchasing its own shares without the prior approval of its shareholders by ordinary resolution, being a resolution passed by a simple majority of votes cast, and other formalities. Such approval may be provided for a maximum period of up to five years.

GENERAL RISK FACTORS

Our internal computer systems, or those used by our third-party CROs or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of the development programs of our product candidates.

Despite the implementation of security measures, our internal computer systems and those of our current and future CROs and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, and telecommunication and electrical failures. The risk of a security breach or disruption, particularly through cyber-attacks or cyber intrusion, including by computer hackers, foreign governments, and cyber terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. While we have not experienced any such material system failure or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations, such as the loss of clinical trial data from completed or future clinical trials. Such loss could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we may rely on third parties for the manufacture of our product candidates and to conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. Any breach in our information technology systems could lead to the unauthorized access, disclosure and use of non-public information, including information from our patient registry or other patient information, which is protected by data privacy and security laws. Any such access, disclosure, or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information, damage to our reputation and the further development and commercialization of our product candidates could be delayed.

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

Our operations, and those of our CROs, CMOs and other contractors and consultants, could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics and other natural or man-made disasters or business interruptions, for which we are predominantly self-insured. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses.

Unstable global economic conditions could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. The most recent global financial crisis caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, including due to the impact of the COVID-19 pandemic, could result in a variety of risks to our business, including a reduced ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy or international trade disputes could also strain our third-party suppliers, possibly resulting in supply disruption. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

We may be unable to adequately protect our information systems from cyber-attacks, which could result in the disclosure of confidential or proprietary information, including personal data, damage our reputation, and subject us to significant financial and legal exposure.

We rely on information technology systems that we or our third-party providers operate to process, transmit and store electronic information in our day-to-day operations. In connection with our product discovery efforts, we may collect and use a variety of personal data, such as name, mailing address, email addresses, phone number and clinical trial information. A successful cyber-attack could result in the theft or destruction of intellectual property, data, or other misappropriation of assets, or otherwise compromise our confidential or proprietary information and disrupt our operations. Cyber-attacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyber-attacks could include wrongful conduct by hostile foreign governments, industrial espionage, wire fraud and other forms of cyber fraud, the deployment of harmful malware, denial-of-service, social engineering fraud or other means to threaten data security, confidentiality, integrity and availability. A successful cyber-attack could cause serious negative consequences for us, including, without limitation, the disruption of operations, the misappropriation of confidential business information, including financial information, trade secrets, financial loss and the disclosure of corporate strategic plans. Although we devote resources to protect our information systems, we realize that cyber-attacks are a threat, and there can be no assurance that our efforts will prevent information security breaches that would result in business, legal, financial or reputational harm to us, or would have a material adverse effect on our results of operations and financial condition. Any failure to prevent or mitigate security breaches or improper access to, use of, or disclosure of our clinical data or patients' personal data could result in significant liability under state (e.g., state breach notification laws), federal (e.g., HIPAA, as amended by HITECH), and international (e.g., the GDPR) law and may cause a material adverse impact to our reputation, affect our ability to conduct new studies and potentially disrupt our business.

In addition, the computer systems of various third parties on which we rely, including our CROs and other contractors, consultants and law and accounting firms, may sustain damage from computer viruses, unauthorized access, data breaches, phishing attacks, cybercriminals, natural disasters (including hurricanes and earthquakes), terrorism, war and telecommunication and electrical failures. We rely on our third-party providers to implement effective security measures and identify and correct for any such failures, deficiencies or breaches. If we or our third-party providers fail to maintain or protect our information technology systems and data integrity effectively or fail to anticipate, plan for or manage significant disruptions to our information technology systems, we or our third-party providers could have difficulty preventing, detecting and controlling such cyber-attacks and any such attacks could result in losses described above as well as disputes with physicians, patients and our partners, regulatory sanctions or penalties, increases in operating expenses, expenses or lost revenues or other adverse consequences, any of which could have a material adverse effect on our business, results of operations, financial condition, prospects and cash flows. Any failure by such third parties to prevent or mitigate security breaches or improper access to or disclosure of such information could have similarly adverse consequences for us.

The GDPR, United States state laws and other international laws to which we may be subject require businesses to notify regulators and data subjects in the event of a data breach. If we are unable to prevent or mitigate the impact of

such security or data privacy breaches, we could be exposed to litigation and governmental investigations, which could lead to fines, damages, reputational damage and a potential disruption to our business.

Our operating results may fluctuate significantly, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations or our guidance.

Our quarterly and annual operating results may fluctuate significantly in the future, which makes it difficult for us to predict our future operating results. From time to time, we may enter into license or collaboration agreements with other companies that include development funding and significant upfront and milestone payments and/or royalties, which may become an important source of our revenue. Accordingly, our revenue may depend on development funding and the achievement of development and clinical milestones under current and any potential future license and collaboration agreements and, if approved, sales of our product candidates. These upfront and milestone payments may vary significantly from period to period and any variance could cause a significant fluctuation in our operating results from one period to the next.

Further, our operating results may fluctuate due to a variety of other factors, many of which are outside of our control and may be difficult to predict, including the following:

- the timing and cost of, and level of investment in, research and development activities relating to our current programs, additional follow-on indications for ATL001, and any future product candidates, which will change from time to time;
- the timing and outcomes of clinical trials for our current programs, additional follow-on indications for ATL001, and any future product candidates;
- the cost of manufacturing ATL001 and any of our future product candidates, which may vary depending on FDA guidelines and requirements, the quantity of production and the terms of our agreements with manufacturers;
- our ability to adequately support our future growth;
- potential unforeseen business disruptions that increase our costs or expenses;
- future accounting pronouncements or changes in our accounting policies; and
- the changing and volatile global economic environment.

The cumulative effect of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period-to-period basis may not be meaningful. Investors should not rely on our past results as an indication of our future performance. This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our revenue or operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our ADSs could decline substantially. The price of our ADSs could decline even when we have met any previously publicly stated revenue and/or earnings guidance we may provide.

Shareholder protections found in provisions under the United Kingdom City Code on Takeovers and Mergers, or the Takeover Code, will not apply if our place of central management and control remains outside of the United Kingdom (or the Channel Islands or the Isle of Man).

We believe that, as of the date of this Annual Report, our place of central management and control is not in the United Kingdom (or the Channel Islands or the Isle of Man) for the purposes of the jurisdictional criteria of the Takeover Code. Accordingly, we believe that we are not currently subject to the Takeover Code and, as a result, our shareholders are not currently entitled to the benefit of certain takeover offer protections provided under the Takeover Code, including the rules regarding mandatory takeover bids.

In the event that this changes, or if the interpretation and application of the Takeover Code by the Panel on Takeovers and Mergers, or Takeover Panel, changes (including changes to the way in which the Takeover Panel assesses the

application of the Takeover Code to English companies whose shares are listed outside of the United Kingdom), the Takeover Code may apply to us in the future.

The Takeover Code provides a framework within which takeovers of companies which are subject to the Takeover Code are regulated and conducted. The following is a brief summary of some of the most important rules of the Takeover Code:

- When any person acquires, whether by a series of transactions over a period of time or not, an interest in shares which (taken together with shares already held by that person and an interest in shares held or acquired by persons acting in concert with him or her) carry 30% or more of the voting rights of a company that is subject to the Takeover Code, that person is generally required to make a mandatory offer to all the holders of any class of equity share capital or other class of transferable securities carrying voting rights in that company to acquire the balance of their interests in the company.
- When any person who, together with persons acting in concert with him or her, is interested in shares representing not less than 30% but does not hold more than 50% of the voting rights of a company that is subject to the Takeover Code, and such person, or any person acting in concert with him or her, acquires an additional interest in shares which increases the percentage of shares carrying voting rights in which he or she is interested, then such person is generally required to make a mandatory offer to all the holders of any class of equity share capital or other class of transferable securities carrying voting rights of that company to acquire the balance of their interests in the company.
- A mandatory offer triggered in the circumstances described in the two paragraphs above must be in cash (or be accompanied by a cash alternative) and at not less than the highest price paid within the preceding 12 months to acquire any interest in shares in the company by the person required to make the offer or any person acting in concert with him or her.
- In relation to a voluntary offer (i.e., any offer which is not a mandatory offer), when interests in shares representing 10% or more of the shares of a class have been acquired for cash by an offeror (i.e., a bidder) and any person acting in concert with it in the offer period and the previous 12 months, the offer must be in cash or include a cash alternative for all shareholders of that class at not less than the highest price paid for any interest in shares of that class by the offeror and by any person acting in concert with it in that period. Further, if an offeror acquires for cash any interest in shares during the offer period, a cash alternative must be made available at not less than the highest price paid for any interest in the shares of that class.
- If, after making an offer for a company, the offeror or any person acting in concert with them acquires an interest in shares in an offeree company (i.e., a target) at a price higher than the value of the offer, the offer must be increased to not less than the highest price paid for the interest in shares so acquired.
- An offeree company must appoint a competent independent advisor whose advice on the financial terms of the offer must be made known to all the shareholders, together with the opinion of the board of directors of the offeree company.
- Special or favorable deals for selected shareholders are not permitted, except in certain circumstances where independent shareholder approval is given and the arrangements are regarded as fair and reasonable in the opinion of the financial advisor to the offeree.
- All shareholders must be given the same information.
- Each document published in connection with an offer by or on behalf of the offeror or offeree must state that the directors of the offeror or the offeree, as the case may be, accept responsibility for the information contained therein.
- Profit forecasts, quantified financial benefits statements and asset valuations must be made to specified standards and must be reported on by professional advisors.
- Misleading, inaccurate or unsubstantiated statements made in documents or to the media must be publicly corrected immediately.
- Actions during the course of an offer by the offeree company, which might frustrate the offer are generally prohibited unless shareholders approve these plans. Frustrating actions would include, for example, lengthening the notice period for directors under their service contract or agreeing to sell off material parts of the target group.

- Stringent requirements are laid down for the disclosure of dealings in relevant securities during an offer, including the prompt disclosure of positions and dealing in relevant securities by the parties to an offer and any person who is interested (directly or indirectly) in 1% or more of any class of relevant securities.
- Employees of both the offeror and the offeree company and the trustees of the offeree company's pension scheme must be informed about an offer. In addition, the offeree company's employee representatives and pension scheme trustees have the right to have a separate opinion on the effects of the offer on employment appended to the offeree board of directors' circular or published on a website.

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

We are incorporated under the laws of England and Wales. The rights of holders of our ordinary shares and Class A ordinary shares and, therefore, certain of the rights of holders of ADSs, are governed by the laws of England and Wales, including the provisions of the Companies Act 2006, and by our Articles. These rights differ in certain respects from the rights of shareholders in typical U.S. corporations.

The principal differences include the following:

- Under English law, subject to certain exceptions and disapplications, each shareholder generally has preemptive rights to subscribe on a proportionate basis to any issuance of ordinary shares or Class A ordinary shares or rights to subscribe for, or to convert securities into, ordinary shares or Class A ordinary shares for cash. Under U.S. law, shareholders generally do not have preemptive rights unless specifically granted in the certificate of incorporation or otherwise.
- Under English law and our Articles, certain matters require the approval of 75% of shareholders representing 75% of the ordinary shares voting (in person or by proxy), including amendments to the Articles. This may make it more difficult for us to complete corporate transactions deemed advisable by our board of directors. Under U.S. law, generally only majority shareholder approval is required to amend the certificate of incorporation or to approve other significant transactions.
- In the United Kingdom, takeovers may be structured as takeover offers or as schemes of arrangement. Under English law, a bidder seeking to acquire us by means of a takeover offer would need to make an offer for all of our outstanding ordinary shares/ADSs. If acceptances are not received for 90% or more of the ordinary shares/ADSs under the offer, under English law, the bidder cannot complete a "squeeze out" to obtain 100% control of us. Accordingly, acceptances of 90% of our outstanding ordinary shares (including those represented by ADSs) will likely be a condition in any takeover offer to acquire us, not 50% as is more common in tender offers for corporations organized under Delaware law. By contrast, a scheme of arrangement, the successful completion of which would result in a bidder obtaining 100% control of us, requires the approval of a majority of shareholders voting at the meeting and representing 75% of the ordinary shares (including those represented by ADSs) voting at the meeting for approval.
- Under English law and our Articles, shareholders and other persons whom we know or have reasonable cause to believe are, or have been, interested in our shares may be required to disclose information regarding their interests in our shares upon our request, and the failure to provide the required information could result in the loss or restriction of rights attaching to the shares, including prohibitions on certain transfers of the shares, withholding of dividends and loss of voting rights. Comparable provisions generally do not exist under U.S. law.

Our Articles provide that the courts of England and Wales are the exclusive forum for the resolution of all shareholder complaints other than complaints asserting a cause of action arising under the Securities Act or the Exchange Act, and that the United States District Court for the Southern District of New York will be the exclusive forum for the resolution of any shareholder complaint asserting a cause of action arising under the Securities Act or the Exchange Act.

Our Articles provide that, unless we consent by ordinary resolution to the selection of an alternative forum, the courts of England and Wales shall, to the fullest extent permitted by law, be the exclusive forum for: (i) any derivative action or proceeding brought on our behalf; (ii) any action or proceeding asserting a claim of breach of fiduciary duty owed by any of our directors, officers or other employees to us; (iii) any action or proceeding asserting a claim arising out of any provision of the Companies Act 2006 or our Articles (as may be amended from time to time); or (iv) any action

or proceeding asserting a claim or otherwise related to our affairs, or the England and Wales Forum Provision. The England and Wales Forum Provision will not apply to any causes of action arising under the Securities Act or the Exchange Act. Our Articles further provide that unless we consent by ordinary resolution to the selection of an alternative forum, the United States District Court for the Southern District of New York shall be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act or the Exchange Act, or the U.S. Federal Forum Provision. In addition, our Articles provide that any person or entity purchasing or otherwise acquiring any interest in our shares is deemed to have notice of and consented to the England and Wales Forum Provision and the U.S. Federal Forum Provision; provided, however, that our shareholders cannot and will not be deemed to have waived our compliance with the U.S. federal securities laws and the rules and regulations thereunder.

The England and Wales Forum Provision and the U.S. Federal Forum Provision in our Articles may impose additional litigation costs on our shareholders in pursuing any such claims. Additionally, the forum selection clauses in our Articles may limit the ability of our shareholders to bring a claim in a judicial forum that they find favorable for disputes with us or our directors, officers or employees, which may discourage the filing of lawsuits against us and our directors, officers and employees, even though an action, if successful, might benefit our shareholders. In addition, while the Delaware Supreme Court ruled in March 2020 that federal forum selection provisions purporting to require claims under the Securities Act be brought in federal court are "facially valid" under Delaware law, there is uncertainty as to whether other courts, including the courts of England and Wales and other courts within the U.S., will enforce our U.S. Federal Forum Provision. If the U.S. Federal Forum Provision is found to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our results of operations and financial condition. The U.S. Federal Forum Provision may also impose additional litigation costs on our shareholders who assert that the provision is not enforceable or invalid. The courts of England and Wales and the United States District Court for the Southern District of New York may also reach different judgments or results than would other courts, including courts where a shareholder considering an action may be located or would otherwise choose to bring the action, and such judgments may be more or less favorable to us than our shareholders.

If we were classified as a passive foreign investment company, there could be material adverse U.S. federal income tax consequences to U.S. Holders.

Under the Internal Revenue Code of 1986, as amended, or the Code, we are a passive foreign investment company, or PFIC, for any taxable year in which (i) 75% or more of our gross income consists of passive income, or the income test, or (ii) 50% or more of the average quarterly value of our assets consists of assets that produce, or are held for the production of, passive income, or the asset test. For purposes of these tests, passive income includes dividends, interest, gains from the sale or exchange of investment property and certain rents and royalties. In addition, for purposes of the above calculations, a non-U.S. corporation that directly or indirectly owns at least 25% by value of the shares of another corporation is treated as holding and receiving directly its proportionate share of assets and income of such corporation. If we are a PFIC for any taxable year during which a U.S. Holder (as defined below under "Item 10.E. Taxation—U.S. Taxation") holds our ordinary shares or ADSs, the U.S. Holder may be subject to material adverse tax consequences regardless of whether we continue to qualify as a PFIC, including ineligibility for any preferred tax rates on capital gains or on actual or deemed dividends, interest charges on certain taxes treated as deferred and additional reporting requirements.

We believe that we were classified as a PFIC for our taxable year ended December 31, 2021. Based on the current and expected composition of our income and assets and the value of our assets, we expect to be a PFIC for the current taxable year ending December 31, 2022. However, no assurances regarding our PFIC status can be provided for any past, current or future taxable years. The determination of whether we are a PFIC is a fact-intensive determination made on an annual basis applying principles and methodologies that in some circumstances are unclear and subject to varying interpretation. Subject to certain exceptions, for purposes of the asset test, if we are treated as a non-publicly traded "controlled foreign corporation," or a CFC (as discussed below), for the year being tested for purposes of the PFIC rules, the value of our assets will be measured by the adjusted tax basis of our assets. If we are a publicly traded CFC or not a CFC for such year, the value of our assets generally will be determined by reference to the market

price of our ordinary shares or ADSs from time to time, which may fluctuate considerably. The income test depends on the nature and composition of our income. The composition of our income and assets is also affected by how fast we spend the cash we raise in any offering.

For further discussion of the PFIC rules and adverse U.S. federal income tax consequences in the event we are classified as a PFIC, see the section titled "Item 10.E. Taxation—U.S. Taxation" in this Annual Report. Each U.S. Holder should consult its own tax advisors with respect to the potential adverse U.S. tax consequences to it if we are or were to become a PFIC.

If we are a "controlled foreign corporation," or CFC, there could be adverse U.S. federal income tax consequences to certain U.S. Holders.

Each "Ten Percent Shareholder" (as defined below) in a non-U.S. corporation that is classified as a CFC for U.S. federal income tax purposes generally is required to include in income for U.S. federal tax purposes such Ten Percent Shareholder's pro rata share of the CFC's "Subpart F income," "global intangible low-taxed income" and investment of earnings in U.S. property, even if the CFC has made no distributions to its shareholders. A non-U.S. corporation generally will be classified as a CFC for U.S. federal income tax purposes if Ten Percent Shareholders own, directly or indirectly, more than 50% of either the total combined voting power of all classes of stock of such corporation entitled to vote or of the total value of the stock of such corporation. A "Ten Percent Shareholder" is a United States person (as defined by the Code) who owns or is considered to own (directly, indirectly or constructively) 10% or more of the value of all classes of stock or total combined voting power of all classes of stock entitled to vote of such corporation. In addition, if a non-U.S. corporation owns at least one U.S. subsidiary, even if such non-U.S. corporation is not a CFC, under current law, any current non-U.S. subsidiaries and any future newly formed or acquired non-U.S. subsidiaries of the non-U.S. corporation will be treated as CFCs. Subpart F income generally includes dividends, interest, rents, royalties, gains from the sale of securities and income from certain transactions with related parties. In addition, a Ten Percent Shareholder that realizes gain from the sale or exchange of shares in a CFC may be required to classify a portion of such gain as dividend income rather than capital gain.

We believe that we were classified as a CFC through the date of completion of our IPO on April 6, 2021. We believe that we were not classified as a CFC from the date of completion of our IPO to December 31, 2021. The determination of CFC status is complex and includes attribution rules, the application of which is not entirely certain. An individual that is a Ten Percent Shareholder with respect to a CFC generally would not be allowed certain tax deductions or foreign tax credits that would be allowed to a Ten Percent Shareholder that is a U.S. corporation. Failure to comply with CFC reporting obligations may subject a United States shareholder to significant monetary penalties. We cannot provide any assurances that we will furnish to any Ten Percent Shareholder information that may be necessary to comply with the reporting and tax paying obligations applicable under the CFC rules of the Code. U.S. Holders should consult their own tax advisors with respect to the potential adverse U.S. tax consequences of becoming a Ten Percent Shareholder in a CFC.

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

As a United Kingdom incorporated and tax resident entity, we are subject to United Kingdom corporate taxation on tax-adjusted trading profits. Due to the nature of our business, we have generated losses since inception and therefore have not paid any United Kingdom corporation tax. As of December 31, 2021, we had cumulative United Kingdom carryforward tax losses of $71.0 million. Subject to any relevant criteria and restrictions (including those that limit the percentage of profits that can be reduced by carried forward losses and those that can restrict the use of carried forward losses where there is a change of ownership of more than half of our ordinary shares and a major change in the nature, conduct or scale of the trade), we expect these to be eligible for carry forward and utilization against future operating profits.

As a company that carries out extensive research and development activities, we seek to benefit from the United Kingdom research and development tax relief programs, being the Small and Medium-sized Enterprises R&D tax relief program, or SME Program, and, to the extent that our projects are grant funded or relate to work subcontracted to us by third parties, the Research and Development Expenditure Credit program, or RDEC Program. Under the SME Program, we may be able to surrender some of our trading losses that arise from our qualifying research and development activities for a cash rebate of up to 33.35% of such qualifying research and development expenditures. The majority of our research, clinical trials management and manufacturing development activities are eligible for inclusion within these tax credit cash rebate claims. We may not be able to continue to claim payable research and development tax credits in the future if we cease to qualify as a SME, based on size criteria concerning employee headcount, turnover and gross assets. The UK Finance Act of 2021 introduced a cap on payable credit claims under the SME Programme in excess of £20,000 with effect from April 2021 by reference to, broadly, three times the total PAYE and NICs liability of the company, subject to an exception which prevents the cap from applying. That exception requires the company to be creating, taking steps to create or managing intellectual property, as well as having qualifying research and development expenditure in respect of connected parties which does not exceed 15% of the total claimed. If such exception does not apply, this could restrict the amount of payable credit that we claim.

We may benefit in the future from the United Kingdom's "patent box" regime, which allows certain profits attributable to revenue from patented products (and other qualifying income) to be taxed at an effective rate of 10% by giving an additional tax deduction. When taken in combination with the enhanced relief available on our research and development expenditures, we expect a long-term rate of corporation tax lower than the statutory 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 for any reason we are unable to qualify for such advantageous tax legislation, or we are unable to use net operating loss and tax credit carryforwards and certain built-in losses to reduce future tax payments then our business, results of operations and financial condition may be adversely affected. This may impact our ongoing requirement for investment and the timeframes within which additional investment is required.

Changes and uncertainties in the tax system in the countries in which we have operations could materially adversely affect our financial condition and results of operations, and reduce net returns to our shareholders.

We conduct business globally and file income tax returns in the United Kingdom and the U.S. The tax treatment of the company or any of the group companies could be materially adversely affected by several factors, including: changing tax laws, regulations and treaties, or the interpretation thereof; tax policy initiatives and reforms under consideration (such as those related to the Organisation for Economic Co-operation and Development's, or OCED, Base Erosion and Profit Shifting, or BEPS, Project, the European Commission's state aid investigations and other initiatives); the practices of tax authorities in jurisdictions in which we operate (the United Kingdom and the U.S.); and the resolution of issues arising from tax audits or examinations and any related interest or penalties. Such changes may include (but are not limited to) the taxation of operating income, investment income, dividends received or (in the specific context of withholding tax) dividends paid.

We are unable to predict what tax reform may be proposed or enacted in the future or what effect such changes would have on our business, but such changes, to the extent they are brought into tax legislation, regulations, policies or practices in jurisdictions in which we operate, could affect our financial position, future results of operations, cash flows in a particular period and overall or effective tax rates in the future in countries where we have operations, reduce post-tax returns to our shareholders and increase the complexity, burden and cost of tax compliance.

Tax authorities may disagree with our positions and conclusions regarding certain tax positions, or may apply existing rules in an unforeseen manner, resulting in unanticipated costs, taxes or non-realization of expected benefits.

A tax authority may disagree with tax positions that we have taken, which could result in increased tax liabilities. For example, Her Majesty's Revenue & Customs, or HMRC, the Internal Revenue Service, or IRS, or another tax authority could challenge our allocation of income among various jurisdictions and the amounts paid between our affiliated

companies pursuant to our intercompany arrangements and transfer pricing policies. Similarly, a tax authority could assert that we are subject to tax in a jurisdiction where we believe we have not established a taxable connection, often referred to as a "permanent establishment" under international tax treaties, and such an assertion, if successful, could increase our expected tax liability in one or more jurisdictions.

A tax authority may take the position that material income tax liabilities, interest and penalties are payable by us, for example where there has been a technical violation of contradictory laws and regulations that are relatively new and have not been subject to extensive review or interpretation, in which case we expect that we might contest such assessment. Contesting such an assessment may be lengthy and costly and if we were unsuccessful in disputing the assessment, the implications could increase our anticipated effective tax rate, where applicable, or result in other liabilities.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

We are subject to the periodic reporting requirements of the Exchange Act. We are continuing to refine our disclosure controls and procedures to provide reasonable assurance that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures, no matter how well-conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met.

These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

If we fail to establish and maintain proper and effective internal control over financial reporting, our operating results and our ability to operate our business could be harmed.

Ensuring that we have adequate internal financial and accounting controls and procedures in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that needs to be re-evaluated frequently. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with generally accepted accounting principles. We continue the process of documenting, reviewing, and improving our internal controls and procedures for compliance with Section 404 of the Sarbanes-Oxley Act, which requires annual management assessment of the effectiveness of our internal control over financial reporting. We continue to recruit additional finance and accounting personnel with certain skill sets that we need as a public company.

Implementing any appropriate changes to our internal controls may distract our officers and employees, entail substantial costs to modify our existing processes, and take significant time to complete. These changes may not, however, be effective in maintaining the adequacy of our internal controls, and any failure to maintain that adequacy, or consequent inability to produce accurate financial statements on a timely basis, could increase our operating costs and harm our business. In addition, investors' perceptions that our internal controls are inadequate or that we are unable to produce accurate financial statements on a timely basis may harm the price of our ADSs and make it more difficult for us to effectively market and sell our products to new and existing customers.

We may be at an increased risk of securities class action litigation.

Historically, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology and pharmaceutical companies have experienced significant stock price volatility in recent years. If we were to be sued, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

Our business and operations may be negatively impacted by the United Kingdom's withdrawal from the EU.

On June 23, 2016, the electorate in the UK voted in favor of leaving the EU, commonly referred to as Brexit, and the UK formally left the EU on January 31, 2020. The transition period during which EU pharmaceutical law remained applicable to the UK ended on December 31, 2020. The EU and the UK have concluded a trade and cooperation agreement, or TCA, which was provisionally applicable since January 1, 2021 and has been formally applicable since May 1, 2021. The TCA includes specific provisions concerning pharmaceuticals, which include the mutual recognition of Good Manufacturing Practice, or GMP, inspections of manufacturing facilities for medicinal products and GMP documents issued, but does not foresee wholesale mutual recognition of UK and EU pharmaceutical regulations. Since the regulatory framework in the UK covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from EU directives and regulations, Brexit could materially impact the future regulatory regime which applies to drugs and the approval of drug candidates in the UK, now that the UK legislation has the potential to diverge from EU legislation. It remains to be seen how Brexit will impact regulatory requirements for product candidates and products in the UK in the long-term. The long-term impact of Brexit, including on our business and our industry, will depend on how the terms of the TCA take effect in practice and any other agreements that are negotiated in relation to the UK's future relationship with the EU.

Since the expiry of the transition period, Great Britain is no longer covered by centralized marketing authorizations (under the Northern Irish Protocol, centralized marketing authorizations will continue to be recognized in Northern Ireland). For a period of two years from January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or MHRA, the UK medicines regulator, may rely on a decision taken by the European Commission on the approval of a new marketing authorization in the centralized procedure, in order to more quickly grant a new Great Britain marketing authorization. A separate application will, however, still be required. Any new regulations in the future could add time and expense to the conduct of our business, as well as the process by which our drug candidates receive regulatory approval in the UK, the EU and elsewhere.

In addition, as we are headquartered in the UK, it is possible that the continued effects of Brexit may impact some or all of our current operations. For example, now the transition period has ended, Brexit will impact our ability to freely move employees from our headquarters in the UK to other locations in Europe and the ability of European healthcare practitioners to move freely to the UK in order to complete part of their training or work on our clinical trials there. In addition, we intend to continue to manufacture our cNeT product candidates at our two UK manufacturing sites, the Royal Free Hospital and the Cell and Gene Therapy Catapult and, once operational, our modular manufacturing facility at Hayes in the UK. Manufacturing product candidates in the UK could, now the Brexit transition period has expired, affect the clearance or timing of the release of our clinical trial materials out of the UK. Any such delays could result in our clinical trial sites outside of the UK not having sufficient clinical trial materials and could adversely affect the timing and completion of our clinical trials.

We expect that, now that the transition period has expired, Brexit could lead to divergent national laws and regulations as the United Kingdom determines which EU laws to replicate or replace, including those related to the regulation of medicinal products, as described above. Any of these longer-term effects of Brexit, and others we cannot anticipate, could negatively impact our business and results of operations.

Item 4. Information on the Company.

A. History and Development of the Company

Achilles Therapeutics Limited was incorporated under the laws of England and Wales in May 2016, under the name AchillesTX Limited and, until the completion of our corporate reorganization in November 2021, was the holding company for Achilles Therapeutics US, Inc. In October 2016, AchillesTX Limited changed its name to Achilles Therapeutics Limited. In January 2021, Achilles Therapeutics Limited changed its name to Achilles Therapeutics UK Limited. Achilles Therapeutics plc was incorporated under the laws of England and Wales in November 2020 as the holding company for Achilles Therapeutics Holdings Limited, under the name Achilles TX Limited. In November

2020, following the incorporation of Achilles TX Limited, Achilles Therapeutics Holdings Limited was incorporated under the laws of England and Wales as a wholly owned subsidiary of Achilles Therapeutics plc, to become a holding company for Achilles Therapeutics UK Limited and Achilles Therapeutics US, Inc. following completion of a corporate reorganization. In April 2021, following the completion of our U.S. initial public offering, our American Depositary Shares began trading on the Nasdaq, under the symbol "ACHL". Our agent for service of process in the United States is Cogency Global Inc.

On April 6, 2021, we completed our initial public offering, or IPO. In connection with the IPO, we sold an aggregate of 9,750,000 ADSs representing the same number of ordinary shares, at a public offering price of $18.00 per ADS. Net proceeds to us were $160.6 million, after deducting underwriting discounts and commissions and other offering expenses. Upon completion of the IPO, we adopted new Articles of Association suitable for a listed public limited company.

Our registered office is located at 245 Hammersmith Road, London, W6 8PW, United Kingdom, and our telephone number is +44 (0)20 8154 4600. Our website address is www.achillestx.com. The information contained on, or that can be accessed through, our website is not a part of, and shall not be incorporated by reference into, this Annual Report. We have included our website address as an inactive textual reference only.

Our capital expenditures for the years ended December 31, 2021, 2020 and 2019 amounted to $7.6 million, $11.8 million and $0.9 million, respectively. Capital expenditures primarily consisted of purchases of property and equipment and leasehold improvements, which largely consisted of operating and lab equipment. We expect our capital expenditures to increase in the near term as we continue to advance our research and development programs, seek to expand our internal manufacturing capabilities, and otherwise grow our operations. We anticipate our capital expenditures in 2022 will be financed from our existing cash and cash equivalents.

The SEC maintains an internet site at http://www.sec.gov that contains reports, information statements, and other information regarding issuers that file electronically with the SEC.

B. Business Overview

We are a clinical stage immuno-oncology biopharmaceutical company developing transformative precision T cell therapies to treat multiple types of solid tumors. We are focused on advancing cancer therapies through our pioneering work in the field of tumor evolution and our belief that clonal neoantigens represent the most specific class of cancer cell targets. Our platform enables us to identify mutations formed early in the development of a cancer that give rise to antigens that are expressed by all of a patient's cancer cells but are absent from healthy tissue. We refer to this novel class of solid tumor targets as clonal neoantigens. To identify clonal neoantigens in a patient, we have developed a proprietary bioinformatic platform called PELEUS. This platform employs sophisticated statistical algorithms trained on the unique tumor genetic data derived from our exclusive license to data from the TRACERx study, which aims to analyze tumor samples from more than 840 non-small cell lung cancer, or NSCLC, patients. Once we have identified the clonal neoantigens, our proprietary manufacturing process, VELOS, uses the patient's T cells and blood-derived dendritic cells to create a clonal neoantigen-reactive T cell, or cNeT, therapy that specifically targets multiple clonal neoantigens to eradicate the tumor or tumors. We are currently conducting two open-label Phase I/IIa trials to evaluate our cNeT product candidate, ATL001, in advanced NSCLC and metastatic or recurrent melanoma and expect to report additional patient data from these trials in the second half of 2022. We are also using our Material Acquisition Platform, or MAP, network, which consists of a network of participating medical facilities, to collect tissue samples from other tumor types, such as head and neck squamous cell carcinoma, or HNSCC, renal cell carcinoma, or RCC, triple negative breast cancer, or TNBC, and bladder cancer, to develop our PELEUS platform to identify clonal neoantigens in these tumor types. Our investigational new drug application, or IND, for HNSCC was accepted by the FDA in January 2022 using VELOS Process 1 manufacturing and we expect to make additional submissions for our other earlier stage programs in the future.

Cancers originate from mutations in the DNA of individual cells. Some of these mutations promote uncontrolled proliferation, metastasis and evasion of the immune system. Tumors within any given patient evolve in a Darwinian branched manner, where the mutations present at the point of a cell becoming cancerous will be carried to all future cells and are therefore present in every future tumor cell of the patient. Additional mutations continue to arise in

response to environmental pressures, carcinogens and genomic instability. These additional mutations increase the intra-tumor genomic variation and are present in some tumor cells but not others.

Mutations can give rise to neoantigens expressed in the tumor cells. The neoantigens arising from the early mutations present at the time of cell transformation are referred to as clonal neoantigens while those that arise later in tumor development are referred to as subclonal neoantigens. As a result of this branched evolution, clonal neoantigens are expressed in every tumor cell, while subclonal neoantigens are expressed only by a fraction of tumor cells. Despite the recent advances in cancer therapy, no therapy to date has been able to specifically identify and target only the clonal neoantigens found throughout the tumor. We believe this is a key reason for limitations in efficacy and durability of many of today's cancer therapies.

In the last decade numerous clinical trials have validated the therapeutic potential of the immune system in the fight against cancer. Immunotherapy approaches include checkpoint inhibitors, or CPIs, which inhibit the downregulation of endogenous T cell activity, and adoptive cell therapies, or ACTs, that expand a patient's own tumor-targeting T cells in vitro followed by their transfer back into the patient. There are different types of ACTs, primarily differentiated by the approach used to target the T cells to the tumor, including chimeric antigen receptor therapy, or CAR-T, T cell receptor therapy, or TCR-T, and tumor-infiltrating lymphocytes, or TIL, therapy. These approaches are based on harnessing T cells to attack tumor antigens. Despite the clinical successes of CPI and ACT therapies, we believe their clinical benefit has generally been limited by an inability to specifically target the antigens that are uniformly expressed by solid tumors and not expressed on healthy tissue. This has resulted in a lack of durable response, off target activity and toxicity concerns.

TIL therapeutic approaches are based on the observation that tumor reactive T cells are found in a patient's tumor at higher frequencies than in other tissues, such as blood and healthy tissue. In standard TIL therapy, T cells are extracted from a patient's tumor, activated and expanded to large numbers before being reinfused back into the patient. Despite the impressive results of standard TIL therapies seen in clinical trials, we believe their clinical benefit has been limited by their inability to specifically target clonal neoantigens, thereby targeting the entire tumor, while sparing healthy tissue. This lack of specificity is a result of the inability of standard TIL therapies to control selection of targeted antigens; instead, all T cells within the patient's tumor sample are expanded and the resulting composition of the T cell therapy is not known or controlled. In addition, manufacturing processes for standard TIL therapies employ non-physiological T cell expansion methods, which we believe result in less functionally fit T cells in the final TIL product. We believe that this lack of control over T cell specificity and T cell fitness limits the potential of standard TIL therapies and provides an opportunity to develop a precision TIL therapy. In contrast, we have demonstrated the ability to detect, quantify, and track patient-specific clonal neoantigen-reactive T cells, or cNeT. The ability to reliably detect and quantify our active component is a key differentiator of our technology that is unique in the field and which we believe will be critical for the successful development of TIL-based therapies.

OUR APPROACH—PRECISION TILS TARGETING CLONAL NEOANTIGENS IN SOLID TUMORS

We believe that targeting clonal neoantigens is the key to unlocking immunotherapy in solid tumors and have developed our platform to specifically address these targets. By targeting multiple clonal neoantigens, we have the potential to reduce the likelihood of immune escape by tumor cells, thereby enhancing long-term tumor control, while also reducing the potential for off-target toxicity. We utilize our bioinformatics platform, PELEUS, to identify clonal neoantigens in patients and combine these targets with our VELOS manufacturing process, which utilizes a physiological, antigen driven expansion process to create a functionally fitter T cell product. We believe the resulting cNeT product candidates can overcome many of the challenges faced by existing immunotherapies for the treatment of solid tumors.

The foundation of our approach is the PELEUS bioinformatics platform which is designed to identify each patient's tumor-specific clonal neoantigens by comparing DNA sequencing information from healthy tissue and tumor. PELEUS combines data from the TRACERx study with sophisticated proprietary statistical models to distinguish which mutations in a patient's tumor are clonal or subclonal. TRACERx is a study which aims to analyze tumor samples from more than 840 NSCLC patients, with approximately 795 NSCLC patients enrolled to date and which has collected over 3,200 tumor region samples. We have exclusive commercial rights to the TRACERx database of multi-region samples from primary tumor and metastases and whole exome sequencing data for each individual patient for development of neoantigen-targeting cell therapies. The PELEUS algorithm is continuously updated, trained, and

improved with this reference data that gives us what we believe is a unique approach to enable identification of clonal neoantigens.

To create our cNeT product candidates, we first procure tumor tissue and blood samples from the patient. We then extract, sequence and analyze the tumor DNA using PELEUS to identify the patient's unique clonal neoantigens. Using this information, we manufacture clonal neoantigen peptides, load them onto dendritic cells extracted from the patient's blood, and co-culture them with TILs extracted from the patient's tumor to activate and expand a subset of the T cells — we call this proprietary manufacturing process VELOS. This process creates a cNeT product candidate significantly enriched for T cells designed to recognize and specifically target multiple clonal neoantigens across all of the patient's tumor cells. We have designed and are continuing to develop an automated, fully-closed system for cell manufacturing, which we believe will be readily scalable for commercial supply and has the potential to overcome many of the manufacturing challenges associated with other cell therapies.

OUR PIPELINE

We believe our cNeT is uniquely positioned to overcome the challenges faced by existing immunotherapies for the treatment of solid tumors. We have worldwide rights to our cNeT programs and are currently developing them for the treatment of the following solid tumor indications:

Depending on the results of our Phase I/II trials, we plan to engage with the appropriate regulatory authorities to discuss potential pathways to registration.

We are currently conducting a Phase I/IIa, open-label, proof-of-concept trial in each of advanced NSCLC, referred to as CHIRON, and metastatic or recurrent melanoma, referred to as THETIS. We have prioritized the tumor types that we are seeking to address based on criteria we believe will maximize the potential of our programs to demonstrate a clinical benefit, including clonal neoantigen burden, TIL infiltration, tumor accessibility, as well as commercial factors such as high unmet medical need. Our Phase I/IIa trials are evaluating safety and tolerability of cNeT and assessing clinical efficacy based primarily on the change from baseline in tumor size, response rate and duration of response. Data from the first eight patients were presented in November 2021 and we expect to generate additional patient data across both clinical trials in the second half of 2022.

We believe the principles of tumor evolution to be common across many tumor types enabling our cNeT approach to be broadly applicable. As such, we have built up our MAP network to acquire and analyze tumor samples from multiple different indications to facilitate the development of follow-on indications for our cNeT, such as HNSCC, RCC, TNBC and bladder cancer. Our investigational new drug application, or IND, for HNSCC was accepted by the FDA in January 2022 for VELOS Process 1 manufacturing and we expect to make additional submissions for our other earlier stage programs in the future.

OUR TEAM

Our management team has a strong track record of delivery including expertise in cancer immunology, oncology drug development, cell therapy process development, manufacturing and supply chain management. We are led by Dr. Iraj Ali, our Chief Executive Officer. Dr. Ali was formerly a Managing Partner of Syncona, where he served as an Investment Director at Nightstar Therapeutics (acquired by Biogen) and Blue Earth Diagnostics (acquired by Bracco Imaging), and was previously an Associate-Principal at McKinsey & Co. Our Chief Scientific Officer and co-founder is Professor Sergio Quezada, who is a recognized leader in the field of immune regulation and cancer immunology and was a founder of TUSK Therapeutics, an immuno-oncology company acquired by Roche. Our Chief Medical Officer and co-founder is Professor Karl Peggs, who was formerly a Professor of Transplant Science and Cancer Immunotherapy at University College London. Professor Peggs has significant experience in the clinical translation of T cell therapies and is the Director of the Cellular Immunotherapy Unit at University College London Hospitals NHS Trust, or UCLH. Our Scientific Advisory Board also includes our other scientific founders, Professors Charles Swanton and Mark Lowdell, who are leaders in the respective fields of tumor evolution and cell manufacturing.

OUR STRATEGY

Our goal is to become a fully integrated biopharmaceutical company focused on the development, manufacture and commercialization of cNeT for multiple solid tumor types. To achieve this, we are pursuing the following strategies:

- Generate proof-of-concept clinical data for our cNeT approach in two lead solid tumor indications: We initiated the CHIRON and THETIS Phase I/IIa clinical trials in advanced NSCLC and metastatic or recurrent melanoma respectively in 2019. As of February 28, 2022, we have treated ten patients from these trials and data from eight patients were presented in November 2021. We expect to generate additional patient data from both clinical trials in the second half of 2022. We expect to utilize initial data to gain insights into our cNeT therapy to inform the design of future trials of cNeT in other solid tumor settings.

- Expand our cNeT platform into multiple additional solid tumors and earlier lines of therapy: We believe clonal neoantigens represent optimal targets for the durable treatment of solid tumors. Our pioneering work in the identification and therapeutic targeting of these antigens gives us a strategic leadership position in advancing the field of cancer immunotherapy. We are leveraging our fundamental insights into the genetic evolution of tumors, combined with real-world data from multiple patient tumor samples obtained through our proprietary MAP network, to rapidly expand our pipeline into additional solid tumors.

- Continuously develop and innovate our cNeT platform: We believe our PELEUS bioinformatics platform gives us a unique ability to therapeutically target clonal neoantigens, and we continuously work to enhance and improve its predictive capabilities. Our approach is designed to enable a granular understanding of cell expansion and trafficking in each patient, which we plan to exploit to optimize the clinical potential of our cNeT platform. With this mechanistic understanding, we can direct our research and development efforts to refine our processes with the goal of delivering T cell product candidates optimized for functional fitness, anti-cancer activity and safety. We continuously evaluate complementary technologies to enhance cNeT activity in vivo and plan to explore alternative sources of T cells beyond tumor (e.g., blood) to initiate the manufacture of cNeT.

- Build a scalable, automated manufacturing process: We recognize the critical strategic importance of manufacturing to the success of the cNeT approach and have learned from the challenges currently facing many other cancer cell therapies. We are designing our VELOS manufacturing process to be automated, fully-closed and robust with a competitive cost of goods. We continue to invest in improving manufacturing time, yield, and delivery of our product candidates to patients, and in expanding our manufacturing capacity to deliver on our ambitious clinical development and commercialization goals. Our current and planned manufacturing footprint in the UK is expected to be sufficient to meet our near-term clinical trial requirements. Our priority over the near-to-medium term is to expand this capacity into the U.S., with the goal of establishing a network of regional manufacturing sites globally. Our ultimate aim, if approved, is to be able to supply thousands of doses of commercial product annually.

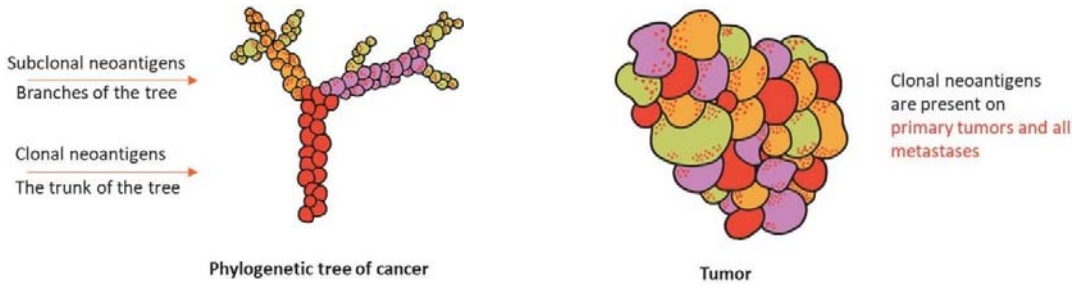
- Opportunistically collaborate with strategic partners to realize the full potential of our technology. We intend to establish our own fully integrated internal capabilities to develop and commercialize our product candidates in Europe and the United States. In parallel, we plan to explore strategic collaborations with partners who bring complementary technical skills, experience and geographic reach to expand the scope of our activities and accelerate our development timelines to maximize the full potential of our platform and realize the transformative therapeutic potential of cNeT therapies to treat patients in need.

TUMOR EVOLUTION AND THE IMMUNE SYSTEM

The Genetic Basis of Cancer

Cancers originate from mutations in the DNA of individual cells that promote uncontrolled proliferation, metastasis and evasion of the immune system. Tumors evolve in a Darwinian branched manner, whereby the mutations that are present in a cell before it becomes cancerous will be carried by all daughter cells of the growing cancer. These mutations are called clonal neoantigens, represented as the red "trunk" in the figure below. After the cell becomes cancerous, additional mutations may continue to arise in some cancer cells in response to genomic instability or environmental challenge. These additional mutations are called subclonal neoantigens – represented as the "branches" in the figure below. Clonal neoantigens are expressed in every tumor cell, while subclonal neoantigens are expressed by only a fraction of tumor cells. Since subclonal neoantigens are not present in all cancer cells, therapies that only target subclonal neoantigens only address a subset of the cancer cells and therefore allow the non-targeted cancer cells to continue to evolve and evade immune attack.

DEPICTION of DARWINIAN TUMOR EVOLUTION



Red = clonal neoantigens
Purple, Green and Orange = subclonal neoantigens

Cancer and the Immune System

A key line of defense of the immune system's response to tumors are T cells, which are white blood cells that mature mainly in the thymus. One of the primary functions of T cells is to detect and eliminate abnormal or "non-self" cells. T cells can be classified into two major subsets, CD4+ T "helper" cells and CD8+ T "effector" cells. CD8+ T cells can directly attack and kill cells that they recognize as abnormal or "non-self." CD4+ T cells provide help to the immune response by secreting cytokines that enhance the activation, expansion, migration and effector functions of other types of immune cells in response to "non-self" cells. In addition, they can also directly kill tumor cells. Central and peripheral tolerance mechanisms prevent T cells from reacting to self-antigens, enabling them to differentiate between human leukocyte antigens, or HLA-peptide complexes that are "self" and those that are "foreign" or "non-self."

When the DNA of tumor cells mutates, it results in the expression of "non-self" peptides. These peptides are then displayed on the cell surface as an HLA-peptide complex, which can be recognized and targeted by T cells, leading to subsequent destruction of the cell expressing them. Cancerous cells evolve as they divide and develop mechanisms to avoid the immune response. For example, tumor cells are able to activate immune checkpoint proteins on the surface of T cells that act to down-regulate the immune response to tumors. This also results in the recruitment of immunosuppressive cells to the tumor microenvironment, or TME, production of immune-suppressive factors, and

reduced antigen presenting capacity, which reduces the ability of T cells to recognize cancerous cells as foreign. As a result, endogenous tumor reactive T cells are present in insufficient quantities and with inadequate levels of activity against the tumor.

Overview of Current Therapies and their Limitations

Immuno-oncology is an emerging field of cancer therapy that is designed to activate the immune system to enhance and/or create anti-cancer immune responses, as well as to overcome immunosuppressive mechanisms that cancer cells have developed. In the last decade, clinical trials have demonstrated the utility of the immune system in the fight against cancer, including some studies that have demonstrated impressive clinical responses against late-stage metastatic disease. Immuno-oncology therapies approved or in development include vaccines and checkpoint inhibitors, which are designed to re-activate the immune response to cancer, and genetically engineered immune cells, such as CAR-T and TCR-T therapies, which are designed to recognize and attack cancerous cells. While these existing immuno-oncology therapies have shown some impressive results in treating cancer, they each have limitations. An alternative approach, known as TIL therapy, aims to extract T cells from the patient's tumor, expand them outside the body and reinfuse the expanded cells back into the patient.

***Checkpoint inhibitors*:** Immune checkpoints mediate peripheral tolerance by down-regulating T cell activity and have been targeted with CPI therapies to block their inhibitory function. Despite showing great potential in treating solid tumors, there are several shortcomings to CPIs. Most importantly, CPIs are designed to overcome the immunosuppressive TME by activating T cells regardless of their specificity, leaving their activity dependent on the presence of tumor reactive T cells. As a result, only a fraction of patients treated with CPIs respond to the therapy. Furthermore, they can promote systemic activation of self-reactive T cells, resulting in immune-related adverse events.

***Adoptive cell therapies*:** Adoptive cell therapies, or ACTs, are based on the *in vitro* expansion of tumor-targeting T cells followed by their transfer into the patient. This process allows for the expansion of large numbers of T cells *ex vivo* away from the immunosuppressive nature of the TME. ACTs are primarily differentiated by the approach used to direct the T cells to target tumor cells and include:

- *CAR-T therapy*: T cells are genetically engineered to target a molecule expressed on the surface of a tumor cell, such as CD19, a molecule present on the surface of hematological cancers. CAR-Ts have demonstrated significant response rates in hematological cancers but remain of limited use in non-hematological cancers due to the lack of sufficiently specific surface targets, as most potential common solid tumor target candidates are also expressed by normal tissue, which increases the chances of serious off-tumor effects.

- *TCR-T therapy*: TCR-T cell therapies engineer T cells to target a selected tumor associated antigen, or TAA, in the context of the patient's own HLA molecules. TAAs are endogenous antigens that are expressed preferentially, but not exclusively, by tumor cells. The selected TAA can be expressed by normal tissue, which leads to a lack of specificity and off-target toxicity concerns. In addition, they are not uniformly expressed by tumor cells which leads to the potential for tumor escape. While there have been clinical successes in solid tumors, each TCR-T cell therapy can only be developed for a specific HLA type, limiting its applicability to the population of patients with that specific HLA type.

- *Standard TIL approaches*: In standard TIL approaches, T cells are extracted from a patient's tumor, activated, and expanded to large numbers before being reinfused into the patient. These therapies are limited due to the lack of control over the specificity of selected antigens, the fitness of the T cells manufactured, and toxicity profile, which is in part driven by the non-physiological doses of IL-2 required for manufacturing and administration in the clinical setting. These limitations are compounded by a patient's pre-existing comorbidities.

Background on Standard TIL Therapy

In clinical trials, standard TIL therapy has demonstrated some of the most impressive results in treating solid tumors to date. These therapies have been observed to induce significant response rates as well as including some complete

responses, or CRs, in clinical trials for melanoma, cervical carcinoma and NSCLC. Despite the clinical benefits provided by standard TIL therapy, we believe the technology has been limited by several factors, including:

- *Specificity and durability*—Standard TIL therapy does not have control over the specific reactivity of the T cells infused into a patient. In this therapy, all T cells within a patient's tumor sample are expanded and the resulting target specificity of the T cell therapy is not known or controlled. Such an expanded standard TIL product may include a mixture of bystander T cells that are unable to identify and target the tumor, and T cells that recognize nonclonal or subclonal neoantigens. We believe that this lack of control over T cell specificity, without specifically targeting clonal neoantigens, contributes to the observed lack of a durable response to standard TIL therapy in a proportion of patients.

- *T cell fitness*—Standard TIL expansion uses non-antigen specific methods to induce T cell proliferation, as well as non-physiological doses of IL-2 during the manufacturing process. These artificial methods for T cell expansion, coupled with chronic stimulation in the absence of dendritic cell-driven co-stimulation can lead to terminal differentiation and exhaustion of the T cell product. These exhausted or terminally differentiated T cells are considered less functionally fit to attack tumors due to their reduced capacity to proliferate and release cytokines *in vivo* after being dosed back into the patient.

- *Toxicity concerns*—The use of high levels of IL-2 in the standard TIL manufacturing process can lead to T cell dependence on IL-2 and the need to administer high dose IL-2 *in vivo* after the TILs are infused back into the patient in order to drive T cell survival. However, non-physiological levels of IL-2 have been associated with a range of toxicities in the clinical setting. Patients that have high tumor burden and comorbidities are more susceptible to the potential toxicity concerns associated with high levels of IL-2.

- *Manufacturing and scalability*—The manufacturing process for standard TIL therapy was developed in an academic setting and was not designed for commercial scale. These academic manufacturing processes lack automation and require human intervention at multiple steps, which increases manufacturing time and cost. Further, these systems are usually not fully closed end-to-end, which increases good manufacturing practice, or GMP, compliance costs, and were not designed to minimize cost of goods or redundancy in materials.

- *Potency assay difficulties* - Regulatory authorities require demonstration that the product contains an active component of a specific identity and potency. Potency can be defined as the specific ability of the product to effect a given result that should take effect through the product's mechanism of action. We believe this may encumber standard TIL therapy companies.

OUR SOLUTION

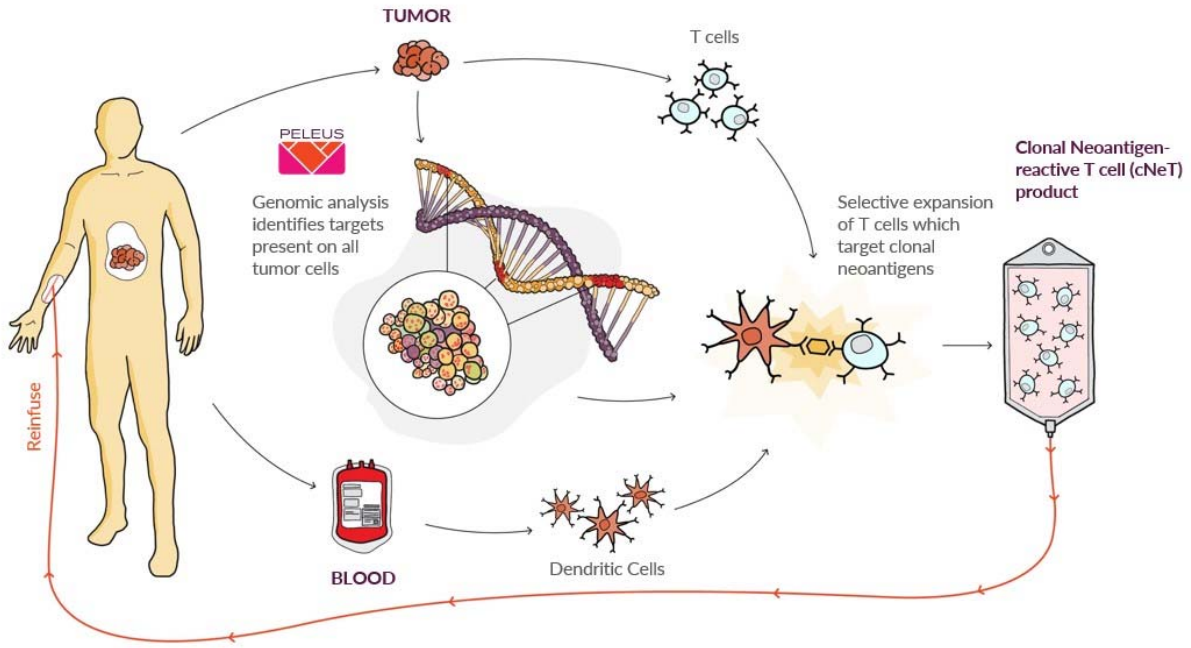
Our approach uses a precision TIL-based therapy to target what we believe to be the most specific tumor antigens, clonal neoantigens, in solid tumors. We believe that tumor clonal neoantigens represent optimal tumor targets because they are recognized by the immune system as foreign antigens and are absent in normal, healthy tissue but present in all of a patient's tumor cells.

We believe that our approach of selectively targeting clonal neoantigens to elicit a robust and durable clinical response is supported by third party studies. These studies have observed that neoantigens were relevant in producing anti-tumor activity, since patients with a high number of neoantigens showed improved progression free survival and overall survival when treated with CPIs and TIL therapies. Furthermore, clinical case studies have observed that adoptive transfer of neoantigen reactive T cells to cancer patients have shown impressive tumor control supporting the hypothesis that neoantigen-targeting T cells are the active component of TIL therapy. While these studies support the development of standard TIL therapies and other immuno-therapies that target neoantigens, third party studies have further observed that clonal neoantigens contributed more than subclonal neoantigens to patient survival. In one study of treatment naïve lung cancer patients, it was observed that high numbers of clonal neoantigens in the tumors correlated with disease-free survival, while this relationship was not evident with subclonal neoantigens.

To address the limitations of current immuno-oncology approaches, we developed cNeT. As outlined in the figure below, the first step of our process involves the procurement of tumor and blood samples from the patient. Once the

tumor and blood are procured, we extract and sequence DNA. These sequencing data are fed into our PELEUS bioinformatic platform to identify the patient's unique clonal neoantigens. In parallel, we expand CD4+ and CD8+ T cells and generate dendritic cells from the tumor and blood, respectively. After PELEUS identifies the sequences of clonal neoantigens from the tumor genome, we manufacture clonal neoantigen peptides, load them onto dendritic cells and co-culture the dendritic cells with TILs to activate and expand a subset of the T cells. This process is designed to create a cNeT product candidate that is enriched with T cells designed to recognize and specifically target multiple clonal neoantigens in all of the patient's tumor cells. Our current VELOS process has an end-to-end time of approximately nine weeks, with a goal of further reducing the time to six to eight weeks.

Our cNeT Approach



Our cNeT is designed to be:

- *Specific and durable*—We are able to design our cNeT to specifically target multiple clonal neoantigens present in a patient's tumor. We believe this specificity for multiple targets will reduce the likelihood of tumor escape and increase the rates of durable complete response.

- *Functionally fit*—The use of dendritic cells to drive physiological, antigen-driven T cell expansion reduces the need for non-physiological IL-2 driven expansion and allows the production of fit T cell populations of CD4+ and CD8+ T cells capable of significant expansion and persistence in the patient. Our VELOS manufacturing process allows us to modulate the levels of IL-2 used in the manufacture and administration of our cNeT product candidates, which in turn allows us to tailor the treatment regimen and IL-2 usage to the patient's specific tumor burden and comorbidities to reduce toxicity concerns.

- *Well-tolerated*—Clonal neoantigens are absent from healthy tissue, which we believe minimizes the risk of off-tumor toxicity.

- *Designed to be cost effectively manufactured at scale* - The manufacturing process for cNeT has been designed, from its inception, to be compatible with industrialization and scalability while considering cost of goods. We have designed, and are developing, our manufacturing process to be fully-automated in a closed end-to-end system, in order to decrease cost and maximize yield.

- *Measurable and quantifiable* - With our platform we can quantify the cNeT component as a percentage of the total T cells (cNeT reactivity) and calculate the expected cNeT dose of each product. cNeT reactivity can be used as both a release criterion and potency measure. We believe that cNeT is the active component of TIL and will correlate with anti-tumor effect. Further phenotypic and functional characteristics of cNeT can be measured to develop potency assays. We have developed a timeline for interaction with regulatory authorities and aim to have an agreed upon plan prior to registrational studies.

Our approach also allows us to determine the dose of active cNeT cells in each patient's cNeT therapy. We use a flow cytometric assay to detect which T cells may be able to produce inflammatory cytokines in each patient in response to the clonal neoantigen peptides which allows us to calculate the fraction of cNeT present in the total CD3+ T cell dose. We believe this information will allow us to investigate potential relationships between cNeT dose, cNeT persistence and clinical response. We plan to use these correlations to further develop our understanding of the cellular mechanism of TIL therapy and support the design and the evaluation of next-generation processes for cNeT manufacture.

OUR PELEUS BIOINFORMATICS PLATFORM – A UNIQUE, PROPRIETARY TOOL FOR IDENTIFYING CLONAL NEOANTIGENS

PELEUS is a bioinformatics platform that is designed to identify each patient's tumor-specific neoantigens by comparing DNA sequencing information from healthy tissue and tumor. Furthermore, PELEUS uses statistical models to further distinguish which of these neoantigens are clonal and subclonal. After identifying the clonal neoantigens, PELEUS selects which of these are most likely to generate an immune response by leveraging data and know-how from the TRACERx study.

We have exclusive commercial access to data, for use in fields including neoantigen cell therapies, from TRACERx, which is a UK national study, funded by Cancer Research UK, to collect NSCLC samples from patients at diagnosis and relapse. The program has been running for more than four years and has enrolled approximately 795 NSCLC patients to date and collected over 3,200 tumor region samples, with a target enrollment of more than 840 patients. TRACERx collects multi-region samples from primary tumor and metastases (where available) over multiple points in time, generating whole exome sequencing data for each sample to understand each patient's tumor genomic evolution in detail. By searching for the overlap of coding mutations across multiple tumor regions across hundreds of patients, we have used TRACERx to identify the fundamental features that define clonal neoantigens. Our PELEUS algorithm is based on this reference data and is continuously updated, trained and improved as additional patients are recruited to the study. While TRACERx is focused on patients with lung cancer, we believe the principles of tumor evolution utilized by PELEUS are broadly applicable across multiple tumor types. We are using our MAP network to expand the tumor database of PELEUS with additional samples from other tumor types. Our MAP network has expanded to include fourteen active sites in the UK, EU and U.S., with twenty-five tumor procurement channels in six tumor indications. We refer to each tumor type that can be collected at a site as a separate procurement channel so one site provides either one or multiple procurement channels. We plan to continue to grow our network as we develop and advance our current and future cNeT programs.

PELEUS identifies clonal neoantigens for each individual patient in a multi-step process. First, tumor and blood samples are collected from the patient and sequenced, using whole exome sequencing and RNA sequencing. The genetic profile of the tumor is compared to that of healthy tissue using blood to identify mutations specific to the tumor. The resulting sequence information is then processed by PELEUS in a three-step process.

- **Step 1:** ***Identify tumor mutations***—PELEUS utilizes a state-of-the-art ensemble approach that combines multiple different algorithms to identify tumor-specific mutations. The sequencing data obtained from the tumor samples originates from a combination of tumor cells and healthy tissues that dilute the tumor signal. The challenge of identifying cancer-specific mutations is further compounded by sequencing errors, as well as non-cancer-specific mutations in the tissue surrounding the tumor. This creates a significant amount of "noise" in each data sample. The unique scale of the TRACERx data has allowed us to develop highly sophisticated proprietary algorithms to improve the signal-to-noise ratio and allow us to reliably identify true cancer-specific mutations from real-world patient samples.

- **Step 2:** ***Identify clonal mutations***—PELEUS assesses the evidence for whether each mutation is present in all tumor cells in order to determine clonal versus subclonal status. This is achieved using a proprietary Bayesian statistical model which combines multiple lines of evidence.

- **Step 3:** ***Identify expressed mutations and predict immunogenicity***—PELEUS evaluates factors which influence the likelihood of each clonal neoantigen generating an immune response, such as neoantigen expression and predicted binding affinity. This enables us to prioritize clonal neoantigen targets for inclusion in our VELOS manufacturing process to selectively expand both CD4+ and CD8+ T cell reactivity.

OUR VELOS MANUFACTURING PROCESS

The viability of a personalized cell therapy product depends critically on manufacturing success and ability to scale sufficiently to address patient demand in a cost-effective manner. Therefore, from inception, we have made it a core strategic priority to invest in optimizing and scaling manufacturing capacity.

The emergence of high throughput next generation DNA sequencing has enabled the rapid and cost-effective genetic characterization of tumor samples on a per patient basis. We leverage these advances, combined with our understanding of tumor evolution, to build upon the initial success of standard TIL therapy and deliver highly precise and functionally fitter T cells that are designed to target multiple clonal neoantigens.

Our VELOS manufacturing process has been designed from the outset to be suitable for scaled commercial use. This approach is in contrast to many other cell therapy processes in development today that have been transferred out of academia. Our process benefits from learnings over years of experience in ACT and is designed for commercial use with a focus on GMP compliance and the use of closed systems.

Background and Challenges of Cell Therapy Manufacturing

Developing a reliable and robust manufacturing process for personalized cell therapies that can ensure adequate product safety, potency, and consistency at an economically viable cost of goods has been one of the most significant challenges in the field of cell and gene therapy. Key challenges include:

- **Academic manufacturing processes**—Historically, cell therapy manufacturing processes have been developed in academic institutions for early-stage clinical trials treating a small number of patients. These are often open processes that require the highest-grade cleanroom environment to protect from contamination. Operating and facility costs to maintain these manufacturing environments are substantial, require a large footprint and high numbers of staff.

- **Manual processing leads to challenges at commercial scale**—Traditional academic approaches to cell therapy manufacturing have been both time consuming and labor intensive due to the high number of operator-dependent manual processes involved. Reverse engineering these academic processes to be suitable for late phase clinical trials and commercialization is both time consuming and cost intensive, introduces risk to overall development timelines, and challenges in maintaining product characteristics.

- **Human clinical trial material is variable**—Patient-to-patient variability in clinical trial material is inherent in autologous therapies. Validation of manufacturing processes are often performed with surrogate healthy volunteer donor material or cell lines due to lack of commercially available patient material.

- **Supply chain and logistics are complex and time consuming**—The shipment of tumor and blood samples direct from surgery to manufacturing hubs requires a complex temperature controlled and sterile supply chain network to maintain cell and tissue viability.

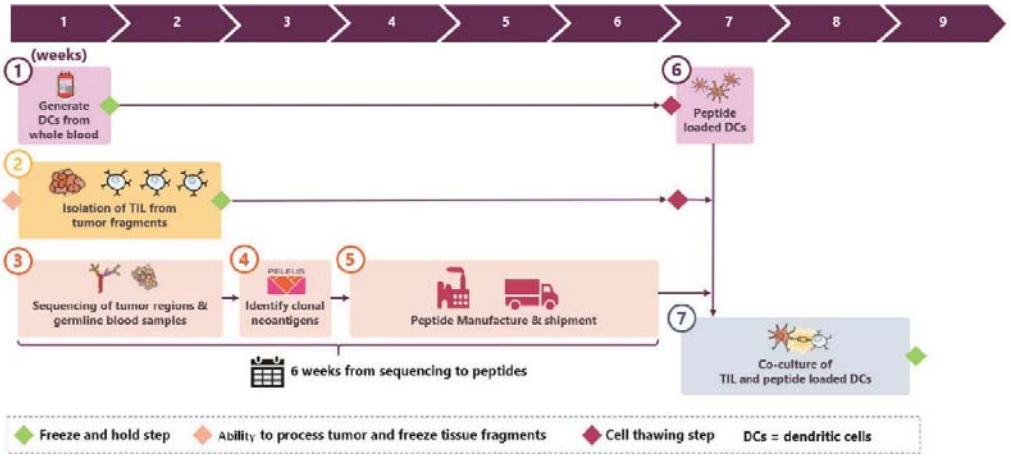
Our Manufacturing Solution

We have invested in our manufacturing process from the outset with the goal of producing our cNeT at a commercial scale, which we believe will allow us to address the challenges faced by traditional methods of cell therapy

manufacture. Our approach is to design a fully closed, end-to-end manufacturing system with integrated automation. We believe this will enable lower operating costs by reducing the number of labor-intensive manual operator steps and eliminate the requirement for the higher-grade manufacturing environment needed for open processing. We believe that this approach is essential for industrial scale-up, as it drives a reduction in process variability between operators, minimizes failure rates, and improves reproducibility. Our approach has been to invest in developing new technology, both in-house and with partners, to deliver an automated and standardized platform that permits rapid scale out while controlling commercial cost of goods. Our proprietary process benefits from the deep experience of our management team and founders in the field of ACT, combined with a core focus on GMP compliance and the use of closed systems.

Key Steps in our VELOS Process

Our Current VELOS Manufacturing Process



The key steps in our manufacturing process include:

1. **Generation of dendritic cells from whole blood**—Monocytes are isolated from the patient's whole blood using a process of immunomagnetic selection and subsequently differentiated into dendritic cells in culture. The harvested dendritic cells are then cryopreserved for later use.

2. **Isolation of TIL from tumor**—Tumor samples are cleaned, dissected into small fragments, and placed into culture with cytokines. TILs are isolated from the fragments, harvested, and cryopreserved for later use.

3. **Sequencing of tumor regions**—Following dissection of the patient's tumor sample, multiple fragments are selected and sent for DNA and RNA sequencing.

4. **Selection of clonal neoantigens**—DNA and RNA sequencing data from each patient are analyzed by PELEUS to identify a unique set of clonal neoantigens.

5. **Manufacture of patient specific peptides**—Each patient's clonal neoantigens are used to manufacture a personalized set of clonal neoantigen peptides.

6. **Peptide loading of dendritic cells**—Following receipt of the clonal neoantigen peptides, the patient's dendritic cells are removed from storage, thawed and put back into cell culture and loaded with the peptides.

7. **Co-culture of TIL and peptide-loaded dendritic cells**—The thawed TIL intermediate is co-cultured with the dendritic cells that have been loaded with the patient's clonal neoantigen peptides. The co-culture step results in

the selective expansion and enrichment of cNeT, prior to final formulation and cryopreservation to enable flexibility for shipping to clinical sites as required for patient treatment.

In the fourth quarter of 2021, regulatory authorities in the UK, Germany, France and Spain with respect to CHIRON and in the UK with respect to THETIS allowed for a modified manufacturing process and a switch from our original Process 1 to a higher dose Process 2. VELOS Process 2 includes an optimized cytokine cocktail throughout the manufacturing process and additional media supplements for T cell expansion following the dendritic cell-driven co-culture step. VELOS Process 2 retains an identical manufacturing timeline to Process 1. We are continuously improving our process with the goal of decreasing end-to-end time to six to eight weeks.

The manufacturing success rate for VELOS Process 1 as of January 13, 2022 across both CHIRON and THETIS trials was 63% in the last 27 patients. We anticipate an improvement in manufacturing success with Process 2 and the generation of higher cNeT doses.

OUR PIPELINE

We believe our cNeT technology is uniquely positioned to overcome many of the challenges faced by existing therapies for solid tumors. We have prioritized the tumor types that we are seeking to address based on criteria that we believe will maximize the potential of our programs to demonstrate a clinical benefit, including expected clonal neoantigen burden, TIL infiltration and tumor accessibility, as well as high unmet medical need and future commercial potential.

Our pipeline is illustrated in the chart below:

Depending on the results of our Phase I/II trials, we plan to engage with the appropriate regulatory authorities to discuss potential pathways to registration.

We are currently conducting two open-label Phase I/IIa trials, CHIRON and THETIS, to evaluate our cNeT programs in advanced NSCLC and metastatic or recurrent melanoma, respectively. Our Phase I/IIa trials are evaluating safety and tolerability of cNeT and assessing clinical efficacy based primarily on the change from baseline in tumor size, response rate and duration of response. Data from the first eight patients were presented in November 2021 and we expect to generate data from additional patients across both clinical trials in the second half of 2022.

We believe the principles of tumor evolution to be common across many tumor types, which could enable our cNeT approach to be broadly applicable. As such, we have built up our MAP network to acquire and analyze tumor samples

from multiple different indications to facilitate the development of follow-on indications for our cNeT, such as HNSCC, RCC, TNBC and bladder cancer.

We have identified these initial tumor indications using the following criteria:

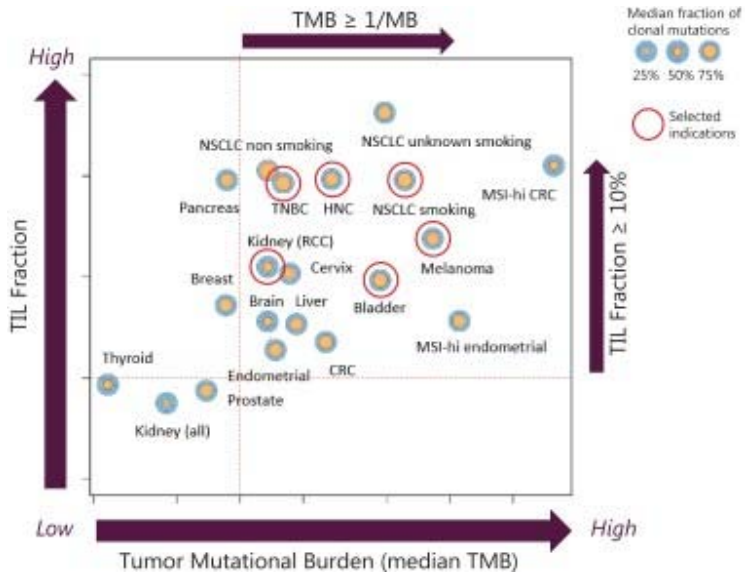
- **Tumor mutational burden**—Tumor mutational burden is a measure of the number of mutations in the coding region of tumor DNA as compared to healthy tissue DNA. This mutational burden will generally increase over time as new mutations accumulate through exposure to environmental carcinogens (e.g., smoking, sunlight) and this is also generally associated with an increase in neoantigen and clonal neoantigen frequency. These clonal neoantigens are the target for our cNeT product candidates.

- **The extent of T cell infiltration into the tumor**—Tumors will typically be targeted and infiltrated by varying numbers of T cells that are able to recognize tumor neoantigens. We have prioritized tumors that typically demonstrate high levels of T cell infiltration for our initial indications since tumor infiltrating T cells are the starting material for our cNeT.

- **The accessibility of tumor tissue**—In order to extract the tumor infiltrating T cells that are required as our starting material, the ability to safely procure adequate primary or metastatic tumor tissue through a surgical procedure is critical for manufacture. We have therefore prioritized indications where tumors are typically present in sufficient volumes and in locations that can be readily accessed to extract the tumor sample without compromising its quality.

- **Unmet need and commercial opportunity**—In order to maximize the beneficial impact for cancer patients, we have sought to address indications with the highest addressable market potential, as defined by various factors including unmet medical need, typical co-morbidities and outcomes with current and likely future treatment options.

The figure below compares the amount of T cell infiltration into a tumor and the corresponding tumor mutational burden for various cancer types. The area shaded orange in each circle reflects the median fraction of clonal mutations for that tumor type. As depicted below, the indications we are targeting in both our lead and follow-on indications typically have high levels of tumor mutational burden, clonal mutational burden and TIL infiltration as compared to other solid tumors.



OUR PROGRAMS

cNeT (ATL001) for Non-Small Cell Lung Cancer and Melanoma

Our lead cNeT programs (product candidate ATL001) are currently in two ongoing Phase I/IIa clinical trials for the treatment of advanced NSCLC and metastatic or recurrent melanoma. Our Phase I/IIa clinical trials will evaluate safety and tolerability of these programs as a monotherapy with the option for investigation of cNeT in combination with a PD-1 inhibitor. The trials will also evaluate, among other measures, change from baseline in tumor size, response rate and duration of response. We expect to receive further interim data from both clinical trials in the second half of 2022.

Non-Small Cell Lung Cancer

Lung cancer remains the most common cause of cancer related death worldwide, with approximately 236,000 new cases and 132,000 deaths annually in the U.S. The majority of cases are caused by smoking and patients are most often diagnosed with advanced invasive or metastatic disease, which is incurable despite current combination regimens utilizing chemotherapy and immune checkpoint inhibitors. Most patients experience disease progression within a year of starting treatment and there are currently no effective standard treatments for these patients.

Melanoma

In the U.S., approximately 106,000 patients are diagnosed with melanoma annually and there are 7,000 melanoma-related deaths each year. The incidence of melanoma continues to rise and we believe that there remains a substantial unmet need for patients with metastatic or recurrent melanoma who become resistant to check-point inhibitors, as there are no effective treatment options available to these patients.

Clinical Trial Designs for NSCLC and Melanoma

We are currently conducting two open-label, proof-of-concept clinical trials in advanced NSCLC and metastatic or recurrent melanoma:

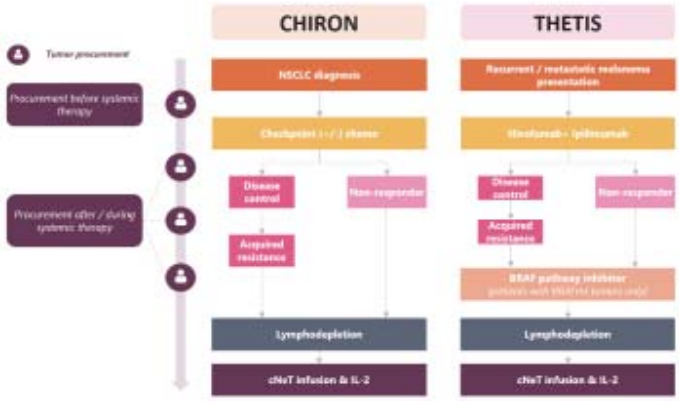
- **CHIRON**—a Phase I/IIa clinical trial to evaluate the safety, tolerability and clinical activity of cNeT in up to 60 patients with advanced NSCLC, ongoing at eight UK sites. Our IND was accepted by the FDA in December 2019 and we plan on expanding our trial in up to ten sites in the U.S. and Europe in 2022.

- **THETIS**—a Phase I/IIa clinical trial to evaluate the safety, tolerability and clinical activity of cNeT in up to 60 patients with metastatic or recurrent melanoma. We are currently conducting this trial at six UK sites and submitted an IND to the FDA in November 2020 to enable expansion to U.S. sites in 2022. Further clinical trial applications in the European Union are planned for 2022.

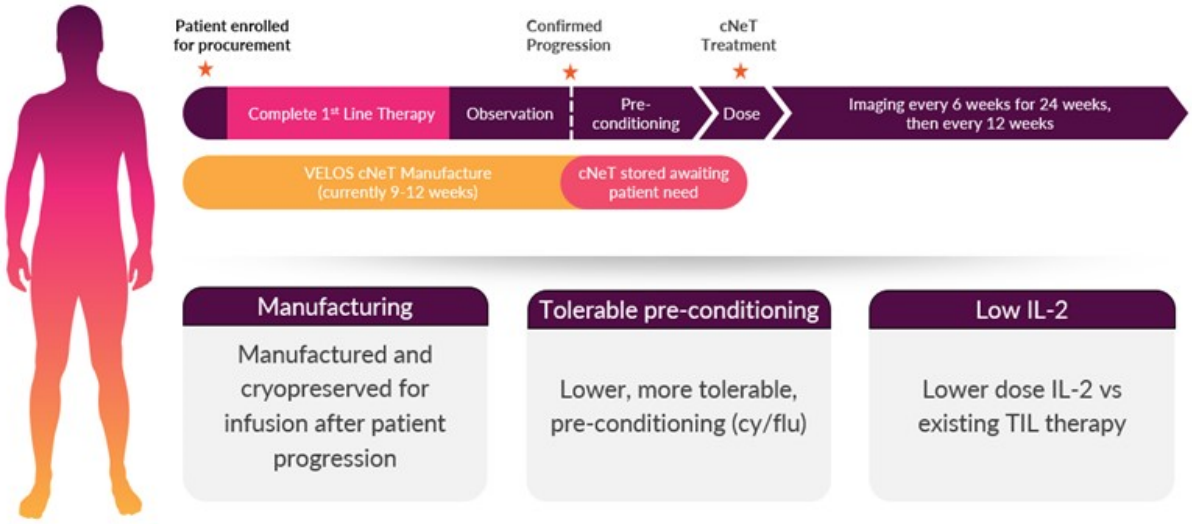
Our trial protocol allows us the option to include an additional cohort for each of CHIRON and THETIS to evaluate cNeT in combination with a PD-1 inhibitor (pembrolizumab in CHIRON and nivolumab in THETIS). We expect to report further patient data from both clinical trials in the second half of 2022.

As the first step in each of these trials, enrolled patients undergo procurement of tumor and blood samples to allow genetic characterization of the tumor and manufacture of the cNeT product candidate. Tissue procurement can occur prior to, during and after completion of standard systemic therapy, as depicted in the diagrams below. During the period between tissue procurement and final cNeT manufacture, patients can continue to be treated with standard of care therapy for their specific cancer. Once manufacture of the patient's specific cNeT is complete, it can be cryopreserved until required for administration.

cNeT treatment paradigm



The trial design of CHIRON and THETIS is illustrated below:



Our dosing regimen is based on experience across dosing of standard TIL, genetically modified T cell therapies and both anti-viral and anti-cancer therapies generated using dendritic cell co-culture systems. Compared to standard TIL therapy, we use lower doses of cyclophosphamide and IL-2, which we believe will be better tolerated in advanced NSCLC and metastatic or recurrent melanoma patients with co-morbidities. The ongoing Phase I/IIa clinical trials do not use a standard dose escalation design since, as a personalized cell therapy product, cNeT yields will vary from patient to patient. Instead, the maximum number of cNeT manufactured will be administered to each patient, within a 100-fold dose range of 1 x 10^7 –1x 10^9 cNeT.

Patients in both trials receive a non-myeloablative lymphodepleting regimen of cyclophosphamide (300mg/ m2/day) and fludarabine (30mg/m2/day), after which they receive their dose of cNeT, followed by ten daily subcutaneous injections of IL-2. Patients receive scans to assess tumor size every six weeks for the first six months, followed by scans every three months for the duration of the trial.

The primary endpoint of both trials is safety and tolerability. The secondary endpoints include change in tumor size from baseline, overall survival and objective response rate, disease control rate, time to response and progression-free

survival based on RECIST criteria. Depending on the results of our Phase I/II monotherapy trials, we plan to engage with the appropriate regulatory authorities to discuss potential pathways to registration. If we advance ATL001 for NSCLC or metastatic or recurrent melanoma in combination with a PD-1 inhibitor, we expect to conduct additional Phase II clinical trials before advancing to a Phase III registrational trial. Other exploratory translational science analyses will aid interpretation of the observed clinical data, addressing such questions as how dose, phenotype, functionality and engraftment kinetics may affect clinical outcomes.

Clinical Data for NSCLC and Melanoma

As of November 12, 2021, we have analyzed initial data from the first eight patients in the CHIRON and THETIS clinical trials, three patients with NSCLC and five with melanoma. Patients had received a median of 2.5 lines of therapy prior to receiving cNeT. All had progressive disease at the time of lymphodepletion prior to cNeT infusion and each patient has completed their first scheduled scan six weeks post-cNeT infusion to assess tumor size. The eight patients received a median dose of 14.2 x 10^6 cNeT, which is at the lower end of our prospectively targeted therapeutic dose range of 1 x 10^7 – 1 x 10^9 cNeT. Data from these eight patients has demonstrated a favorable cNeT tolerability profile, and provided encouraging initial evidence of cNeT engraftment. Based on observations from these data, we plan to increase the administered cNeT doses in our next series of monotherapy patients.

cNeT Tolerability

Overall, the tolerability profile of cNeTs was observed to be similar to that of standard TIL products that have not been enriched for cNeT reactivities, with the lymphodepletion regimen accounting for most of the observed higher-grade adverse events, being neutropenia, and febrile neutropenia/neutropenic sepsis and none of the higher-grade adverse events (grade 3 or 4) more commonly associated with the use of higher doses of interleukin-2 (IL-2). There were no suspected unexpected serious adverse reactions, or SUSARs reported since the previous update on the first six patients earlier in 2021. Overall, in the cohort there were three events of cytokine release syndrome and one immune effector cell-associated neurotoxicity syndrome, or ICANS, event deemed to be possibly related to cNeT treatment. A previously disclosed case of encephalopathy was subsequently deemed unlikely related to cNeT treatment following an Independent Data and Safety Monitoring Committee, or IDSMC, review.

We observed two neurological serious adverse events, or SAEs, that were deemed SUSARs related or possibly related to ATL001. The first was an instance of ICANS. The event was also deemed potentially related to IL-2. The patient was treated with dexamethasone and tocilizumab and their acute condition improved. The patient, however, subsequently died due to progression of the underlying cancer. The second SAE presented as a non-specific encephalopathy (grade 1), which led to hospitalization. The episode of encephalopathy responded to corticosteroids and the patient was discharged from the hospital. Two additional patients subsequently died due to progression of the underlying cancer. On January 4, 2021 a formal review of safety data from these first six patients was conducted by an IDSMC, to review the data from these first six patients. The IDSMC recommended that the two clinical trials should continue as planned with no required modifications.

After the patient experiencing the second SAE (non- specific encephalopathy) was discharged from the hospital, the SAE persisted with recurrence of symptoms on attempted withdrawal of steroids and parallel evidence of disease progression. Neurological symptoms worsened 109 days after administration of cNeT. The event was deemed a possible ICANS event. The patient also continued to experience disease progression and was ultimately put on end of life care and medical treatment was ceased, with the ICANS (grade 5) remaining unresolved at the time of death. We had two subsequent reviews of this case with the IDSMC (March 15, 2021 and April 12, 2021). The unanimous view of the committee was that it was unlikely that the neurotoxicity was caused by ATL001 based on the small number of cells infused, the limited early engraftment of cNeT, the late progression of the neurotoxicity beyond the time that engraftment was no longer detected, the lack of preferential expression of any of the cNeT target antigens in the brain and the lack of evidence of T cell-mediated neuropathology within the brain at post mortem. They recommended we continue both trials with no required modifications.

cNeT Activity

We observed stable disease at six-weeks post-dosing in five out of the eight patients and progressive disease in three patients. One patient had a reduction in the size of two of their four tumor lesions by approximately 55% and 90%, respectively. In 88% (7 of 8) of the cNeT products dosed, we observed tumor reactivity to individual patient-specific mutated peptides. In these seven products, the number of individual reactivities ranged from two to twenty-eight and cNeT were detected in the blood of 71% (5 of 7) of the patients following infusion at time points up to six weeks post dosing. It has been observed in prior studies of CAR-T cell therapies that engraftment and expansion of tumor-reactive T cells post infusion is correlated to clinical response. This correlation has not been evaluable with standard TIL therapies due to the lack of routine characterization of the active component of the infused cells, and the associated inability to track the active component post dosing. Since we characterize our cell product candidates at the level of individual cNeT reactivities, we are able to determine engraftment, peak expansion, and durability of persistence of clonal neoantigen-reactive T cells. We will continue to assess these features and any associations with clinical outcomes in subsequent patients that we plan to treat with higher cNeT doses.

Next Steps

Based on these initial results from the CHIRON and THETIS clinical trials and work from our product development laboratories, we submitted the necessary regulatory filings to use a modified manufacturing process incorporating additional cytokines that we believe will yield higher cNeT doses that we call VELOS Process 2. Enrollment of patients for the higher cNeT dose process commenced in the fourth quarter of 2021 in the UK. We expect initial data from patients dosed at these higher dose levels in the second half of 2022. In addition, we have received regulatory approval to open a combination cohort in the THETIS trial evaluating the addition of nivolumab (a PD-1 inhibitor) following cNeT infusion, and expect to begin patient dosing in the first half of 2022 with initial data expected in the second half of 2022.

Follow-On Indications

In addition to our two primary indications in advanced NSCLC and metastatic or recurrent melanoma, we are pursuing follow-on indications that include advanced HNSCC, RCC, TNBC and bladder cancer. Each of these indications is characterized by a high tumor and clonal mutational burden, high T cell infiltration into the tumor, readily accessible tumors, and high unmet medical need, which makes them attractive targets for our cNeT programs.

As with NSCLC and melanoma, we expect that these follow-on programs will allow for tumor procurement before or during the first line of systemic therapy for advanced disease, with cNeT manufacture during the treatment phase and delivery of the product upon disease progression.

Our investigational new drug application, or IND, for HNSCC was accepted by the FDA in January 2022 for VELOS Process 1 manufacturing and we expect to make additional submissions for our other earlier stage programs in the future.

Head and neck squamous cell carcinoma

In the U.S., there are approximately 67,000 new cases of HNSCC diagnosed and 15,000 deaths annually, with most cases being smoking related. The tumor mutational burden of HNSCC is similar to that of NSCLC, and it is typically an immunogenic tumor that is generally responsive to treatment with checkpoint inhibitors. As such, we believe that our cNeT therapy can be used to drive a robust anti-tumor response in this disease. Disease recurrence is very common and in this incurable setting, the first-line treatment consists of chemotherapy and checkpoint inhibitors. Following failure of first line therapy, approximately six months after starting treatment, there are few treatment options remaining.

Renal cell carcinoma

In the U.S., there are approximately 76,000 new cases and almost 14,000 deaths from RCC each year. RCC is a promising indication for a cNeT product as tumors have a very high TIL infiltration and a high proportion of the tumor

mutational load consists of mutations which are likely to lead to the generation of neoantigens. Despite recent advances in using immune checkpoint inhibitors in combination with a range of tyrosine kinase inhibitors as first line therapies, there still remains significant unmet need with few available treatment options for patients who progress from first-line therapies.

Triple negative breast cancer

In the U.S., there are approximately 284,000 diagnoses of invasive breast cancer each year of which approximately 11% are TNBC. TNBC is most often diagnosed in younger patients and is a more aggressive form of breast cancer with lower survival rates than other types of breast cancer. The high tumor mutational burden and TIL infiltration make it an attractive target for a cNeT therapy. In the metastatic setting, the PD-L1 inhibitor atezolizumab in combination with nab-paclitaxel is becoming an established first line standard of care, after which there are very few effective treatment options.

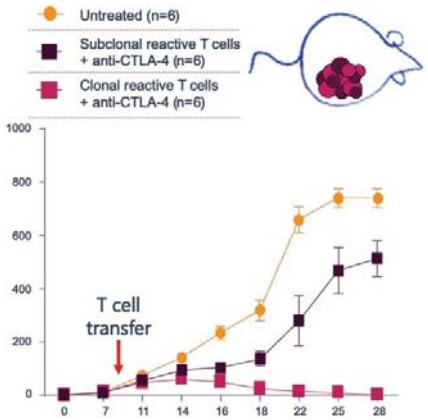
Bladder cancer

In the U.S., there are approximately 84,000 new cases and 17,000 deaths from bladder cancer each year. Bladder cancer has a similar clonal mutational burden to NSCLC and is responsive to CPIs. After decades with few new approved treatments for advanced bladder cancer, five CPIs have been approved since 2016. Originally approved in the second line treatment setting, they have now moved to the first line maintenance setting, leaving few treatment options following disease recurrence.

OUR PRECLINICAL STUDIES SUPPORTING THE SPECIFICITY AND FITNESS OF OUR cNeT PRODUCT CANDIDATES

To evaluate whether T cells targeting clonal neoantigens could generate a more complete and durable response than T cells targeting subclonal neoantigens, we used a melanoma mouse tumor model containing clonal and subclonal neoantigens. After tumor growth was visible, the mice were either left untreated or treated with T cells targeting the clonal or the subclonal neoantigen. We observed that the transfer of T cells targeting a subclonal neoantigen resulted in partial control of, or delayed, tumor growth with eventual relapse and tumor growth in all treated mice. In contrast, we observed that mice treated with T cells targeting a clonal neoantigen experienced a complete and durable response through to the completion of the study at day 28.

Clonal Neoantigen Targeting T Cell Therapies Led to Durable Complete Responses in Mouse Models of Cancer



Our goal is to deliver a cNeT product candidate with greater specificity to clonal neoantigens as well as higher functional T cell fitness as compared to standard TIL, in order to maximize tumor control. We have compared the specificity of standard TILs with cNeT derived from the same patient, and demonstrated the potential of cNeT to better recognize and target clonal neoantigens compared to CD8+ and CD4+ T cells generated with the standard TIL.

We observed that more than 80% of cNeT recognized the clonal neoantigens from the patient's tumor while less than 30% of CD8+ TILs recognized those same antigens. Importantly, approximately 60% of the CD4+ cNeT recognized clonal neoantigens while none of the standard TIL CD4+ T cells recognized these same clonal neoantigens. We believe these data support the potential of our process to generate a product candidate that is enriched for CD8+ and CD4+ T cells that recognize clonal neoantigens as compared to standard TIL.

cNeT Process Delivered Higher Clonal Reactivity than Standard TIL Therapy

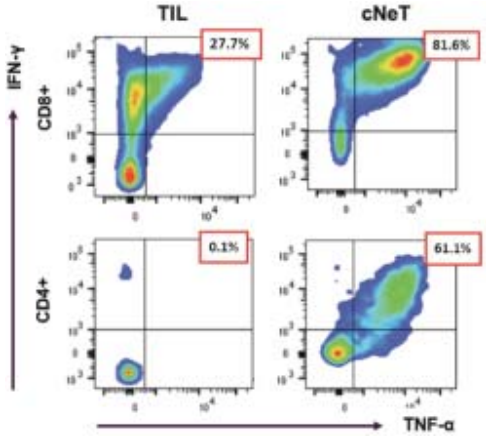


FIGURE A

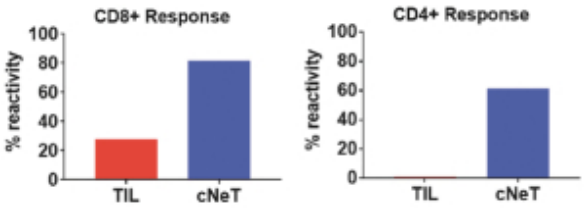


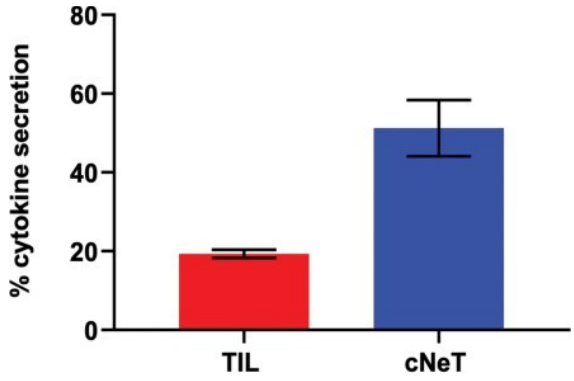
FIGURE B

Figure A is a flow cytometric analysis depicting the ability of cNeT to produce IFN-g and TNF-a, which are accepted T cell activation markers. Figure B represents the percentage of IFN-g and TNF-a produced by CD8+ and CD4+ T cells.

Separately, we assessed T cell fitness using T cell receptor independent polyclonal stimulation of the cNeT and standard expanded TIL product candidate. By stimulating T cells with anti-CD3, all the T cells in the assay were tested for their maximal capacity to produce effector cytokines, regardless of their reactivity. This assay is widely used by academics and industry to test overall activity of T cells.

The data below depicts the potential of cNeT to outperform standard TIL cells in the production of effector cytokines, which we believe support improved fitness of our cNeT.

cNeT Produced Higher Amounts of Effector Cytokines than Standard TILs



Material Acquisition Platform

Our Material Acquisition Platform, or MAP, network is our proprietary network for collection of donor tumor tissue and blood from cancer patients. We created, and are continuing to grow, our MAP network as a strategic asset to

secure continued access to patient tumor and blood samples which are procured from patients undergoing standard-of-care cancer surgery across multiple solid tumor indications. The samples accessed through our MAP network are used in the development of our VELOS process and the expansion of the PELEUS database. In addition, our MAP network provides access to patient samples from multiple additional tumor types that can inform the basis of our future pipeline development. Our MAP network also acts to improve our supply chain operations with respect to interventional studies, by identifying and building non-standard site pathways for patient access and transportation pathways from procurement centers to our manufacturing facilities and back to patients.

Our network of MAP sites also provides an opportunity to procure and archive cancer samples from patients earlier in their treatment pathway, for example when surgery is undertaken for curative treatment in patients determined to be at high risk of future relapse. Archived tumor samples and TIL intermediates have the potential to be partially processed and then stored until the patient experiences disease progression, at which point cNeT manufacture could be completed and the final therapy supplied. This potentially provides an additional pathway to shorten the effective supply time of our cNeT in the event of a patient's disease progression, and would offer patients a more rapidly available, customized treatment option. Furthermore, by procuring tumor samples earlier in the patient treatment pathway and prior to exposure to multiple lines of therapy, we believe these samples have the potential to yield T cells of both higher fitness and quantity. The ability to collect tumor samples earlier in the treatment paradigm also allows us to explore the potential for cNeT in earlier lines of therapy in future.

Our MAP network has delivered more than 100 samples from 14 active sites in the UK, EU and U.S., with 25 tumor procurement channels, in 6 tumor indications including lung, melanoma, head and neck, renal, bladder and breast. We refer to each tumor type that can be collected at a site as a separate procurement channel so one site provides either one or multiple procurement channels. This material will be used to enable potential Clinical Trial Application and IND filings for these indications.

OUR CURRENT MANUFACTURING CAPACITY AND EXPANSION PLANS

Recognizing the strategic importance of manufacturing to the development and commercial success of our personalized cell therapy approach, we continue to take steps to scale-up and expand our capabilities in this regard.

We have secured dedicated manufacturing capacity to support our clinical trials at two UK sites: The Royal Free Hospital and the Cell and Gene Therapy Catapult. The Royal Free Hospital (Centre for Cell, Gene and Tissue Therapeutics) is an MHRA-licensed facility for the manufacture of investigational medicinal products and holds a Human Tissue Authority license for the import and storage of cells and tissues. The manufacturing agreement provides services that include quality management systems, qualified persons for product release, quality control labs and GMP storage. In September 2020, we entered into agreements with UCL for office and lab space on the Royal Free Campus to support both GMP development and translational science operations.

In March 2020, we entered into a collaboration agreement with Cell Therapy Catapult Limited, or Catapult, pursuant to which we lease a manufacturing space from Catapult at the Cell and Gene Therapy Catapult Manufacturing Centre in Stevenage and pay Catapult to support GMP operations at the manufacturing facility. Activities for licensing this site are ongoing and we anticipate the site being licensed in the second quarter of 2022.

Additionally, we lease a warehouse in west London, where we expect to construct a flexible GMP modular facility, to scale our manufacturing footprint where modular cleanrooms can be brought online in a phased approach. We expect the fully controlled facility to support in-house capability for peptide manufacture and supply that we believe will reduce cost of goods and shorten manufacturing times. The modular facility is intended to support our registration trials, commercial supply for Europe and provide the optionality to support U.S. operations. Over time, we will establish further regional manufacturing facilities.

Through the continued strategic expansion of our manufacturing footprint across multiple sites, we plan to scale up capacity from 50 cNeT doses per year in 2021 to 1,250 doses per year by 2026 to supply our clinical trials through to registration of our lead programs. Our ultimate aim is to be able to supply thousands of doses of commercial product annually.

Future Strategy for Automation

Automation will enable improvements to our manufacturing success rate, a reduction in operator dependencies and related costs and will support the industrial scale-up of GMP operations. Additionally, the custom devices that support a fully-closed process, while further reducing high operating costs associated with open processes, enable the potential for new intellectual property and security of the manufacturing process and know-how. We have developed a roadmap for automation by focusing on several key areas across the end-to-end manufacturing process to drive the future commercial delivery of cNeT. Some of the key initiatives in our automation strategy include:

- **Tumor collection and processing device:** We are developing a closed system to process patient tumor samples. This system is designed to be utilized for procurement of the tumor sample at the time of surgery and delivered to the manufacturing site. We believe this will increase sample throughput and minimize operator variability, while decreasing the time required to process samples. Additionally, this closed system approach allows manufacturing in a simpler and lower cost cleanroom environment.

- **Automation for co-culture:** We are evaluating different fully closed bioreactor systems to be used in the industrial manufacturing process of our cNeT. These bioreactors will enable us to reduce costs through higher output and fewer manual operations. Our goal is to utilize these bioreactors to increase cell yield through optimized cell feeding methods enabled through real time monitoring of cell cultures.

We have entered into and are evaluating several strategic partnerships to support the development of automation and devices to deliver an industrial manufacturing process.

TRANSLATIONAL SCIENCE PROGRAM

We believe that by prospectively targeting identified clonal neoantigens, we have a unique opportunity to more fully characterize cNeT at the product and single cell level, providing a detailed understanding of their kinetics and function in patients and potential association to clinical responses. We have built a Translational Science Program, or TSP, that is run in parallel with our clinical studies and is designed to allow us to better understand specific features of our cNeT and their mechanism of action.

We collect samples to analyze each patient's TME prior to cNeT manufacturing, as well as the manufactured cNeT including dose, number of reactivities, immune phenotype and specific T cell receptor sequences. Upon administration into the patient, we will track cNeT engraftment, expansion, phenotype, activity and transcriptional profile. In parallel to tracking cNeT, we will also evaluate circulating tumor DNA as a liquid biomarker of tumor burden.

The increasingly detailed molecular understanding of cNeT and their mechanism of action in patients will further inform and control the development of next generations of our VELOS manufacturing process by focusing on functional fitness, anti-cancer activity and safety as well as alternative starting material for cNeT manufacture (e.g., blood). By using blood as a starting material, we aim to provide patient optionality and broaden patient access and supply for those patients where tumor collection by surgery may not always be possible.

COMMERCIALIZATION

At our current stage of development, we have not yet established a commercial organization or distribution capabilities. We are developing our clinical-stage programs for the treatment of patients with late-stage solid tumors, most of whom are treated in specialized treatment centers or hospitals. We aim to use selected centers to pilot and establish systems necessary for product delivery by the time of launch. By focusing on these centers, we can begin to build our commercialization capabilities with limited resources.

We have worldwide commercial rights for our potential products. We currently plan to build our global commercialization capabilities internally over time such that we are able to commercialize any product candidate for which we may obtain regulatory approval. We may selectively pursue strategic collaborations with third parties in order to maximize the commercial potential of our product candidates. We generally expect to launch any of our

products that receive regulatory approval in the United States first, followed by the European Union, and then in other major markets.

COMPETITION

There is significant investment across the biotechnology and pharmaceutical industries in developing novel and proprietary therapies for the treatment of cancer. While we believe that our differentiated, precision and scientific expertise in the field of cancer immunotherapy provides us with competitive advantages, we face potential competition from various sources, including larger and better-funded pharmaceutical, specialty pharmaceutical and biotechnology companies, as well as from academic institutions, governmental agencies and public and private research institutions. We anticipate that we will face intense and increasing competition as new drugs and therapies enter the market and advanced technologies become available.

Advanced T cell therapies are under evaluation in solid tumors by multiple biotechnology and pharmaceutical companies, including Kite Pharma Inc. (a Gilead company), Iovance Biotherapeutics Inc., or Iovance, Adaptimmune Therapeutics PLC, Autolus Therapeutics PLC, Instil Bio, Inc., or Instil, Pact Pharma, Inc., Neogene Therapeutics, B.V., BioNTech SE, Turnstone Biologics Corp., Genocea Biosciences, Inc., Obsidian Therapeutics, Inc. and KSQ Therapeutics, Inc. In particular, Iovance and Instil are developing TIL therapies for treatment of various cancers, including melanoma, which will compete directly with our product candidate, ATL001, in the relevant indication.

We cannot predict whether new types of immunotherapies including novel checkpoint inhibitors may be enhanced and show greater efficacy, and we may have direct and substantial competition from such immunotherapies in the future. In addition, more effective small molecules, cancer vaccines and other approaches may be developed and used as first line or second line treatments, which would reduce the opportunity for our T cell therapies.

Many of our competitors, either alone or with their strategic collaborators, have substantially greater financial, technical and human resources than we do. Accordingly, our competitors may be more successful than we are in obtaining approval for treatments and achieving widespread market acceptance and may render our treatments obsolete or non-competitive. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of our competitors. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical study sites and patient registration for clinical studies, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

We anticipate that we will face intense and increasing competition as new products and therapies enter the market and advanced technologies become available. We expect any treatments that we develop and commercialize to compete on the basis of, among other things, efficacy, safety, delivery, price and the availability of reimbursement from government and other third-party payers.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive or better reimbursed than any products that we may commercialize. Our competitors also may obtain FDA, EMA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position for either their product or a specific indication before we are able to enter the market.

LICENSE AGREEMENT WITH CANCER RESEARCH TECHNOLOGY LIMITED

In May 2016, we entered into a License Agreement, or the License Agreement, with Cancer Research Technology Limited, or CRT, pursuant to which we obtained access rights to intellectual property and know-how from the TRACERx Study. Under the License Agreement, we were granted an exclusive, sublicensable license to the TRACERx patents and bioinformatic data for use in: (i) the therapeutic field of neoantigen cell therapies and adoptive cell transfer; and (ii) the neoantigen diagnostic field, for use in research and the potential development of products for commercialization. We were further granted, during the vaccine option period, an exclusive license to the TRACERx

patents and the bioinformatic data in the private neoantigen therapeutic vaccine field for research and development but not in the development of products for commercial sale, and a non-exclusive license to the same in the public neoantigen therapeutic vaccine field. We also obtained a non-exclusive license to the TRACERx bioinformatic pipeline, patient sequencing and medical data, know-how, and materials.

CRT additionally granted us certain rights to new patent applications filed by the Founding Institutions in respect of inventions resulting from the TRACERx study through February 2023, including automatic exclusive licenses to patent rights relating to non-severable improvements of technology covered by the original TRACERx patents and non-exclusive rights to severable improvements. CRT granted us the right of first negotiation to license certain patents rights generated by our founders outside of the TRACERx study which relate to the licensed technology.

In July 2017, we obtained a non-exclusive license to the LOHHLA patent under the License Agreement. In October 2018, we obtained an exclusive license to the LOHHLA patent under an addendum to the License Agreement. Under the License Agreement, we hold an option to exploit products in the therapeutic vaccine field, or the Vaccine Option. In March 2021, we extended the Vaccine Option from May 2021 to May 2023 with a payment of less than £0.1 million or $0.1 million.

In May 2018, we entered into an amendment to the License Agreement that created an additional sample period through July 2020 and specified additional patient tumor and blood materials to be subject to the License Agreement related to the immunology side study. The License Agreement was subsequently amended in July 2020, November 2020 and March 2021.

Upon execution of the License Agreement, we granted CRT 396,125 B ordinary shares and 67,793 C ordinary shares. The C ordinary shares granted to CRT were forfeited and transferred to the deferred shares during the year ended December 31, 2019, as the applicable performance conditions were not met. The B ordinary shares granted to CRT were converted into ordinary shares upon IPO. We recorded $0.3 million of IP research and development expense in 2016. We are obligated to pay CRT milestone success payments up to an aggregate of £6.5 million for therapeutic products, and milestone success payments up to an aggregate £0.8 million for non-therapeutic products, as well as sub-single digit to low-single digit percentage royalty on net sales of products that utilize the licensed intellectual property, subject to certain customary reductions. The royalty obligations continue on a product-by-product and country-by-country basis until the later of: (i) the date there ceases to be a valid patent claim covering such product in the country in which it is sold; or (ii) with respect to contribution royalty products, ten years from the first commercial sale of the product, and with respect to a patent royalty product, five years from the first commercial sale of the product. On a product-by-product basis, we may also elect to provide other cash consideration at fair market value and forgo the milestone or royalty payment.

Unless terminated earlier, the term of the agreement continues until the later of the expiration of the royalty term in each country and such time as no further milestone payments are due, and upon such termination, the licenses granted shall become fully-paid, royalty-free, irrevocable, and perpetual. We have the right to terminate the license agreement for convenience in its entirety upon 90 days' notice. Each party may terminate the agreement if the other party is in material breach subject to a 90 day remedy period. We have the right to acquire ownership of the TRACERx patents upon either: (i) the occurrence of a royalty product for use in the therapeutic field; (ii) CRT shareholders cease to hold any of our ordinary shares; (iii) we undergo an initial public offering; or (iv) we are acquired by a third party for more than £25.0 million. Upon IPO, we gave notice to CRT to exercise the option to acquire the TRACERx patents with no consideration in accordance with the terms of the License Agreement. The acquisition was not finalized as of December 31, 2021.

INTELLECTUAL PROPERTY

Our success depends, in part, on our ability to obtain and maintain intellectual property protection for our product candidates, technology and know-how, to defend and enforce our intellectual property rights, in particular, our patent rights, to preserve the confidentiality of our know-how and trade secrets, and to operate without infringing the proprietary rights of others. We seek to protect our product candidates and technologies by, among other methods, filing U.S. and foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development of our business. We also rely on trade secrets, know-how, continuing technological innovation and in-licensing of third-party intellectual property to develop and maintain our proprietary position. We,

or our collaborators and licensors, file patent applications directed to our key product candidates in an effort to establish intellectual property positions to protect our product candidates as well as processes for producing our product candidates and uses of our product candidates for the prevention and/or treatment of diseases.

With regard to ATL001, we in-license from Cancer Research Technology Limited, or CRT, a family of pending patent applications and granted patents with claims directed to a method of treating cancer, including non-small cell lung cancer and melanoma, and claims directed to a T cell composition comprising a CAR-T or TCR-T that binds a clonal neoantigen that includes three pending U.S. patent applications, one granted EP patent, one granted Singapore patent and 21 foreign patent applications pending in various jurisdictions such as Australia, Europe, Canada, China, Japan and South Korea. Patent applications in this family, if issued, are expected to expire in 2036 without giving effect to any potential patent term extensions and patent term adjustments and assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees.

With regards to ATL001, we own a pending international (PCT) patent application filed at the European Patent Office, or EPO, with claims directed to treatment regimens for using T cell therapy in combination with a specific cytokine in the treatment of cancer. If a patent were to issue from a national/regional patent application derived from this international patent application, such a patent would be expected to expire in 2041, without giving effect to any potential patent term extensions and patent term adjustments and assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees.

We also in-license from CRT a family of pending patent applications with claims directed to a method for determining the loss of an HLA allele in a tumor, which is referred to as the "LOHHLA" bioinformatics tool, which enables prediction of neoantigens that are presented by an HLA molecule that has not been lost by the tumor, and hence are still available for targeting by immunotherapy, and methods of treating cancer by targeting neoantigens that are predicted to be presented by an HLA molecule that has not been lost from the tumor, which family includes a pending U.S. patent application and eight foreign patent applications pending in various jurisdictions, namely Australia, Canada, China, Europe, Hong Kong, India, Russia and Japan. Patent applications in this family, if issued, are expected to expire in 2038 without giving effect to any potential patent term extensions and patent term adjustments and assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees.

We own a pending international (PCT) patent application filed at the EPO, with claims directed to a tumor sample collection and disaggregation device. If a patent were to issue from a national/regional patent application derived from this international patent application, such a patent would be expected to expire in 2041, without giving effect to any potential patent term extensions and patent term adjustments and assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees.

We own a pending patent application filed in Great Britain at the UK Intellectual Property Office, or UKIPO, with claims directed to a method of determining whether a tumor-specific mutation is likely to be clonal in a subject. If a patent were to issue from a patent application claiming priority from this Great Britain patent application, such a patent would be expected to expire in 2042 (provided it is timely filed in 2022), without giving effect to any potential patent term extensions and patent term adjustments and assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees.

We own a pending patent application filed in Great Britain at the UKIPO with claims directed to a batch release assay for a pharmaceutical product comprising T cells. If a patent were to issue from a patent application claiming priority from this Great Britain patent application, such a patent would be expected to expire in 2042 (provided it is timely filed in 2022), without giving effect to any potential patent term extensions and patent term adjustments and assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees.

We own a pending patent application filed in Great Britain at the UKIPO with claims directed to a method of producing a population of T cells which comprises antigen-specific T cells. If a patent were to issue from a patent application claiming priority from this Great Britain patent application, such a patent would be expected to expire in 2042 (provided it is timely filed in 2022), without giving effect to any potential patent term extensions and patent term adjustments and assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees.

We own a pending patent application filed in Great Britain at the UKIPO with claims directed to a blood collection device. If a patent were to issue from a patent application claiming priority from this Great Britain patent application, such a patent would be expected to expire in 2042 (provided it is timely filed in 2022), without giving effect to any potential patent term extensions and patent term adjustments and assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees.

GOVERNMENT REGULATION

The FDA and other U.S. regulatory authorities at federal, state, and local levels, as well as in foreign countries, extensively regulate, among other things, the research, development, testing, manufacture, quality control, import, export, safety, effectiveness, labeling, packaging, storage, distribution, record keeping, approval, advertising, promotion, marketing, post-approval monitoring, and post-approval reporting of biological product candidates such as those we are developing. We, along with third-party contractors, will be required to navigate the various preclinical, clinical and commercial approval requirements of the governing regulatory agencies of the countries in which we wish to conduct studies or seek approval or licensure of our product candidates. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources.

U.S. Biological Products Development Process

In the United States, biological products are subject to regulation under the Federal Food, Drug, and Cosmetic Act, or FDC Act, the Public Health Service Act, or PHS Act, and other federal, state, local and foreign statutes and regulations. The process required by the FDA before a biological product candidate may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests and animal studies performed in accordance with FDA's good laboratory practice, or GLP, requirements and applicable requirements for the humane use of laboratory animals or other applicable regulations;

- submission to the FDA of an application for an IND which must become effective before human clinical trials may begin;

- approval of the protocol and related documentation by an independent institutional review board, or IRB, or ethics committee at each clinical trial site before each study may be initiated;

- performance of adequate and well-controlled human clinical trials according to the FDA's good clinical practice, or GCP, requirements and any additional requirements for the protection of human research subjects and their health information, to establish the safety, purity, and potency of the proposed biological product candidate for its intended use;

- preparation and submission to the FDA of a biologic license application, or BLA, after completion of all pivotal clinical trials that includes substantial evidence of safety, purity, and potency from results of nonclinical testing and clinical trials;

- satisfactory completion of an FDA pre-license inspection of the manufacturing facility or facilities where the biological product is produced to assess compliance with cGMP requirements to assure that the facilities, methods and controls are adequate to preserve the biological product's identity, strength, quality and purity and, if applicable, the FDA's current good tissue practices, or cGTPs, for the use of human cellular and tissue products;

- satisfactory completion of an FDA Advisory Committee review, if applicable;

- a determination by the FDA within sixty (60) days of its receipt of a BLA to file the application for review;

- potential FDA audit of selected nonclinical study and clinical trial sites that generated the data in support of the BLA to assess compliance with GLP or GCP, as applicable;

- payment of user fees for FDA review of the BLA (unless a fee waiver applies); and

- FDA review and approval, or licensure, of the BLA to permit commercial marketing of the product for particular indications for use in the United States.

Before testing any biological product candidate in humans, the product candidate enters the preclinical testing stage. Preclinical tests, also referred to as nonclinical studies, include laboratory evaluations of product biological characteristics, chemistry, toxicity and formulation, as well as animal studies to assess the potential safety and activity of the product candidate. The conduct of the preclinical tests must comply with federal regulations and requirements including GLPs.

The clinical trial sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. Some preclinical testing may continue even after the IND is submitted. An IND is a request for authorization from the FDA to ship an unapproved, investigational product in interstate commerce and to administer it to humans, and must become effective before clinical trials may begin.

The IND automatically becomes effective thirty (30) days after receipt by the FDA, unless the FDA places the clinical trial on a clinical hold within that thirty (30)-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA also may impose clinical holds on a biological product candidate at any time before or during clinical trials due to, among other considerations, unreasonable or significant safety concerns, inability to assess safety concerns, lack of qualified investigators, a misleading or materially incomplete investigator brochure, study design deficiencies, interference with the conduct or completion of an a study designed to be adequate and well-controlled for the same or another investigational product, insufficient quantities of investigational product, lack of effectiveness, or non-compliance. If the FDA imposes a clinical hold, studies may not recommence without FDA authorization and then only under terms authorized by the FDA.

Clinical trials involve the administration of the biological product candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the study sponsor's control. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety, including stopping rules that assure a clinical trial will be stopped if certain adverse events should occur. Each protocol and any amendments to the protocol must be submitted to the FDA as part of the IND. Clinical trials must be conducted and monitored in accordance with the FDA's regulations comprising the GCP requirements, including the requirement that all research subjects provide informed consent. Further, each clinical trial and its related documentation must be reviewed and approved by an Institutional Review Board, or IRB, at or servicing each site at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of study participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the form and content of the informed consent that must be signed by each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed.

Clinical trials typically are conducted in three sequential phases that may overlap or be combined:

- Phase 1. The biological product candidate is initially introduced into healthy human subjects and tested for safety. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients. These studies are designed to test the safety, dosage tolerance, absorption, metabolism and distribution of the biological product candidate in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence of effectiveness.

- Phase 2. The biological product candidate is evaluated in a limited patient population with a specific disease or condition to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance, optimal dosage and dosing schedule. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.

- Phase 3. The biological product candidate is administered to an expanded patient population to further evaluate dosage, clinical efficacy, potency, and safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the product candidate and provide an adequate basis for approval and product labeling.

In some cases, the FDA may require, or companies may voluntarily pursue, additional clinical trials after a biological product is approved to gain more information about the product. These post-approval clinical trials, sometimes referred to as Phase 4 clinical trials, may also be made a condition to approval of the BLA. Failure to exhibit due diligence with regard to conducting required Phase 4 clinical trials could result in withdrawal of approval for products.

Concurrent with clinical trials, companies usually complete additional animal studies and also must develop additional information about the physical characteristics of the biological product as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. To help reduce the risk of the introduction of adventitious agents with use of biological products, the PHS Act emphasizes the importance of manufacturing control for products whose attributes cannot be precisely defined. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the sponsor must develop methods for testing the identity, strength, quality, potency and purity of the final biological product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the biological product candidate does not undergo unacceptable deterioration over its shelf life.

During all phases of clinical development, the FDA requires extensive monitoring and auditing of all clinical activities, clinical data, and clinical trial investigators. Annual progress reports detailing the results of the clinical trials must be submitted to the FDA. Written IND safety reports must be promptly submitted to the FDA and the investigators for serious and unexpected adverse events, any findings from other studies, tests in laboratory animals or *in vitro* testing that suggest a significant risk for human subjects, or any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must submit an IND safety report within fifteen (15) calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information. Regulatory authorities, the IRB or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk or that the trial is unlikely to meet its stated objectives. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as an Independent Data Safety and Monitoring Committee, or IDSMC, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. There are also requirements governing the reporting of ongoing clinical studies and clinical study results to public registries.

U.S. Review and Approval Processes

After the completion of clinical trials of a biological product candidate, FDA approval of a BLA must be obtained before commercial marketing of the biological product. The BLA must include results of product development, laboratory and animal studies, human studies, information on the manufacture and composition of the product, proposed labeling and other relevant information.

Within sixty (60) days following submission of the application, the FDA reviews a BLA submitted to determine if it is substantially complete before the FDA accepts it for filing. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission and may request additional information. In this event, the BLA must be resubmitted with the additional information. The resubmitted application also is subject to review

before the FDA accepts it for filing. In most cases, the submission of a BLA is subject to a substantial application user fee, although the fee may be waived under certain circumstances. Under the performance goals and policies implemented by the FDA under the Prescription Drug User Fee Act, or PDUFA, for original BLAs, the FDA targets ten months from the filing date in which to complete its initial review of a standard application and respond to the applicant, and six months from the filing date for an application with priority review. Therefore, the BLA review process typically takes twelve (12) months from the date the application is submitted to the FDA because the FDA has approximately two months to make a "filing" decision. The FDA does not always meet its PDUFA goal dates, and the review process is often significantly extended by FDA requests for additional information or clarification. For example, the review process and the PDUFA goal date may be extended by three months if the FDA requests or the BLA sponsor otherwise provides additional information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date.

Once the submission is accepted for filing, the FDA begins an in-depth substantive review of the BLA. The FDA reviews the BLA to determine, among other things, whether the proposed product is safe and potent, or effective, for its intended use, and has an acceptable purity profile, and whether the product is being manufactured in accordance with cGMP to assure and preserve the product's identity, safety, strength, quality, potency and purity. The FDA may refer applications for novel biological products or biological products that present difficult or novel questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

During the BLA review process, the FDA also will determine whether a risk evaluation and mitigation strategy, or REMS, is necessary to assure the safe use of the biological product candidate. A REMS is a safety strategy implemented to manage a known or potential serious risk associated with a product and to enable patients to have continued access to such medicines by managing their safe use, and could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. If the FDA concludes a REMS is needed, the sponsor of the BLA must submit a proposed REMS; the FDA will not approve the BLA without a REMS, if required.

Before approving a BLA, the FDA typically will inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. For a cell therapy product that includes human cells, tissues or tissue-based products, or HCT/Ps, which are human cells or tissue intended for implantation, transplant, infusion, or transfer into a human recipient, the FDA also will not approve the product if the manufacturer is not in compliance with cGTPs. These are FDA regulations that govern the methods used in, and the facilities and controls used for, the manufacture of HCT/Ps. The primary intent of the cGTP requirements is to ensure that cell and tissue based products are manufactured in a manner designed to prevent the introduction, transmission and spread of communicable disease. FDA regulations also require tissue establishments to register and list their HCT/Ps with the FDA and, when applicable, to evaluate donors through appropriate screening and testing. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure that the clinical trials were conducted in compliance with IND study requirements and GCP requirements. To assure cGMP, cGTP and GCP compliance, an applicant must incur significant expenditure of time, money and effort in the areas of training, record keeping, production and quality control.

Under the Pediatric Research Equity Act, or PREA, a BLA or supplement to a BLA for a novel product (e.g., new active ingredient, new indication, etc.) must contain data to assess the safety and effectiveness of the biological product for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers for PREA requirements. Unless otherwise required by regulation, PREA does not apply to any biological product for an indication for which orphan designation has been granted.

Notwithstanding the submission of relevant data and information, the FDA may ultimately decide that the BLA does not satisfy its regulatory criteria for approval and deny approval. If the FDA decides not to approve the BLA in its present form, the FDA will issue a Complete Response letter that usually describes all of the specific deficiencies in the BLA identified by the FDA. The deficiencies identified may be minor, for example, requiring labeling changes,

or major, for example, requiring additional clinical trials. Additionally, the Complete Response letter may include recommended actions that the applicant might take to place the application in a condition for approval. If a Complete Response letter is issued, the applicant may either resubmit the BLA, addressing all of the deficiencies identified in the letter, or withdraw the application.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, including to subpopulations of patients, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings precautions or interactions be included in the product labeling. The FDA may impose restrictions and conditions on product distribution, prescribing, or dispensing in the form of a REMS, or otherwise limit the scope of any approval. In addition, the FDA may require post marketing clinical trials, sometimes referred to as Phase 4 clinical trials, designed to further assess a biological product's safety and effectiveness, and testing and surveillance programs to monitor the safety of approved products that have been commercialized.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a biological product intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making a biological product available in the United States for this type of disease or condition will be recovered from sales of the product. Orphan product designation must be requested before submitting a BLA. After the FDA grants orphan product designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

Orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications, including a full BLA, to market the same biological product for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity, or if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. Competitors, however, may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity.

A designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or, as noted above, if a second applicant demonstrates that its product is clinically superior to the approved product with orphan exclusivity or the manufacturer of the approved product is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

Expedited Development and Review Programs

The FDA offers various programs, including fast track designation, breakthrough therapy designation, accelerated approval, priority review and regenerative medicine advanced therapy, or RMAT, designation, that are intended to expedite or simplify the process for the development and FDA review of biological products that are intended for the treatment of serious or life-threatening diseases or conditions. To be eligible for fast track designation, biological product candidates must be intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a biological product candidate may request the FDA to designate the biologic as a fast track product at any time during the clinical development of the product. The sponsor of a fast track product has opportunities for more frequent interactions with the applicable FDA review team during product development and, once a BLA is submitted, the product candidate may be eligible

for priority review. A fast track product may also be eligible for rolling review, where the FDA may consider for review sections of the BLA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the BLA, the FDA agrees to accept sections of the BLA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the BLA.

Under the FDA's Breakthrough Therapy program, a biological product candidate may be eligible for breakthrough therapy designation if it is intended to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product candidate, alone or in combination with one or more other drugs or biologics, may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Breakthrough therapy designation provides all the features of fast track designation in addition to intensive guidance on an efficient development program beginning as early as Phase 1, and FDA organizational commitment to expedited development, including involvement of senior managers and experienced review staff in a cross-disciplinary review, where appropriate.

Any marketing application for a biological product submitted to the FDA for approval, including a product candidate with a Fast Track designation and/or Breakthrough Therapy Designation, may be eligible for other types of FDA programs intended to expedite the FDA review and approval process, such as priority review and accelerated approval. Any product candidate is eligible for priority review if it is designed to treat a serious or life-threatening disease or condition, and if approved, would provide a significant improvement in safety or effectiveness compared to available alternatives for such disease or condition. The FDA will attempt to direct additional resources to the evaluation of an application for a biological product candidate designated for priority review in an effort to facilitate the review. Under priority review, the FDA's goal is to review an application within six months of the 60-day filing date, compared to ten months for a standard review.

Additionally, FDA may grant accelerated approval to a product candidate intended to treat a serious or life- threatening disease or condition upon a determination that the product has an effect on 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. As a condition of approval, the FDA may require that a sponsor of a biological product receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. Products receiving accelerated approval may be subject to expedited withdrawal procedures if the sponsor fails to conduct the required post-marketing studies or if such studies fail to verify the predicted clinical benefit. In addition, the FDA generally requires, unless otherwise informed by the agency, pre-approval of promotional materials for products receiving accelerated approval, which could adversely impact the timing of the commercial launch of the product.

In 2017, the FDA established a new RMAT designation as part of its implementation of the 21st Century Cures Act. The RMAT designation program is intended to fulfill the 21st Century Cures Act requirement that the FDA facilitate an efficient development program for, and expedite review of, any biological product that meets the following criteria: (i) the biological product qualifies as a RMAT, which is defined as a cell therapy, therapeutic tissue engineering product, human cell and tissue product, or any combination product using such therapies or products, with limited exceptions; (ii) the biological product is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition; and (iii) preliminary clinical evidence indicates that the biological product has the potential to address unmet medical needs for such a disease or condition. RMAT designation provides all the benefits of breakthrough therapy designation, including more frequent meetings with the FDA to discuss the development plan for the product candidate and eligibility for rolling review and priority review. Product candidates granted RMAT designation may also be eligible for accelerated approval on the basis of a surrogate or intermediate endpoint reasonably likely to predict long-term clinical benefit, or reliance upon data obtained from a meaningful number of clinical trial sites, including through expansion of trials to additional sites.

Fast track designation, breakthrough therapy designation, priority review, accelerated approval, and RMAT designation do not change the standards for approval but may expedite the development or approval process. Even if a product candidate qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Post-Approval Requirements

Rigorous and extensive FDA regulation of biological products continues after approval, particularly with respect to cGMP. Biologic manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP, which impose certain procedural and documentation requirements. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP that may affect the identity, potency, purity, or safety of a marketed product, and FDA also imposes reporting requirements. Manufacturers and other parties involved in the drug supply chain for prescription drug products must also comply with product tracking and tracing requirements and for notifying the FDA of counterfeit, diverted, stolen and intentionally adulterated products or products that are otherwise unfit for distribution in the United States. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance. Following approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual program fees for any marketed products. Other post-approval requirements applicable to biological products, include, among other things, record-keeping requirements, reporting of adverse effects, reporting updated safety and efficacy information, and complying with electronic record and signature requirements.

In addition, after a BLA is approved, the product also may be subject to official lot release. As part of the manufacturing process, the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official release by the FDA, the manufacturer submits samples of each lot of product to the FDA together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot.

Discovery of previously unknown problems or the failure to comply with the applicable regulatory requirements may result in restrictions on the marketing of a product or withdrawal of the product from the market as well as possible civil or criminal sanctions. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant or manufacturer to administrative or judicial civil or criminal sanctions and adverse publicity. FDA sanctions could include refusal to approve pending applications, withdrawal of an approval, clinical holds, warning or untitled letters, product recalls, product seizures, safety alerts, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, mandated corrective advertising or communications with doctors or other stakeholders, debarment, restitution, disgorgement of profits, or civil or criminal penalties.

In addition, the FDA closely regulates the marketing, labeling, advertising and promotion of biological products. A company can make only those claims relating to safety and efficacy, purity and potency that are approved by the FDA and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available products for uses that are not described in the product's labeling and that differ from those tested and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products.

U.S. Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of the FDA approval of the use of our biological product candidates, some of our U.S. patents may be eligible for limited patent term extension under the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of fourteen (14) years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of a BLA plus the time between the submission date of a BLA and the approval of that application. Only one

patent applicable to an approved biological product is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. In addition, a patent can only be extended once and only for a single product. The U.S. PTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we may intend to apply for restoration of patent term for one of our patents, if and as applicable, to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant BLA.

The Affordable Care Act, or ACA, signed into law on March 23, 2010, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or the BPCIA, which created an abbreviated approval pathway for biological products shown to be similar to, or interchangeable with, an FDA-approved reference biological product. Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical trial or trials. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product and, for products administered multiple times, the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. However, complexities associated with the larger, and often more complex, structure of biological products, as well as the process by which such products are manufactured, pose significant hurdles to implementation that are still being worked out by the FDA.

A reference biological product is granted four and twelve (12) year exclusivity periods from the time of first licensure of the product. FDA will not accept an application for a biosimilar or interchangeable product based on the reference biological product until four years after the date of first licensure of the reference product, and FDA will not approve an application for a biosimilar or interchangeable product based on the reference biological product until twelve (12) years after the date of first licensure of the reference product. “First licensure” typically means the initial date the particular product at issue was approved in the United States. Date of first licensure does not include the date of licensure of (and a new period of exclusivity is not available for) a biological product if the licensure is for a supplement for the biological product or for a subsequent application by the same sponsor or manufacturer of the biological product (or licensor, predecessor in interest, or other related entity) for a change (not including a modification to the structure of the biological product) that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device or strength, or for a modification to the structure of the biological product that does not result in a change in safety, purity, or potency. Therefore, one must determine whether a new product includes a modification to the structure of a previously approved product that results in a change in safety, purity, or potency to assess whether the licensure of the new product is a first licensure that triggers its own period of exclusivity. Whether a subsequent application, if approved, warrants exclusivity as the “first licensure” of a biological product is determined on a case-by-case basis with data submitted by the sponsor.

A biological product can also obtain pediatric market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued “Written Request” for such a study. The BPCIA is complex and continues to be interpreted and implemented by the FDA. In addition, government proposals have sought to reduce the 12-year reference product exclusivity period. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. As a result, implementation and the ultimate impact of the BPCIA is subject to significant uncertainty.

Additional Regulation

In addition to the foregoing, state and federal laws regarding environmental protection and hazardous substances, including the Occupational Safety and Health Act, the Resource Conservancy and Recovery Act and the Toxic Substances Control Act, affect our business. These and other laws govern our use, handling and disposal of various biological, chemical and radioactive substances used in, and wastes generated by, our operations. If our operations result in contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and governmental fines. We believe that we are in material compliance with applicable environmental laws and that continued compliance therewith will not have a material adverse effect on our business. We cannot predict, however, how changes in these laws may affect our future operations.

Government Regulation Outside of the United States

In addition to regulations in the United States, we are subject to a variety of regulations in other jurisdictions governing, among other things, research and development, clinical trials, testing, manufacturing, safety, efficacy, labeling, packaging, storage, record keeping, distribution, reporting, advertising and other promotional practices involving biological products as well as authorization and approval of our products.

Because biologically sourced raw materials are subject to unique contamination risks, their use may be restricted in some countries.

The requirements and process governing the conduct of clinical trials, product approval, pricing and reimbursement vary from country to country. In all cases, the clinical trials must be conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension of clinical trials, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

European Union Clinical Trials Regulation

Whether or not we obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application much like the IND prior to the commencement of human clinical trials. In the European Union, for example, a CTA must be submitted for each clinical trial to each country's National Competent Authority, or NCA, and at least one independent Ethics Committee, or EC, much like the FDA and an IRB, respectively. Once the CTA is approved in accordance with a country's requirements, the corresponding clinical trial may proceed. Under the current regime (the EU Clinical Trials Directive 2001/20/EC and corresponding national laws) all suspected unexpected serious adverse reactions to the investigated drug that occur during the clinical trial have to be reported to the NCA and ECs of the Member State where they occurred.

In April 2014, the EU adopted a new Clinical Trials Regulation (EU) No 536/2014, which has replaced the former Clinical Trials Directive 2001/20/EC. It overhauls the current system of approvals for clinical trials in the EU. Specifically, the new regulation, which is directly applicable in all Member States (meaning that no national implementing legislation in each EU Member State is required), aims at simplifying and streamlining the approval of clinical trials in the EU. For instance, the new Clinical Trials Regulation provides for a streamlined application procedure via a single entry point and strictly defined deadlines for the assessment of clinical trial applications. The new Clinical Trials Regulation (EU) No 536/2014 came into effect on January 31, 2022.

European Union Drug Review and Approval

In the European Union, medicinal products, including advanced therapy medicinal products, or ATMPs, are subject to extensive pre- and post-market regulation by regulatory authorities at both the European Union and national levels. Under Article 2(1) of Regulation (EC) No 1394/2007, or the "ATMP Regulation," ATMPs include somatic cell therapy products, which are cells that have undergone substantial manipulation so that biological characteristics, physiological functions or structural properties relevant for the intended clinical use have been altered, where such cells are to be administered to human beings in order to cure, diagnose or prevent disease. Our current development products are somatic cell therapy medical products which would be regulated as ATMPs in the European Union.

To obtain regulatory approval of an ATMP under the European Union regulatory system, we must submit a marketing authorization application, or MAA, under the centralized procedure administered by the EMA. The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid across all of the EEA (which is made up of all the European Union Member States, as well as Iceland, Norway and Liechtenstein). As provided for in the ATMP Regulation, the scientific evaluation of MAAs for ATMPs is primarily performed by a specialized scientific committee called the Committee for Advanced Therapies, or CAT. The CAT prepares a draft opinion on the quality, safety and efficacy of the ATMP which is the subject of the MAA, which is

sent for final approval to the Committee for Medicinal Products for Human Use, or CHMP. The CHMP recommendation is then sent to the European Commission, which adopts a decision binding in all EEA Member States. The maximum timeframe for the evaluation of an MAA for an ATMP is 210 days from receipt of a valid MAA, excluding clock stops when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CAT and/or CHMP. Clock stops may extend the timeframe of evaluation of an MAA considerably beyond 210 days. Where the CHMP gives a positive opinion, the EMA provides the opinion together with supporting documentation to the European Commission, who make the final decision to grant a marketing authorization, which is issued within 67 days of receipt of the EMA's recommendation. Accelerated evaluation may be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and, in particular, from the viewpoint of therapeutic innovation. If the CHMP accepts such a request, the timeframe of 210 days for assessment will be reduced to 150 days (excluding clock stops), but it is possible that the CHMP may revert to the standard time limit for the centralized procedure if it determines that the application is no longer appropriate to conduct an accelerated assessment.

The application used to submit the BLA in the United States is similar to that required in the European Union, with the exception of, among other things, certain specific requirements set out in the ATMP Regulation, for example certain particulars to be contained in the summary of product characteristics.

In the European Union, if human tissues and cells are used as starting materials in an ATMP, the donation, procurement and testing of the cells are covered by the Tissues and Cells Directive (2004/23/EC), or Human Tissue Directive. The competent authority in the UK under the Human Tissue Directive is the Human Tissue Authority, or HTA, which is responsible for licensing certain activities in the UK related to the donation, procurement and testing of cells used for the manufacture of ATMPs under the Human Tissue (Quality and Safety for Human Application) Regulations 2007. The processing, storage and distribution of the ATMP itself is governed by the medicines regulations and marketing authorization process set out above, however a separate license from the HTA may be needed for the initial procurement, processing, testing and storage (if for more than 48 hours) of the human cells which are to be subsequently used in the ATMP manufacture. Any organization involved in these activities in the UK will require an HTA license.

Data and Marketing Exclusivity in the EEA

The EEA also provides opportunities for market exclusivity. Upon receiving marketing authorization in the EEA, innovative medicinal products generally receive eight years of data exclusivity and an additional two years of market exclusivity. If granted, data exclusivity prevents generic or biosimilar applicants from referencing the innovator's pre-clinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar marketing authorization in the EEA, during a period of eight years from the date on which the reference product was first authorized in the EEA. During the additional two-year period of market exclusivity, a generic or biosimilar marketing authorization can be submitted, and the innovator's data may be referenced, but no generic or biosimilar product can be marketed until the expiration of the market exclusivity. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to authorization, is held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity so that the innovator gains the prescribed period of data exclusivity, another company may market another version of the product if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Orphan Drug Designation and Exclusivity in the EEA

Products receiving orphan designation in the EEA can receive ten years of market exclusivity, during which time no "similar medicinal product" for the same indication may be placed on the market. A "similar medicinal product" is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. An orphan product can also obtain an additional two years of market exclusivity where an agreed Pediatric Investigation Plan for pediatric studies has been

complied with. No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications.

The criteria for designating an "orphan medicinal product" in the EEA are similar in principle to those in the United States. Under Article 3 of Regulation (EC) 141/2000, a medicinal product may be designated as orphan if it meets the following criteria: (i) it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; and (ii) either the prevalence of such condition must not be more than five (5) in ten thousand (10,000) persons in the EEA when the application is made; or without the benefits derived from orphan status, it must be unlikely that the marketing of the medicine would generate sufficient return in the EEA to justify the investment needed for its development; and (iii) there exists no satisfactory method of diagnosis, prevention or treatment of such condition, or if such a method exists, the product will be of significant benefit to those affected by the condition, as defined in Regulation (EC) 847/2000. Orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers made available by the EU and its Member States to support research into, and the development and availability of, orphan drugs. The application for orphan drug designation must be submitted before the application for marketing authorization. The applicant will receive a fee reduction for the MAA if the orphan drug designation has been granted, but not if the designation is still pending at the time the marketing authorization is submitted. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The ten (10)-year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation, for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity. Otherwise, orphan medicine marketing exclusivity may be revoked only in very select cases, such as if:

- it is established that a similar medicinal product is safer, more effective or otherwise clinically superior;
- the marketing authorization holder consents; or
- the marketing authorization holder cannot supply enough orphan medicinal product.

Pediatric Development in the EEA

In the EEA, companies developing a new medicinal product must agree upon a Pediatric Investigation Plan, or PIP, with the EMA's Pediatric Committee, or PDCO, and must conduct pediatric clinical trials in accordance with that PIP, unless a waiver applies, (e.g., because the relevant disease or condition occurs only in adults). The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the drug for which marketing authorization is being sought. The marketing authorization application for the product must include the results of pediatric clinical trials conducted in accordance with the PIP, unless a waiver applies, or a deferral has been granted by the PDCO of the obligation to implement some or all of the measures of the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults, in which case the pediatric clinical trials must be completed at a later date. Products that are granted a marketing authorization with the results of pediatric clinical trials conducted in accordance with the PIP are eligible for a six month extension of the protection under a supplementary protection certificate (if any is in effect at the time of approval) even where the trial results are negative. In the case of orphan medicinal products, a two year extension of the orphan market exclusivity may be available. This pediatric reward is subject to specific conditions and is not automatically available when data in compliance with the PIP are developed and submitted.

Post-Approval Controls

Following approval, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of the medicinal product. These include the following:

- The holder of a marketing authorization must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance, who is responsible for oversight of that system. Key

obligations include expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports, or PSURs.

- All new MAAs must include a risk management plan, or RMP, describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the product. The regulatory authorities may also impose specific obligations as a condition of the marketing authorization. Such risk-minimization measures or post-authorization obligations may include additional safety monitoring, more frequent submission of PSURs, or the conduct of additional clinical trials or post-authorization safety studies. RMPs and PSURs are routinely available to third parties requesting access, subject to limited redactions.

- All advertising and promotional activities for the product must be consistent with the approved SmPC and therefore all off-label promotion is prohibited. Direct-to-consumer advertising of prescription medicines is also prohibited in the United Kingdom and European Union. In the European Union, although general requirements for advertising and promotion of medicinal products are established under EU directives, the details are governed by regulations in each European Union Member State and can differ from one country to another.

European Union Medical Devices Regulation

Some of our devices used to collect blood and tissue used in the manufacture of our medicinal products may be considered a class IIa medical device under the EU Medical Devices Regulations 2017/745, or EU MDR. The EU MDR became fully applicable in all EU Member States from May 26, 2021 (therefore not including the UK). All medical devices require a CE mark to be placed on the market in the European Union. In order to obtain a CE mark, a notified body must conduct a conformity assessment of the device to confirm whether it complies with the essential safety and efficacy requirements in the EU MDR. Such requirements will differ depending on the class of the device. The conformity assessment usually involves an audit of the manufacturer's quality system and a review of the technical documentation from the manufacturer on the safety and performance of the device. If the notified body considers that the device is in conformity with the EU MDR, it will issue a conformity assessment certificate and the manufacturer of the device can place a CE mark on the device, allowing it to be marketed in any EU Member State.

As stated above, our product candidates may require use of an *in vitro* diagnostic to identify appropriate patient populations. As in the U.S., these diagnostics, referred to as companion diagnostics, are regulated as medical devices in the European Union and will be governed by the In-Vitro Diagnostic Devices Regulation (EU) 2017/746, or EU IVDR. The EU IVDR will become fully applicable in all EU Member States on May 26, 2022 (therefore not including the UK). The EU IVDR introduced more stringent requirements than the current EU In Vitro Diagnostics Directive 98/79/EC and manufacturers will need to apply to a notified body for a conformity assessment of their device under the EU IVDR in order for their device to be marketed after May 26, 2022. As manufacturers are currently able to place devices on the market under the EU IVDR, any new devices should be assessed under this regime rather than the previous Directive. Before a notified body can issue a CE certificate for a companion diagnostic, it must seek a scientific opinion from the EMA on the suitability of the companion diagnostic to the medicinal product concerned if the medicinal product falls exclusively within the scope of the centralized marketing authorization procedure.

Brexit and the Regulatory Framework in the United Kingdom

In June 2016, the electorate in the United Kingdom voted in favor of leaving the European Union (commonly referred to as "Brexit"). Thereafter, in March 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. The United Kingdom formally left the European Union on January 31, 2020. A transition period began on February 1, 2020, during which European Union pharmaceutical law remained applicable to the United Kingdom, which ended on December 31, 2020. Since the regulatory framework for pharmaceutical products and medical devices in the United Kingdom covering quality, safety and efficacy of pharmaceutical products, medical devices, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from European Union directives and regulations, Brexit could materially impact the future regulatory regime which applies to products and the approval of product candidates and devices in the United Kingdom, as the UK legislation now has the potential to diverge from EU legislation. It remains to be seen

how Brexit will impact regulatory requirements for product candidates and devices in the United Kingdom in the long-term. The MHRA has recently published detailed guidance for industry and organizations to follow now that the transition period is over, which will be updated as the UK's regulatory position on medicinal products and medical devices evolves over time.

Centralized marketing authorizations which have been granted before January 1, 2021 automatically became Great Britain marketing authorizations on January 1, 2021, unless the marketing authorization holder opted out. Following January 1, 2021, an entirely separate application can be made to the MHRA for a Great Britain marketing authorization, which will be required alongside the centralized authorization for the EEA. Alternatively, for two years from January 1, 2021, Great Britain will adopt decisions taken by the European Commission on the approval of new marketing authorizations in the centralized marketing authorization procedure. In this case, MAAs for Great Britain (which will mirror the MAA used for the centralized application in the EEA) should be submitted to the MHRA following receipt of the CHMP opinion, and will be determined following conformation of notification of the EC decision.

As the EU MDR and EU IVDR became fully applicable after January 1, 2021, they will not apply to Great Britain. Instead, the Medical Devices Regulations 2002, or UK MDR, will apply. Following Brexit, before being placed on the market in Great Britain, all medical devices will not only require a CE mark but will also need to be registered with the MHRA. The MHRA will only register devices where the manufacturer has a registered place of business in the UK, or has appointed a UK Responsible Person who has a registered place of business in the UK. Devices must either conform to the UK MDR, or EU MDR or EU IVDR (until June 30, 2023 only) in order to be registered with the MHRA. There will be grace period to allow time for compliance with the new registration process which will depend on the class and type of device.

Other Healthcare Laws and Compliance Requirements

In addition to FDA restrictions on the marketing of pharmaceutical products, we may be subject to various federal and state laws targeting fraud and abuse in the healthcare industry. Healthcare providers, physicians, and third party payors play a primary role in the recommendation and prescription of drug products for which we obtain marketing approval. Arrangements with third party payors, healthcare providers and physicians, in connection with the clinical research, sales, marketing and promotion of products, once approved, and related activities, may expose a pharmaceutical manufacturer to broadly applicable fraud and abuse and other healthcare laws and regulations. In the United States, these laws include, without limitation, state and federal anti-kickback, false claims, physician transparency, and patient data privacy and security laws and regulations, including but not limited to those described below:

- the federal Anti-Kickback Statute, or AKS, which makes it illegal for any person or entity, including a prescription drug manufacturer (or a party acting on its behalf) to knowingly and willfully solicit, receive, offer or pay any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, that is intended to induce or reward, referrals including the purchase recommendation, order or prescription of a particular drug for which payment may be made under a federal healthcare program, such as the Medicare and Medicaid programs. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution;

- the federal civil and criminal false claims laws, including the False Claims Act, which impose criminal and civil penalties, including through civil "qui tam" or "whistleblower" actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid, or other federal health care programs that are false or fraudulent; knowingly making or causing a false statement material to a false or fraudulent claim or an obligation to pay money to the federal government; or knowingly concealing or knowingly and improperly avoiding or decreasing such an obligation. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;

- the civil monetary penalties law, which prohibits, among other things, the offering or giving of remuneration, which includes, without limitation, any transfer of items or services for free or for less than fair market value (with limited exceptions), to a Medicare or Medicaid beneficiary that the person knows or should know is likely to influence the beneficiary's selection of a particular supplier of items or services reimbursable by a federal or state governmental program;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payer (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false, fictitious, or fraudulent statements or representations in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it;

- HIPAA, as amended by HITECH, and their respective implementing regulations, which impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions;

- the federal Physician Payments Sunshine Act, created under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, the ACA, and its implementing regulations, which requires applicable manufacturers of drugs, devices, biological products and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program to report annually to the Centers for Medicare and Medicaid Services, or CMS, under the Open Payments Program, information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made to certain non-physician providers such as physician assistants and nurse practitioners;

- federal government price reporting laws, which require us to calculate and report complex pricing metrics in an accurate and timely manner to government programs;

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

- analogous state and foreign laws and regulations, such as state and foreign anti-kickback, false claims, consumer protection and unfair competition laws which may apply to pharmaceutical business practices, including but not limited to, research, distribution, sales and marketing arrangements as well as submitting claims involving healthcare 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 promulgated by the federal government that otherwise restricts payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to file reports with states regarding pricing and marketing information, such as the tracking and reporting of gifts, compensations and other remuneration and items of value provided to healthcare professionals and entities; state and local laws requiring the registration of pharmaceutical sales representatives; and state and foreign laws governing the privacy and

security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. Efforts to ensure that our business arrangements comply with applicable healthcare laws involve substantial costs. It is possible that governmental and enforcement authorities will conclude that a pharmaceutical manufacturer's business practices do not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If a pharmaceutical manufacturer's operations, including its arrangements with physicians and other healthcare providers, some of whom receive stock options as compensation for services provided, are found to be in violation of any of such laws or any other governmental regulations that apply, governmental and enforcement authorities may institute action. If the pharmaceutical manufacturer is not successful in defending itself or asserting its rights, those actions could have a significant impact on its business, including the imposition of significant civil, criminal and administrative penalties, damages, disgorgement, monetary fines, imprisonment, possible exclusion or suspension from participation in Medicare, Medicaid and other federal healthcare programs, integrity and oversight agreements to resolve allegations of non-compliance, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of operations, any of which could adversely affect a pharmaceutical manufacturer's ability to operate its business and the financial results of operations. Additionally, private individuals have the ability to bring actions on behalf of the U.S. government under the federal False Claims Act as well as under the false claims laws of several states against a pharmaceutical manufacturer. The approval and commercialization of a pharmaceutical manufacturer's product candidates outside the United States will also likely subject it to foreign equivalents of the healthcare laws mentioned above, among other foreign laws. Lastly, if any of the physicians or other healthcare providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs, which may also adversely affect our business.

The risk of our being found in violation of these laws is increased by the fact that many of these laws have not been fully interpreted by the regulatory authorities or the courts, their provisions are open to a variety of interpretations, and are currently the subject of legal challenge. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. The shifting compliance environment and the need to build and maintain a robust system to comply with multiple jurisdictions with different compliance and reporting requirements increases the possibility that a healthcare company may violate one or more of the requirements. Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial cost.

Healthcare Reform

In both the United States and certain foreign jurisdictions, there have been a number of legislative and regulatory changes to the health care system. In particular, in 2010 the ACA was enacted, which, among other things, 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.

There have been a number of significant changes to the ACA and its implementation. The Tax Cuts and Jobs Act of 2017, or Tax Act, includes a provision that repealed effective January 1, 2019 the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." On December 14, 2018, a federal district court in Texas ruled the individual mandate is a critical and inseverable feature of the ACA, and therefore, because it was repealed as part of the Tax Act, the remaining provisions of the ACA are invalid as well. Additionally, on December 18, 2019, the U.S. Court of Appeals for the Fifth Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. The U.S. Supreme Court is currently reviewing the case, although it is unclear how the Supreme Court will rule. In addition, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the ACA-mandated "Cadillac" tax on high-cost employer- sponsored health coverage and, effective January

1, 2021, also eliminates the health insurer tax. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court's decision, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is unclear how other healthcare reform measures of the Biden administration or other efforts, if any, to challenge, repeal or replace the ACA will impact our business.

The Bipartisan Budget Act of 2018, also amended the ACA, effective January 1, 2019, by increasing the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and closing the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." Similarly, on April 9, 2018, CMS issued a final rule that, effective January 1, 2020, will gives states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces by relaxing certain requirements for essential health benefits required under the ACA for plans sold through such marketplaces.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, included aggregate reductions of Medicare payments to providers of 2% per fiscal year. These reductions went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022. Then, a 1% payment reduction will occur beginning April 1, 2022 through June 30, 2022, and the 2% payment reduction will resume on July 1, 2022. The American Taxpayer Relief Act of 2012 further reduced Medicare payments to several providers, including hospitals 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 has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. At a federal level, President Biden signed an Executive Order on July 9, 2021 affirming the administration's policy to: (i) support legislative reforms that would lower the prices of prescription drug and biologics, including by allowing Medicare to negotiate drug prices, by imposing inflation caps, and, by supporting the development and market entry of lower-cost generic drugs and biosimilars; and (ii) support the enactment of a public health insurance option. Among other things, the Executive Order also directs HHS to provide a report on actions to combat excessive pricing of prescription drugs, enhance the domestic drug supply chain, reduce the price that the Federal government pays for drugs, and address price gouging in the industry; and directs the FDA to work with states and Indian Tribes that propose to develop section 804 Importation Programs in accordance with the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, and the FDA's implementing regulations. FDA released such implementing regulations on September 24, 2020, which went into effect on November 30, 2020, providing guidance for states to build and submit importation plans for drugs from Canada. On September 25, 2020, CMS stated drugs imported by states under this rule will not be eligible for federal rebates under Section 1927 of the Social Security Act and manufacturers would not report these drugs for "best price" or Average Manufacturer Price purposes. Since these drugs are not considered covered outpatient drugs, CMS further stated it will not publish a National Average Drug Acquisition Cost for these drugs. If implemented, importation of drugs from Canada may materially and adversely affect the price we receive for any of our product candidates. Further, on November 20, 2020 CMS issued an Interim Final Rule implementing the Most Favored Nation, or MFN, Model under which Medicare Part B reimbursement rates would have been be calculated for certain drugs and biologicals based on the lowest price drug manufacturers receive in Organization for Economic Cooperation and Development countries with a similar gross domestic product per capita. However, on December 29, 2021 CMS rescinded the Most Favored Nations rule. Additionally, on November 30, 2020, HHS published a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. Pursuant to court order, the removal and

addition of the aforementioned safe harbors were delayed and recent legislation imposed a moratorium on implementation of the rule until January 1, 2026. Although a number of these and other proposed measures may require authorization through additional legislation to become effective, and the Biden administration may reverse or otherwise change these measures, both the Biden administration and Congress have indicated that they will continue to seek new legislative measures to control drug costs.

Further, on May 30, 2018, the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new product candidates that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a pharmaceutical manufacturer to make its product candidates available to eligible patients as a result of the Right to Try Act.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing.

We expect that additional foreign, federal and state healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, and result in reduced demand for our current product candidates and any future product candidates or additional pricing pressures. It is possible that additional governmental action is taken to address the COVID-19 pandemic. For example, on April 18, 2020, CMS announced that QHP issuers under the ACA may suspend activities related to the collection and reporting of quality data that would have otherwise been reported between May and June 2020 given the challenges healthcare providers are facing responding to the COVID-19 virus.

Legislative and regulatory proposals, and enactment of laws, at the foreign, federal and state levels, directed at containing or lowering the cost of healthcare, will continue into the future.

Secarna License

On October 20, 2021, we entered into an agreement, or the Secarna Agreement, with Secarna Pharmaceuticals GmbH & Co. KG, or Secarna, whereby Secarna granted us a non-exclusive worldwide license under certain patent and other intellectual property rights, to use the Secarna technology in the ex vivo manufacture of a T cell pharmaceutical product.

We are obligated to pay Secarna development milestone payments up to a maximum aggregate of €6.5 million and one-time commercial milestone payments up to €26.0 million, as well as tiered low-single digit percentage royalty payments on net sales of products, subject to certain customary reductions. The royalty obligations continue until the later of: (i) the date there ceases to be a valid patent claim covering such product in the country in which it is sold or (ii) ten years from the first commercial sale of the product. For the year ended December 31, 2021, we recorded expenses of €0.7 million related to the Secarna Agreement.

Unless terminated earlier, the term of the Secarna Agreement continues until the later of the expiration of the royalty term in each country and such time as no further milestone payments are due, and upon such termination, the licenses granted shall become fully-paid, royalty-free, irrevocable, and perpetual. The Company has the right to terminate the Secarna Agreement for convenience in its entirety upon 90 days' notice. Each party may terminate the agreement if the other party is in material breach subject to a 60 day remedy period.

C. Organizational Structure.

As of December 31, 2021, we had three subsidiaries. The following table sets out for our principal subsidiaries, country of incorporation and percentage ownership and voting interest held by us (directly or indirectly through subsidiaries).

Company	Country of incorporation	Percentage ownership and voting interest
Achilles Therapeutics Holdings Limited	England and Wales	100.00%
Achilles Therapeutics UK Limited	England and Wales	100.00%
Achilles Therapeutics US, Inc.	United States	100.00%

D. Property, Plant and Equipment.

Our corporate headquarters are located in Hammersmith Road, London in the United Kingdom, where we currently lease a facility containing our research and development, laboratory and office space, which consists of approximately 25,000 square feet. Our lease expires in 2030 with a break clause in 2025.

We lease a facility in Philadelphia, United States containing research and development, laboratory and office space, which consists of approximately 7,000 square feet. Our lease expires in 2024.

We also lease a warehouse in west London that expires in 2030 with approximately 64,000 square feet. We expect to construct a flexible GMP modular facility to scale up our manufacturing footprint at this location.

We have other smaller leases that are primarily used for office and laboratory space. See Note 9, "Leases," to our financial statements appearing at the end of this Annual Report, for further discussion.

We believe that our current facilities are adequate for our current needs and that suitable additional or substitute space at commercially reasonable terms will be available as needed to accommodate any future expansion of our operations.

Item 4A. Unresolved Staff Comments.

None.

Item 5. Operating and Financial Review and Prospects.

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and related notes appearing elsewhere in this Annual Report. Some of the information contained in this discussion and analysis, including information with respect to our plans and strategy for our business and our expectations with respect to liquidity and capital resources, includes forward-looking statements. These forward-looking statements are subject to numerous risks and uncertainties, including, but not limited to, those risks and uncertainties described in Item 3.D. "Risk Factors" and "Special Note Regarding Forward-Looking Statements" in this Annual Report. Our actual results could differ materially from the results described in or implied by these forward- looking statements.

We maintain our books and records in pounds sterling, our results are subsequently converted to U.S. dollars and we prepare our consolidated financial statements in accordance with generally accepted accounting principles in the United States, or U.S. GAAP, as issued by the Financial Accounting Standards Board, or FASB. All references in this Report to "$" are to U.S. dollars and all references to "£" are to pounds sterling. Unless otherwise indicated, certain U.S. dollar amounts contained in this Report have been translated into pounds sterling at the rate of £1.00 to $1.3497 on December 31, 2021. These translations should not be considered representations that any such amounts have been,

could have been or could be converted into pounds sterling at that or any other exchange rate as of that or any other date.

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

A. Operating Results.

Overview

We are a clinical immuno-oncology biopharmaceutical stage company developing transformative precision T cell therapies to treat multiple types of solid tumors. We are focused on advancing cancer therapies through our pioneering work in the field of tumor evolution and our belief that clonal neoantigens represent the most specific class of cancer cell targets. Our platform enables us to identify mutations formed early in the development of a cancer that give rise to antigens that are expressed by all of a patient's cancer cells but are absent from healthy tissue. We refer to this novel class of solid tumor targets as clonal neoantigens. To identify clonal neoantigens in a patient, we have developed a proprietary bioinformatic platform called PELEUS. This platform employs sophisticated statistical algorithms trained on the unique tumor genetic data derived from our exclusive license to data from the TRACERx study, which aims to analyze tumor samples from more than 840 non-small cell lung cancer, or NSCLC, patients. Once we have identified the clonal neoantigens, our proprietary manufacturing process, VELOS, uses the patient's T cells and blood-derived dendritic cells to create a clonal neoantigen-reactive T cell therapy, or cNeT, that specifically targets multiple clonal neoantigens to eradicate the tumor.

Since our inception in 2016, we have devoted substantially all of our resources to conducting research activities and clinical trials, organizing and staffing our company, business planning, raising capital and establishing our intellectual property portfolio. We have initially focused on two solid tumor types: advanced NSCLC and metastatic or recurrent melanoma as well as expanding into a range of additional indications. We do not have any products approved for sale and have not generated any revenue from product sales. We have principally raised capital through the issuance and sale of our convertible preferred shares to outside investors and sales of ADSs through our IPO. Through December 31, 2021, we had received net cash proceeds of $230.9 million from investors in our preferred shares financings and $160.6 million from sales of ADS through our IPO.

We have incurred significant operating losses since inception. We incurred total net losses of $61.1 million, $33.2 million and $14.0 million for the years ended December 31, 2021, 2020 and 2019, respectively. As of December 31, 2021, we had an accumulated deficit of $119.1 million. These losses have resulted primarily from costs incurred in connection with research and development activities and general and administrative costs associated with our operations. We expect that our expenditure will increase substantially in connection with our ongoing activities, particularly as we:

- continue to develop our pipeline of discovery programs and conduct research and clinical activities for our existing programs for advanced NSCLC, metastatic or recurrent melanoma and other solid tumors;
- continue to innovate, improve and develop our technology platform, including continuing to develop and improve our PELEUS bioinformatic platform and VELOS manufacturing process and to evaluate new approaches to our manufacturing process;
- expand our Material Acquisition Platform, or MAP, network to increase our network of clinical sites;
- advance the development of our current programs, additional follow-on indications and any future product candidates into additional solid tumor indications;
- maintain, expand and protect our intellectual property portfolio;
- seek marketing approvals and complete any post-marketing studies, if required, for any of our product candidates that successfully complete clinical trials, if any;
- acquire or in-license additional product candidates and technologies;
- expand our infrastructure and facilities to accommodate our growing employee base and ongoing development activity;
- continue to improve our manufacturing process to create a fully closed end-to-end manufacturing process;

- expand our manufacturing infrastructure and facilities to support the manufacture of larger quantities of our product candidates for clinical development and potential commercialization globally;
- establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval; and
- add operational, financial and management information systems and personnel, including personnel to support our research and development programs, any future commercialization efforts and our operations as a public company.

We will not generate revenue from product sales unless and until we successfully complete clinical development and obtain regulatory approval for ATL001 or any future product candidates. If we obtain regulatory approval for ATL001 or any product candidates, we expect to incur significant expenses related to developing our commercialization capability to support product sales, marketing and distribution. As a result, we will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through the sale of equity, debt financings or other capital sources, including potential collaborations with other companies or other strategic transactions. Our inability to raise capital as and when needed could have a negative impact on our financial condition and ability to pursue our business strategies. There can be no assurances, however, that the current operating plan will be achieved or that additional funding will be available on terms acceptable to us, or at all.

As of December 31, 2021, we had cash and cash equivalents of $266.3 million. We believe our existing cash and cash equivalents will enable us to fund our operating expenses and capital expenditure requirements into the second half of 2024. See "—Liquidity and Capital Resources—Funding Requirements" below.

Impact of the On-Going COVID-19 Coronavirus

The development of ATL001 for our current programs and additional follow-on indications as well as any future product candidates could be disrupted and materially adversely affected in the future by a pandemic, epidemic or outbreak of an infectious disease, such as the on-going COVID-19 pandemic. The spread of COVID-19 has impacted the global economy and has impacted our operations, including the interruption of our research activities, clinical trials and our supply chain. Interruption to our supply chain includes interruption of or delays in receiving supplies from the third parties we rely on to, among other things, conduct our manufacturing process. It is primarily due to staffing shortages, production slowdowns or stoppages and disruptions in delivery systems. As a result of the COVID-19 pandemic, we have experienced delays in enrollment in and dosing of our ongoing Phase I/IIa clinical trial for metastatic or recurrent melanoma and our ongoing Phase I/IIa clinical trial for advanced NSCLC and may continue to do so. The causes of these delays includes government orders and site policies on account of the pandemic, some patients may be unwilling or unable to travel to study sites, enroll in trials, or be unable to comply with clinical trial protocols if quarantines impede patient movement or interrupt healthcare services. These factors could delay our ability to conduct research activities and clinical trials or release clinical trial results, and/or delay our ability to obtain regulatory approval and commercialize ATL001 and any product candidates. Furthermore, COVID-19 could affect our employees or the employees of research sites and service providers on whom we rely as well as those of companies with which we do business, including our suppliers and contract manufacturing organizations, thereby disrupting our business operations. Quarantines and travel restrictions imposed by governments in the jurisdictions in which we and the companies with which we do business operate could materially impact the ability of employees to access research and clinical sites, laboratories, manufacturing sites and offices. We have implemented work-at-home policies and may experience limitations in employee resources. Our increased reliance on personnel working from home may negatively impact productivity, or disrupt, delay, or otherwise adversely impact our business.

We are still assessing our business plans and the impact the COVID-19 pandemic may have on our ability to advance the testing, development and manufacturing of ATL001 and any future product candidates, including as a result of adverse impacts on the research sites, service providers, vendors, or suppliers on whom we rely, or to raise financing to support the development of product candidates. No assurances can be given that this analysis will enable us to avoid part or all of any impact from the spread of COVID-19 or its consequences, including downturns in business sentiment generally or in our sector in particular. We cannot presently predict the scope and severity of any potential business shutdowns or disruptions, but if we or any of the third parties on whom we rely or with whom we conduct business,

were to experience shutdowns or other business disruptions, our ability to conduct our business in the manner and on the timelines presently planned could be materially and adversely impacted.

CRT License

In May 2016, we entered into a License Agreement, or the License Agreement, with Cancer Research Technology Limited, or CRT, pursuant to which we obtained access rights to intellectual property and know-how from the TRACERx Study. Under the License Agreement, we are granted an exclusive, sublicensable license to the TRACERx patents and bioinformatic data for use in: (i) the therapeutic field of neoantigen cell therapies and adoptive cell transfer; and (ii) the neoantigen diagnostic field, for use in research and the potential development of products for commercialization. We are further granted, during the vaccine option period, an exclusive license to the TRACERx patents and the bioinformatic data in the private neoantigen therapeutic vaccine field for research and development but not in the development of products for commercial sale, and a non-exclusive license to the same in the public neoantigen therapeutic vaccine field. We also obtained a non-exclusive license to the TRACERx bioinformatic pipeline, patient sequencing and medical data, know-how, and materials.

CRT additionally granted us certain rights to new patent applications filed by the Founding Institutions in respect of inventions resulting from the TRACERx study through February 2023, including automatic exclusive licenses to patent rights relating to non-severable improvements of technology covered by the original TRACERx patents and non-exclusive rights to severable improvements. CRT granted us the right of first negotiation to license certain patent rights generated by our founders outside of the TRACERx study which relate to the licensed technology.

In July 2017, we obtained a non-exclusive license to the LOHHLA patent under the License Agreement. In October 2018, we obtained an exclusive license to the LOHHLA patent under an addendum to the License Agreement. Under the License Agreement, we hold an option to exploit products in the therapeutic vaccine field, or the Vaccine Option. In March 2021, we extended the Vaccine Option from May 2021 to May 2023 with a payment of less than £0.1 million or $0.1 million.

In May 2018, we entered into an amendment to the License Agreement that created an additional sample period through July 2020 and specified additional materials to be subject to the License Agreement related to the immunology side study. The License Agreement was subsequently amended in July 2020, November 2020 and March, 2021.

Upon execution of the License Agreement, we granted CRT 396,125 B ordinary shares and 67,793 C ordinary shares. The C ordinary shares granted to CRT were forfeited and transferred to the deferred shares during the year ended December 31, 2019, as the applicable performance conditions were not met. The B ordinary shares granted to CRT were converted into ordinary shares upon IPO. The Company recorded $0.3 million of IP research and development expense in 2016. We are obligated to pay CRT milestone success payments up to an aggregate of £6.5 million for therapeutic products, and milestone success payments up to an aggregate £0.8 million for non-therapeutic products, as well as sub-single digit to low-single digit percentage royalty on net sales of products that utilize the licensed intellectual property, subject to certain customary reductions. The royalty obligations continue on a product-by-product and country-by-country basis until the later of: (i) the date there ceases to be a valid patent claim covering such product in the country in which it is sold; or (ii) with respect to contribution royalty products, ten years from the first commercial sale of the product, and with respect to a patent royalty product, five years from the first commercial sale of the product. On a product-by-product basis, we may also elect to provide other cash consideration at fair market value and forgo the milestone or royalty payment.

Less than $0.1 million of expenses were recorded for the year ended December 31, 2021 related to the CRT License Agreement. No expenses were recorded for the year December 31, 2020 related to the CRT License Agreement.

Secarna License

On October 20, 2021, we entered into an agreement, or the Secarna Agreement, with Secarna Pharmaceuticals GmbH & Co. KG, or Secarna, whereby Secarna granted us a non-exclusive worldwide license under certain patent and other intellectual property rights, to use the Secarna technology in the ex vivo manufacture of a T cell pharmaceutical product.

We are obligated to pay Secarna development milestone payments up to a maximum aggregate of €6.5 million ($7.4 million using a rate of €1.132 at December 31, 2021) and one-time commercial milestone payments up to €26 million ($29.4 million using a rate of €1.132 at December 31, 2021), as well as tiered low-single digit percentage royalty payments on net sales of products, subject to certain customary reductions. The royalty obligations continue until the later of: (i) the date there ceases to be a valid patent claim covering such product in the country in which it is sold or (ii) ten years from the first commercial sale of the product. For the year ended December 31, 2021, we recorded expenses of €0.7 million ($0.8 million using an average rate of €1.183 for the year ended December 31, 2021) related to the Secarna Agreement.

Components of our Results of Operations

Revenue

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from the sale of products in the foreseeable future. If our development efforts for ATL001 or any of our future candidates are successful and result in regulatory approval, we may generate revenue in the future from product sales.

Operating Expenses

Research and Development Expenses

Research and development expenses consist primarily of costs incurred in connection with the research and development of ATL001 for our current programs, additional follow-on indications and enhancement of our existing technology platform. Research and development expenses consist of:

- expenses incurred under agreements with contract research organizations, or CROs, as well as investigative sites and consultants that conduct our clinical trials, research activities and other scientific development services;
- manufacturing scale-up expenses and the cost of acquiring and manufacturing clinical trial materials;
- expenses to acquire technologies to be used in research and development;
- employee-related expenses, including salaries, related benefits, travel and share-based compensation expense for employees engaged in research and development functions;
- costs of outside consultants, including their fees, share-based compensation and related travel expenses;
- the costs of laboratory supplies and acquiring, developing and manufacturing clinical trial materials;
- costs related to compliance with regulatory requirements;
- facility-related expenses, which include direct depreciation costs and allocated expenses for rent and maintenance of facilities and other operating costs; and
- upfront, milestone and management fees for maintaining licenses under our third-party licensing agreements.

We expense research and development costs as incurred. We recognize external development costs based on an evaluation of the progress to completion of specific tasks using information provided to us by our service providers. As a result, our research and development expenses may vary substantially from period to period based on the timing of our research and development activities. Payments for these activities are based on the terms of the individual agreements, which may differ from the pattern of costs incurred, and are reflected in our financial statements as a prepaid expense or accrued research and development expenses.

UK research and development tax credits are recorded as an offset to research and development expense. See “Income Tax Expenses.”

Our direct research and development expenses are tracked on an indication-by-indication basis and consist primarily of external costs, such as fees paid to outside consultants, CROs and central laboratories in connection with our research activities, process development, manufacturing and clinical development activities. License fees and other costs incurred after a product candidate has been selected that are directly related to a product candidate are included in direct research and development expenses for that program. License fees and other costs incurred prior to designating a product candidate are included in other program expense. We do not allocate employee costs, costs

associated with our discovery efforts, laboratory supplies, and facilities, including depreciation or other indirect costs, to specific programs because these costs are deployed across multiple programs and, as such, are not separately classified. We use internal resources primarily to oversee the research and development as well as to manage our research activities, process development, manufacturing and clinical development activities. These employees work across multiple programs and, therefore, we do not track their costs by program.

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials and related product manufacturing expenses. As a result, we expect that our research and development expenses will continue to increase over the next several years as we: (i) expedite the clinical development and obtain marketing approval for ATL001 for advanced NSCLC and metastatic or recurrent melanoma; (ii) initiate additional clinical trials for ATL001 or any future product candidates, including for the treatment of head and neck, renal, triple negative breast and bladder; (iii) improve the efficiency and scalability of our manufacturing processes and supply chain including enhancing the capability of our PELEUS platform for selecting clonal neoantigens; and (iv) build our in-house process development, analytical and manufacturing capabilities and continue to discover and develop additional product candidates, increase personnel costs and prepare for regulatory filings related to ATL001 and any future product candidates. We also expect to incur additional expenses related to milestone payments, royalty payments and maintenance fees payable to third parties with whom we have entered into license agreements.

The successful development and commercialization of ATL001 or any of our future product candidates is highly uncertain. This is due to the numerous risks and uncertainties associated with development and commercialization, including the following:

- completing research activities for the development of ATL001 and identifying new cNeT product candidates;
- establishing an appropriate safety profile with IND- and CTA-enabling studies;
- successful patient enrollment in, and the initiation and completion of, clinical trials;
- the timing, receipt and terms of any marketing approvals from applicable regulatory authorities and reimbursement and market access from third-party payors;
- our ability to establish commercial manufacturing capabilities and maintain suitable arrangements with third-party manufacturers for ATL001 and any future product candidates;
- obtaining, maintaining, defending and enforcing patent claims and other intellectual property rights;
- defending against third-party infringement, misappropriation or other violation of intellectual property rights claims;
- significant and changing government regulation;
- establishing and maintaining temperature controlled product logistics;
- launching commercial sales of ATL001 and any future product candidates, if and when approved, whether alone or in collaboration with others; and
- maintaining a continued acceptable safety profile of the product candidates following approval.

A change in the outcome of any of these variables with respect to the development of ATL001 and any future product candidates in development could mean a significant change in the costs and timing associated with the development of these product candidates. For example, if the FDA, EMA or another regulatory authority were to delay our planned start of clinical trials or require us to conduct clinical trials or other testing beyond those that we currently expect, or if we experience significant delays in enrollment in any of our planned clinical trials, we could be required to commit significant additional financial resources and time on the completion of clinical development of that product candidate.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and related benefits, share-based compensation expense, travel and other expenses incurred by personnel in executive, finance and administrative functions. These expenses include professional fees for legal, including patent costs, consulting, accounting and audit services. We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support our continued research activities and development of ATL001 and any future product candidates.

We also anticipate we will continue to incur increased accounting, audit, legal, regulatory, compliance, director and officer insurance costs as well as investor and public relations expenses associated with being a public company. Additionally, if and when we believe a regulatory approval of a product candidate appears likely, we anticipate an increase in payroll and expense as a result of our preparation for commercial operations, especially as it relates to the sales and marketing of our product candidate.

Other Income (Expense), Net

Interest Income

Interest income consists primarily of interest earned on our cash and cash equivalents.

Other Expense

Foreign currency transactions in currencies different from the functional currency of our entity are translated into the functional currency using the exchange rates prevailing at the dates of the transactions. Foreign exchange differences resulting from the settlement of such transactions and from the translation at period-end exchange rates in foreign currencies are recorded in other income (expense), net in the statement of operations and comprehensive loss. As such, our other income (expense), net may be impacted by future changes in exchange rates. See Item 11 - Quantitative and Qualitative Disclosures About Market Risks, for further discussion.

Income Taxes

We are subject to corporate taxation in the United States and the United Kingdom. Due to the nature of our business, we have generated losses since inception and have therefore not paid UK corporation tax. As a company that carries out extensive research and development activities, we seek to benefit from one of two UK R&D tax credit cash rebate regimes: Small and Medium Enterprise, or SME, Program and the Research and Development Expenditure Credit, or RDEC, Program. 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.

Based on criteria established by Her Majesty's Revenue and Customs, or HMRC, a portion of expenditures being carried in relation to our pipeline R&D, clinical trials management and manufacturing development activities were eligible for the SME Program for the years ended December 31, 2019, 2020 and 2021. We claimed the tax credit in 2019 and 2020 which were paid in 2020 and 2021, respectively. We have claimed a tax credit for 2021, which we expect will be paid to us in 2022 from HMRC. We will continue to assess whether it is possible to qualify under the more favorable SME regime for future accounting periods.

Unsurrendered UK losses may be carried forward indefinitely to be offset against future taxable profits, subject to numerous utilization criteria and restrictions. The amount that can be offset each year is limited to £5.0 million plus an incremental 50% of UK taxable profits. After accounting for tax credits receivable, we had accumulated tax losses for carry forward in the UK of $71.0 million as of December 31, 2021. We have recorded an insignificant amount of income tax provisions for the year ended December 31, 2021, which relate to income tax obligations of our operating company in the U.S., which generates a profit for tax purposes.

Benefit from research and development, or R&D, tax credit, is received in the UK and recorded as an offset to research and development expenses. The UK R&D tax credit, as described below, is fully refundable to us and is not dependent on current or future taxable income. As a result, we have recorded the entire benefit from the UK R&D tax credit as a benefit which is included in our net loss before income tax and accordingly, not reflected as part of the income tax provision. If, in the future, any UK R&D tax credits generated are needed to offset a corporate income tax liability in the UK, that portion would be recorded as a benefit within the income tax provision and any refundable portion not dependent on taxable income would continue to be recorded as an offset to research and development expenses.

In the event we generate revenues in the future, we may benefit from the UK "patent box" regime that allows profits attributable to revenues from patents or patented products to be taxed at an effective rate of 10%.

Value Added Tax, or VAT, is broadly charged on all taxable supplies of goods and services by VAT-registered businesses. Under current rates as determined for VAT purposes, the VAT on goods or services supplied is added to all sales invoices and is payable to HMRC. Similarly, VAT paid on purchase invoices is generally reclaimable from HMRC.

Consolidated Results of Operations

Comparison of the Years Ended December 31, 2021 and 2020

The following table summarizes our consolidated results of operations for the years ended December 31, 2021 and 2020 (in thousands):

	Year ended December 31, 2021	2020	Change
Operating expenses:			
Research and development	$ 42,224	$ 22,629	$ 19,595
General and administrative	21,971	11,098	10,873
Total operating expenses	64,195	33,727	30,468
Loss from operations	(64,195)	(33,727)	(30,468)
Other income (expense), net:			—
Other income (expense)	3,133	531	2,602
Total other income (expense), net	3,133	531	2,602
Loss before provision for income taxes	(61,062)	(33,196)	(27,866)
Provision for income taxes	(37)	(3)	(34)
Net loss	$ (61,099)	$ (33,199)	$ (27,900)

Research and Development Expenses

The table below summarizes our research and development expenses incurred by program for the year ended December 31, 2021 and 2020 (in thousands):

	Year ended December 31, 2021	2020	Change
Direct research and development expense by program:			
NSCLC	$ 8,729	$ 5,432	$ 3,297
Melanoma	7,858	4,512	3,346
Other pre-clinical and technology development cost	6,710	2,984	3,726
Unallocated research and development expense:			
Personnel expenses	13,717	7,200	6,517
Other expenses	5,210	2,501	2,709
Total research and development expenses	$ 42,224	$ 22,629	$ 19,595

Research and development expenses were net of research and development tax credit reimbursement of $10.7 million and $5.8 million for the year ended December 31, 2021 and 2020, respectively. The net increase in research and development expenses was $19.6 million for the year ended December 31, 2021 compared to the year ended December 31, 2020. The net increase in direct research and development expense was primarily attributable to a net increase of $3.7 million in IND enabling activities primarily for new follow-on indications, as well as continuing research and development into enhancements to PELEUS, our bioinformatics platform, and our VELOS manufacturing process, a net increase of $3.3 million in our metastatic or recurrent melanoma program specifically in

relation to our ongoing Phase I/II THETIS clinical trial and a net increase of $3.3 million in our NSCLC program specifically in relation to our ongoing Phase I/II CHIRON clinical trial. Our unallocated research and development expense increased by $9.2 million for the year ended December 31, 2021, primarily as a result of increased costs of supporting the increased headcount in our research and development functions and their research efforts and increased facility costs due to the lease of new laboratory space.

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General and Administrative Expenses

The following table summarizes our general and administrative expenses for the year ended December 31, 2021 and 2020 (in thousands):

	Year ended December 31,		
	2021	2020	Change
Personnel expenses	$ 11,227	$ 6,835	$ 4,392
Professional services fees	3,424	2,273	1,151
Facilities and other expense	7,320	1,990	5,330
	$ 21,971	$ 11,098	$ 10,873

General and administrative expenses were $22.0 million for the year ended December 31, 2021, compared to $11.1 million for the year ended December 31, 2020. The increase of $10.9 million consisted primarily of an increase of $5.3 million in facilities and other expenses due to the lease of new office space and increased costs of supporting the expansion of our business, an increase of $4.4 million in personnel expenses due to an overall increase in headcount and the recognition of additional share-based compensation and an increase of $1.2 million in legal and professional fees due to activities related to becoming a public company.

Total Other Income (Expense), Net

Other income (expense), net was income of $3.1 million for the year ended December 31, 2021, compared to income of $0.5 million for the year ended December 31, 2020. The increase in other income of $2.6 million was primarily due to an increase in foreign exchange gains of $2.4 million.

Provision for Income Taxes

The provision for income taxes was less than $0.1 million for each of the years ended December 31, 2021 and 2020, which is related to income tax obligations of our operating company in the U.S., which generates a profit for tax purposes.

Comparison of the Years Ended December 31, 2020 and 2019

The following table summarizes our consolidated results of operations for the years ended December 31, 2020 and 2019 (in thousands):

	Year Ended December 31,		
	2020	2019	Change
Operating expenses:			
Research and development	$ 22,629	$ 9,072	$ 13,557
General and administrative	11,098	4,703	6,395
Total operating expenses	33,727	13,775	19,952
Loss from operations	(33,727)	(13,775)	(19,952)
Other income (expense), net:			
Other income (expense)	531	(215)	746
Total other income (expense), net	531	(215)	746
Loss before provision for income taxes	(33,196)	(13,990)	(19,206)
Provision for income taxes	(3)	—	(3)
Net loss	$ (33,199)	$ (13,990)	$ (19,209)

Research and Development Expenses

The table below summarizes our research and development expenses incurred by program for the year ended December 31, 2020 and 2019 (in thousands):

	Year Ended December 31,		
	2020	2019	Change
Direct research and development expense by program:			
NSCLC	$ 5,432	$ 1,366	$ 4,066
Melanoma	4,512	491	4,021
Other pre-clinical and technology development cost	2,984	1,661	1,323
Unallocated research and development expense:			
Personnel expenses	7,200	4,626	2,574
Other expenses	2,501	928	1,573
Total research and development expenses	$ 22,629	$ 9,072	$ 13,557

Research and development expenses were net of research and development tax credit reimbursement of $5.8 million and $3.1 million for the year ended December 31, 2020 and 2019, respectively. The net increase in research and development expenses was $13.6 million for the year ended December 31, 2020 compared to the year ended December 31, 2019. The net increase in research and development expense was primarily attributable to a net increase of $4.1 million in direct expenses as a result of optimization activities for our advanced NSCLC program, a net increase of $4.0 million in direct expenses of our metastatic or recurrent melanoma program and a net increase of $1.3 million in direct costs related to our good manufacturing practices, or GMP, manufacturing spend and other exploratory program. Our unallocated research and development expense increased by $4.1 million for the year ended December 31, 2020, primarily as a result of increased facility costs due to the lease of new laboratory space and the increased costs of supporting the increased headcount in our research and development functions and their research efforts.

General and Administrative Expenses

The following table summarizes our general and administrative expenses for the years ended December 31, 2020 and 2019 (in thousands):

	Year Ended December 31,		
	2020	2019	Change
Personnel expenses	$ 6,835	$ 3,132	$ 3,703
Professional services fees	2,273	830	1,443
Facilities and other expense	1,990	741	1,249
	$ 11,098	$ 4,703	$ 6,395

General and administrative expenses were $11.1 million for the year ended December 31, 2020, compared to $4.7 million for the year ended December 31, 2019. The increase of $6.4 million consisted primarily of an increase of $3.7 million in personnel expenses due to an overall increase in headcount and the recognition of additional share-based compensation, an increase of $1.4 million in legal and professional fees due to activities related to preparations for becoming a public company and an increase of $1.2 million in facilities and other expenses due to the lease of new office space and increased costs of supporting the expansion of our business.

Total Other Income (Expense), Net

Other income (expense), net was income of $0.5 million for the year ended December 31, 2020, compared to expense of $0.2 million for the year ended December 31, 2019. The increase in other income of $0.7 million was primarily due to an increase of $0.2 million in interest income and an increase of $0.5 million in foreign exchange gain.

Provision for Income Taxes

The provision for income taxes was less than $0.1 million for the year ended December 31, 2020, which is related to income tax obligations of our operating company in the U.S., which generates a profit for tax purposes. There is no provision for income taxes for the year ended December 31, 2019.

B. Liquidity and Capital Resources

Since our inception, we have not generated any revenue from product sales or any other sources and have incurred significant net losses in each period and on an aggregate basis. We have not yet commercialized any product candidates and we do not expect to generate revenue from sales of any product candidates for several years, if at all. We have funded our operations to date primarily with proceeds from the sale of preferred shares and ordinary shares. Through December 31, 2021, we had received net cash proceeds of $230.9 million from investors in our preferred shares financings and $160.6 million net proceeds from the sales of ADSs through our IPO after deducting underwriting discounts and commissions and other offering expenses. As of December 31, 2021, we had cash and cash equivalents of $266.3 million.

We currently have no ongoing material financing commitments, such as lines of credit or guarantees, that are expected to affect our liquidity over the next five years, other than our manufacturing and lease obligations described below.

Cash Flows

The following table summarizes our cash flows for each of the periods presented (in thousands):

	Year ended December 31,		
	2021	**2020**	**2019**
Net cash used in operating activities	$ (59,284)	$ (25,252)	$ (14,142)
Net cash used in investing activities	(7,634)	(11,847)	(942)
Net cash provided by financing activities	160,755	113,704	93,622
Effect of exchange rate changes on cash, cash equivalents and restricted cash	(5,334)	3,650	8,373
Net increase in cash	$ 88,503	$ 80,255	$ 86,911

Net Cash Used in Operating Activities

During the year ended December 31, 2021, net cash used in operating activities was $59.3 million, primarily resulting from our net loss of $61.1 million, adjusted for share-based compensation of $6.3 million, depreciation and amortization of $3.3 million The net loss also was adjusted by $7.4 million related to changes in components of working capital due to: (i) decreased accounts payable for payment of vendors' invoices; (ii) increased accrued research and development, increased accrued expenses incurred in relation to our IPO costs and increased accrued facility costs in conjunction with lease of new laboratory and office space; and (iii) increased prepaid expenses and other current assets in conjunction with accrued UK R&D tax credits. In addition, changes in other assets of $0.5 million primarily due to the capitalization of cloud-based implementation costs during the year ended December 31, 2021 increased cash used.

During the year ended December 31, 2020, net cash used in operating activities was $25.3 million, primarily resulting from our net loss of $33.2 million, adjusted for share-based compensation of $3.0 million and depreciation and amortization of $0.8 million. The net loss was also partially offset by changes in right of use assets and operating lease liabilities of $1.2 million and $5.2 million related to changes in components of working capital due to increased accounts payable, accrued research and development expenses incurred on our preclinical trials and increased accrued facility costs in conjunction with lease of new laboratory and office space. The net loss was also partially offset by changes in other long-term liabilities of $0.6 million due to reinstatement accrual of one leased office. In addition, changes in other assets of $2.8 million due to rent deposit paid during the year ended December 31, 2020 increased cash used.

During the year ended December 31, 2019, net cash used in operating activities was $14.1 million, primarily resulting from our net loss of $14.0 million, adjusted for share-based compensation of $0.7 million and depreciation and amortization of $0.3 million. The net loss was also partially offset by $1.2 million increase in working capital which is primarily related to the accrual of research and development tax credit reimbursement due from the tax authority.

Net Cash Used in Investing Activities

During the years ended December 31, 2021, 2020 and 2019, net cash used in investing activities was $7.6 million, $11.8 million and $0.9 million, respectively, primarily driven by purchases of property and equipment related to lab equipment and leasehold improvements.

Net Cash Provided by Financing Activities

During the year ended December 31, 2021, net cash provided in financing activities was $160.8 million, primarily related to the net proceeds from sales of our ADSs through our IPO.

During the year ended December 31, 2020, net cash provided by financing activities was $113.7 million, consisting of $43.9 million and $69.9 million net cash proceeds from our sale and issuance of Series B and Series C convertible preferred shares, respectively. The increase was also offset by the payment of initial public offering costs of $0.1 million.

During the year ended December 31, 2019, net cash provided by financing activities was $93.6 million, consisting of $13.3 million and $80.3 million net cash proceeds from our sale and issuance of Series A and Series B convertible preferred shares, respectively.

Funding Requirements

We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we advance the research activities, manufacturing and clinical trials of product candidates. In addition, following our IPO, we incur additional costs associated with operating as a public company, including significant legal, accounting, investor relations and other expenses that we did not incur as a private company.

We believe our existing cash and cash equivalents will enable us to fund our operating expenses and capital expenditure requirements into the second half of 2024. We have based these estimates on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we expect. As we progress with our development programs and the regulatory review process, we expect to incur significant expenses related to product manufacturing, pre-commercial activities and commercialization.

Because of the numerous risks and uncertainties associated with research, development and commercialization of product candidates and programs, we are unable to estimate the exact amount of our working capital requirements. Our future funding requirements will depend on and could increase significantly as a result of many factors, including:

- the initiation, progress, timing, costs and results of our pipeline discovery programs and clinical activities for our existing programs for advanced NSCLC and metastatic or recurrent melanoma, and any additional product candidates or follow-on indications that we may develop or pursue;
- the cost to establish, maintain, expand, enforce and defend the scope of our intellectual property portfolio, including the amount and timing of any payments we may be required to make, or that we may receive, in connection with licensing, preparing, filing, prosecuting, defending and enforcing any patents or other intellectual property rights;
- our ability to enroll clinical trials in a timely manner and to quickly resolve any delays or clinical holds that may be imposed on our development programs;
- timing delays with respect to development of our current and any future product candidates, including as a result of the COVID-19 pandemic;
- the costs of expanding our increasing manufacturing infrastructure and facilities to capacity to support the manufacture of larger quantities of our product candidates for clinical development and potential commercialization globally;
- the costs of expanding our facilities to accommodate our expected growth in personnel;
- the costs, timing and outcome of potential future commercialization activities, including manufacturing, marketing, sales and distribution for our product candidates for which we receive marketing approval;
- the extent to which we acquire technologies;
- the sales price and availability of adequate third-party coverage and reimbursement for our product candidates, if and when approved; and
- the costs of operating as a public company.

Until such time, if ever, that we can generate product revenue sufficient to achieve profitability, we expect to finance our cash needs through equity offerings, debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements. To the extent that we raise additional capital through the sale of equity, current ownership interests will be diluted. If we raise additional funds through government or third-party funding, collaboration agreements, strategic alliances, licensing arrangements or marketing and distribution arrangements, we may have to relinquish valuable rights to our

technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we are unable to raise additional funds when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves.

As of December 31, 2021, we are committed to make minimum payments of $13.2 million due for our office and laboratory space leases. See Note 9, "Leases," to our financial statements appearing at the end of this Annual Report for our annual expected payments under our operating lease obligations at December 31, 2021. In addition, we are committed to make payments of $7.4 million, with approximately $6.8 million to be made in 2022, for costs associated with our certain vendors, which we engaged to provide clinical trial materials and contractual commitments for capital expenditures. These purchase commitments included non-cancellable minimum quantities to be purchased as of December 31, 2021.

We enter into contracts in the normal course of business with CROs and other third-party vendors for clinical trials, clinical and commercial supply manufacturing, support for pre-commercial activities, research and development activities and other services and products for our operations. Our agreements generally provide for termination within 30 to 90 days of notice. Such agreements are cancellable contracts and have not been included above.

We may incur potential contingent payments upon our achievement of clinical, regulatory and commercial milestones, as applicable, or we may be required to make royalty payments under the CRT and/or Secarna license agreements. Due to the uncertainty of the achievement and timing of the events requiring payment under these agreements, the amounts to be paid by us are not fixed or determinable at this time and have not been included above.

Emerging Growth Company and Smaller Reporting Company Status

In April 2012, the JOBS Act was enacted. Section 107 of the JOBS Act provides that an "emerging growth company" may take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act for complying with new or revised accounting standards. Therefore, an emerging growth company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected to avail ourselves of this extended transition period and, as a result, we may adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for non-public companies instead of the dates required for other public companies. However, the Company may choose to early adopt these standards.

In addition, as an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable generally to public companies. These provisions include:

- reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- an exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting pursuant to the Sarbanes-Oxley Act; and
- an exemption from new or revised financial accounting standards until they would apply to private companies and from compliance with any new requirements adopted by the Public Company Accounting Oversight Board requiring mandatory audit firm rotation.

We may take advantage of these exemptions for up to the last day of the fiscal year ending after the fifth anniversary of our IPO or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company on the date that is the earliest of: (i) the last day of the fiscal year in which we have total annual gross revenues of $1.07 billion or more; (ii) December 31, 2026, which is the last day of our fiscal year following the fifth anniversary of the date of the completion of our IPO; (iii) the date on which we have issued more than $1.0 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the SEC. We may choose to take advantage of some but not all of these exemptions.

Recently Issued Accounting Pronouncements

A description of recently issued accounting pronouncements that may potentially impact our financial position and results of operations is disclosed in Note 2, "Summary of significant accounting policies" to our financial statements appearing at the end of this Annual Report.

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

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

D. Trend Information.

See Item 4.B. "Information on the Company—Business Overview," Item 5.A. "Operating and Financial Review and Prospects—Operating Results" and Item 5.B. "Operating and Financial Review and Prospects—Liquidity and Capital Resources" within this Annual Report.

E. Critical Accounting Estimates

Critical Accounting Policies and Significant Judgments and Estimates

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

While our significant accounting policies are described in more detail in Note 2 to our financial statements appearing at the end of this Annual Report, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our financial statements.

Accrued Research and Development Expenses

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

- vendors in connection with preclinical development activities; and
- CROs and investigative sites in connection with preclinical studies and clinical trials.

We base our expenses related to research activities and clinical trials on our estimates of the services received and efforts expended pursuant to quotes and contracts with multiple research institutions and CROs that conduct and manage clinical trials on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense.

Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the estimate, we adjust the accrual or the amount of prepaid expenses accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting amounts that are too high or too low in any particular period. To date, there have not been any material adjustments to our prior estimates of accrued research and development expenses.

Share-Based Compensation

We measure share-based awards granted to employees, non-employees and directors based on the fair value on the date of the grant. Forfeitures are accounted for as they occur. We issue share-based awards with service-based vesting conditions and/or performance-based vesting conditions. For equity awards that vest based on a service condition, the share-based compensation expense is recognized on a straight-line basis over the requisite service period. For equity awards that vest based on a combination of service and performance conditions, we recognize share-based compensation expense using a straight-line basis over the requisite service period when the achievement of a performance-based milestone is probable, based on the relative satisfaction of the performance condition as of the reporting date.

Determination of the Fair Value of the Share Options

Prior to our IPO, the estimated fair value of the ordinary shares underlying our ADSs had been determined by our board of directors as of the date of each award grant, with input from management, considering our most recently available third-party valuations of our common stock and our board of directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent valuation through the date of the grant. Subsequent to our IPO, the fair value of our ordinary shares underlying our ADSs is based on quoted market prices. We measure share options granted to employees based on the fair value on the date of the grant and recognize the corresponding compensation expense of those share options over the requisite service period, which is generally the vesting period of the respective share options. We have only issued share options with service-based vesting conditions and record the expense for these awards using the straight-line method.

We estimate the fair value of each share options grant using the Black-Scholes option-pricing model, which uses as inputs the estimated fair value of our ordinary shares and assumptions we make for the volatility of our ordinary shares, the expected term of our share options, the risk-free interest rate for a period that approximates the expected term of our share options and our expected dividend yield.

We determined the assumptions for the Black-Scholes option-pricing model as discussed below. Each of these inputs is subjective and generally requires significant judgment to determine.

- Fair Value of our Ordinary Shares. Prior to the completion of our IPO, our ordinary shares were not publicly traded, and therefore we estimated the fair value of our ordinary shares on the basis referred to above. Subsequent to the IPO, the fair value of each share option grant is estimated on the date of grant using the Black-Scholes option pricing model applying assumptions used in connection with share option grants made during the periods covered.

- Expected Term. The expected term represents the period that the share-based awards are expected to be outstanding. The expected term of share options granted has been determined using the simplified method as there is a limited trading history of our ordinary shares, which uses the midpoint between the vesting date and the contractual term.
- Risk-Free Interest Rate. The risk-free interest rate is based on the U.S. Treasury yield curve in effect at the date of grant for zero-coupon U.S. Treasury constant maturity notes with terms approximately equal to the share-based award's expected term.
- Expected Volatility. Because we have a limited trading history of our ordinary shares, the expected volatility was derived from the average historical stock volatilities of several public companies within our industry that we consider to be comparable to our business over a period equivalent to the expected term of the share-based awards.
- Dividend Rate. The expected dividend is zero as we have not paid and do not anticipate paying any dividends in the foreseeable future.

If any of the assumptions used in the Black-Scholes model change significantly, share-based compensation for future awards may differ materially compared with the awards granted previously.

Leases

Our right of use assets and lease liabilities associated with leases for leasehold properties are recognized at 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, we use the incremental borrowing rates based on indicative borrowing rates that would be available based on the value, currency and borrowing term provided by financial institutions, adjusted for company and market specific factors. This incremental borrowing rate is the rate of interest that we would have to pay to borrow on a collateralized basis an amount equal to the lease payments over a similar term 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. Although we do not expect our estimates of the incremental borrowing rate, or IBR, to generate material differences within a range of sensitivities, judgment is involved in selecting an appropriate rate and the rate selected for each lease will have an impact on the value of the right-of-use asset and corresponding lease liability in the consolidated balance sheets.

Item 6. Directors, Senior Management and Employees.

A. Directors and Senior Management.

The following table sets forth the name, age and position of our senior management and directors as of the date of this Annual Report. Unless otherwise stated, the business address of our members of senior management and our directors

is c/o Achilles Therapeutics plc, 245 Hammersmith Road, London, W6 8PW, United Kingdom. Less than a majority of the directors of our board of directors are citizens or residents of the United States.

Name	Age	Position
Senior Management:		
Iraj Ali, Ph.D.	46	Chief Executive Officer and Director
Robert Coutts	38	Chief Financial Officer
Karl Peggs. M.D.	55	Chief Medical Officer
Sergio Quezada, Ph.D.	47	Chief Scientific Officer
Non—Executive Directors:		
Edwin Moses. Ph.D.[(1)(2)(3)]	67	Chairman of the Board of Directors Director
Michael F. Giordano. M.D. [(2)(3)(4)]	64	Director
Carsten Boess [(1)(2)(3)]	55	Director
Derek DiRocco. Ph.D.[(1)]	41	Director
Julie ONeill	55	Director

(1) Member of Audit Committee
(2) Member of Remuneration Committee
(3) Member of Nominating Committee
(4) Member of Research & Development Committee

Senior Management

Iraj Ali, *Ph.D.* has served as our Chief Executive Officer since January 2018 and a member of our board of directors since March 2016. Previously, Dr. Ali served as a Managing Partner of Syncona Ltd., or Syncona, a leading healthcare investment company focused on founding, building and funding global leaders in life sciences and a major shareholder of our company, from December 2016 to December 2018. Dr. Ali was also an Investment Partner at Syncona from September 2012 to December 2018. Dr. Ali has a Ph.D. in Biochemistry from Cambridge University and a B.S. in Biochemistry from the University of Reading. We believe that Dr. Ali is qualified to serve on our board of directors because of his experience, qualifications, attributes and skills, including his extensive global pharmaceutical experience.

Robert Coutts has served as our Chief Financial Officer since November 2020. Previously, Mr. Coutts served as our Finance Director, from November 2017 to November 2020 and as Subsidiary Financial Controller at Syncona from June 2015 to November 2017. Mr. Coutts has a M.Sc. in Management from the Cass Business School, City University and a B.A. in Politics, Philosophy and Economics from New College, Oxford University and is a qualified chartered accountant.

Karl Peggs, M.D. is one of our founders and has served as our Chief Medical Officer since January 2021. From May 2016 to December 2020, Dr. Peggs served on our board of directors. Dr. Peggs received a M.A. from Cambridge University, a M.B., B.Ch. from Oxford University Medical School and is a Member of the Royal College of Medicine and Fellow of the Royal College of Pathologists.

Sergio Quezada, Ph.D. is one of our founders and has served as our Chief Scientific Officer since April 2020. He has also been a Professor of Cancer Immunology and Immunotherapy at University College London Cancer Institute since January 2011, as well as a Cancer Research UK, or CRUK, senior cancer research fellow since January 2011. Previously, Dr. Quezada co-led the development of novel antibody for the depletion of regulatory T cells for TUSK Therapeutics Ltd., a company focused on developing novel immuno-oncology products. Dr. Quezada holds a Ph.D. from Dartmouth Medical School and a B.S. in Biochemistry and Molecular Biology from the Pontificia Universidad Católica de Chile. From 2004 to 2010, Dr. Quezada completed his post-doctoral training at Memorial Sloan-Kettering Cancer Center.

Non-Executive directors

Edwin Moses, Ph.D. has served as the Chairman and a member of our board of directors since December 2018. He was the Chief Executive Officer of Ablynx N.V., or Ablynx, a biopharmaceutical company, a position he held from March 2006 until Ablynx's acquisition by Sanofi in June 2018. Dr. Moses also served on the board of directors of Ablynx from 2004 until 2018. Dr. Moses received his B.S. and Ph.D. in Chemistry from the University of Sheffield. We believe that Dr. Moses is qualified to serve on our board of directors because of his experience, qualifications, attributes and skills, including his extensive executive experience.

Michael F. Giordano, M.D. has served on our board of directors since September 2018. Dr. Giordano has served as a Clinical Advisor and Interim Chief Medical Officer to Epizyme, Inc., or Epizyme, a biopharmaceutical company, from December 2017 to August 2018. From 1999 to 2017, Dr. Giordano worked at Bristol-Myers Squibb Company, a pharmaceutical company, most recently serving as Senior Vice President and Head of Development, Oncology and Immuno-Oncology from February 2012 to February 2017. Dr. Giordano has also served on the board of directors of Epizyme since March 2018 and on the board of directors of RAPT Therapeutics, Inc. since February 2018. He earned his M.D. and completed his residency and fellowship training at New York Presbyterian-Weill Cornell Medical Center, and received his B.A. in Natural Sciences from The Johns Hopkins University. We believe that Mr. Giordano is qualified to serve on our board of directors because of his experience, qualifications, attributes and skills, including his extensive pharmaceutical experience.

Carsten Boess has served on our board of directors since April 2020. Previously, Mr. Boess was the Executive Vice President of Corporate Affairs at Kiniksa Pharmaceuticals, Ltd., a biotechnology company, from August 2015 until February 2020. Mr. Boess has also served as a director for Rocket Pharmaceuticals, Inc. since January 2016, Avidity Biosciences, Inc. since April 2020, and Health Sciences Acquisition Corp. 2 since August 2020. Mr. Boess received a B.S. and M.S. in Economics and Finance, specializing in Accounting and Finance, from the University of Odense, Denmark. We believe that Mr. Boess is qualified to serve on our board of directors because of his experience, qualifications, attributes and skills, including his extensive executive experience.

Derek DiRocco, Ph.D. has served as a member of our board of directors since September 2019. Dr. DiRocco has been a Principal at RA Capital Management, L.P., or RA Capital, an investment advisory firm that invests in healthcare and life science companies and a major shareholder of our company, since December 2017 and was previously an analyst at RA Capital from June 2015 to December 2017. Dr. DiRocco has served on the board of directors of 89bio, Inc. since April 2018 and on the board of directors for iTeos Therapeutics, Inc. since March 2020. Dr. DiRocco holds a B.A. in Biology from College of the Holy Cross and a Ph.D. in pharmacology from the University of Washington. We believe that Dr. DiRocco is qualified to serve on our board of directors because of his experience, qualifications, attributes and skills, including his extensive biotechnology industry experience.

Julie O'Neill has served as a member of our board of directors since May 2021. Ms. O'Neill has more than two decades of executive experience in senior leadership roles. From January 2015 to September 2018, Ms. O'Neill served as Executive Vice President, Global Operations at Alexion Pharmaceuticals, Inc., or Alexion, a pharmaceutical company, where she led the Global Operations business including product development, manufacturing, quality, supply chain and global real estate functions. Prior to joining Alexion, she served as Vice President of Operations and General Manager of Ireland at Gilead Sciences, Inc., a pharmaceutical company, from 2011 to 2014. Ms. O'Neill serves as a member of the board of directors of ICON plc, DBV Technologies S.A. and Hookipa Pharma Inc. She is also on the Board of Ireland's National Institute for Bioprocessing Research & Training and serves on the Strategy Committee of the State Claims Agency in Ireland. We believe that Ms. O'Neill is qualified to serve on our board of directors because of her experience, qualifications, attributes and skills, including her extensive biotechnology experience.

Board Diversity

The table below provides certain information regarding the diversity of our board of directors as of the date of this Annual Report.

Board Diversity Matrix				
Country of Principal Executive Offices	United Kingdom			
Foreign Private Issuer	Yes			
Disclosure Prohibited under Home Country Law	No			
Total Number of Directors	6			
	Female	**Male**	**Non-Binary**	**Did Not Disclose Gender**
Part I: Gender Identity				
Directors	1	5	0	0
Part II: Demographic Background				
Underrepresented Individual in Home Country Jurisdiction	1			
LGBTQ+	1			
Did Not Disclose Demographic Background	0			

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Family Relationships

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

B. Compensation.

The following section provides the amount of compensation paid, and benefits in-kind granted, by us and our subsidiaries to our directors, members of our senior management and non-employee directors for services in all capacities to us and our subsidiaries for the year ended December 31, 2021.

Director Compensation

For the year ended December 31, 2021, the table below sets forth the compensation paid to our directors (in thousands):

Name	Salary/Fees	Bonus	Pension Benefit	All Other Compensation	Total
Executive Director					
Iraj Ali	$ 413	$ 157	$ 25	$ 1,243	$ 1,838
Non-Executive Directors					
Carsten Boess	$ 95	-	-	$ 109	$ 204
Derek Di Rocco	$ 56	-	-	$ 41	$ 97
Edwin Moses	$ 146	-	-	$ 347	$ 493
Julie O'Neill	$ 50	-	-	$ 41	$ 91
Michael Giordano	$ 83	-	-	$ 167	$ 250

Non-Executive Letters of Appointment

The compensation of our non-executive directors is determined by our board of directors as a whole, based, in part, on a review of current practices in other companies. We have entered into appointment letters with our non-executive directors and these agreements provide for an annual fee and a grant of share options under our share incentive plan arrangement. Non-Executive Directors are subject to re-election annually at the Annual General Meeting.

Employment Agreements

We have entered into employment agreements with our chief executive officer, or CEO, who is our sole executive director and the wider senior management. Each of these employment agreements provides for an initial annual salary, discretionary annual bonus opportunity and equity incentive opportunities, as well as participation in certain retirement and welfare benefit plans. The agreements provide payment in lieu of notice termination rights and we are required to give six months' prior written notice of a termination of employment. These agreements contain intellectual property and confidentiality provisions which survive termination and also contain 12-month non-competition and non-solicitation restrictive covenants.

Incentive Compensation Program

The board of directors maintains an annual incentive compensation program for all employees. The incentive compensation program is designed to offer incentive compensation to our employees by rewarding the achievement of company goals and specifically measured personal goals that are consistent with and support the achievement of the company goals. The key terms of the incentive compensation program are summarized below.

Administration and Eligibility. The board of directors is responsible for the oversight and administration of the incentive compensation program at a company level and manages this through delegation to the remuneration committee of the board. This remuneration committee is responsible for approving any incentive awards to our chief

executive officer and other members of our senior management. The CEO is responsible for approving any incentive awards to other employees, in accordance with parameters set by the remuneration committee.

Form and Determination of Incentive Awards. Incentive award payments are paid in cash. After the end of the plan year under review, the actual achievement of the company and individual goals is determined resulting in the calculation of the individual's total incentive award. Payment of incentive awards is made in February.

Termination of Employment. If a participant in the incentive compensation program gives or receives notice of termination of her or his employment prior to the payment of an incentive award under the incentive compensation program, the employee is not eligible to receive an incentive award.

Amendment. Our board of directors or the remuneration committee of the board, may abolish or alter the incentive compensation program at any time before, during or after a plan year is completed.

Outstanding Equity Awards

The following table summarizes the options that we granted to members of our board of directors and senior management during the year ended December 31, 2021:

	Ordinary Shares Underlying Option Covered	Exercise Price	Expiration Date
Senior Management:			
Iraj Ali	136,305	$ 15.28	6/27/2031
Robert Coutts	51,796	$ 15.28	6/27/2031
Karl Peggs	90,870	$ 15.28	6/27/2031
Sergio Quezada	76,331	$ 15.28	6/27/2031
Non-Executive Directors:			
Carsten Boess	15,000	$ 15.28	6/27/2031
Derek DiRocco	15,000	$ 15.28	6/27/2031
Michael Giordano	15,000	$ 15.28	6/27/2031
Edwin Moses	15,000	$ 15.28	6/27/2031
Julie O'Neill	15,000	$ 15.28	6/27/2031

No options were exercised by any members of our board of directors and senior management during the year ended December 31, 2021.

Employee Shares and Options issued prior to IPO

Under our shareholder and subscription agreements, which were effective until the date of IPO, the Company was authorized to grant equity awards to individuals including a director of and/or a person who is employed by or who directly or indirectly provides consultancy services to us, in the form of D, E, F, G, H, I, J, K, L, M and N ordinary shares, collectively referred to as Employee Shares and share options. All Employee Shares converted into ordinary shares in accordance with the reverse share split implemented on IPO (see Note 1 to our financial statements appearing at the end of this Annual Report). The share options granted prior to IPO were granted pursuant to the terms of the 2020 Share Omnibus Plan, or the 2020 Plan.

Upon and following closing of the IPO, no further equity awards were granted under the 2020 Plan. To the extent outstanding options granted under the 2020 Plan are cancelled, forfeited or otherwise terminated without being exercised and would otherwise have been returned to the share reserve under the 2020 Plan, the number of shares underlying such awards will be available for future grant under our 2021 Omnibus Plan (see below). In anticipation of IPO, we and the holders of Employee Shares entered into individual vesting agreements, or Vesting Agreements, which apply the same terms to vesting of Employee Shares as applied prior to IPO under our pre-IPO Articles of

Association, except that following the IPO Employee Shares that would pre-IPO have converted to deferred shares, will be transferred back to us and cancelled within twelve months of an employee leaving employment with us.

2021 Share Omnibus Plan

In March 2021, our board of directors adopted, and our shareholders approved, the 2021 Share Omnibus Plan, or the 2021 Plan, which became effective upon the effectiveness of our Registration Statement on Form F-1 in connection with the IPO. The 2021 Plan allows the remuneration committee to make equity-based and cash-based incentive awards to our officers, employees, directors and other key persons (including consultants).

We initially reserved 2,572,558 of our ordinary shares for the issuance of awards under the 2021 Plan. The 2021 Plan provides that the number of shares reserved and available for issuance under the plan will automatically increase each January 1, beginning on January 1, 2022, by 4% of the outstanding number of ordinary shares on the immediately preceding December 31, or such lesser number of shares as determined by our remuneration committee. This number is subject to adjustment in the event of a sub-division, consolidation, share dividend or other change in our capitalization. The total number of ordinary shares that may be issued under the 2021 Plan was 2,572,558 shares as of December 31, 2021, of which 1,578,993 shares remained available for future grant.

2021 Employee Share Purchase Plan

Our 2021 Employee Share Purchase Plan, or ESPP, was adopted by our board of directors in March 2021 and approved by shareholders in March 2021 and became effective upon the effectiveness of our Registration Statement on Form F-1 in connection with the IPO. The ESPP initially reserves and authorizes the issuance of up to a total of 467,738 ordinary shares to participating employees. The ESPP provides that the number of shares reserved and available for issuance will automatically increase each January 1, beginning on January 1, 2022 and each January 1 thereafter through January 1, 2022, by the least of (i) 1% of the outstanding number of ordinary shares on the immediately preceding December 31; (ii) 467,738 ordinary shares or (iii) such number of shares as determined by the remuneration committee. The number of shares reserved under the ESPP is subject to change in the event of a share split, share dividend or other change in our capitalization. The total number of ordinary shares that may be issued under the ESPP was 467,738 shares as of December 31, 2021, of which 467,738 shares remained available for future grant. As of December 31, 2021, the initial purchase period under the ESPP had not yet commenced.

Employee Shares

We typically grant incentive shares which vest over a four-year service period with 25% of the award vesting on the first anniversary of the vesting commencement date, and the balance vesting periodically over the remaining three years.

Unvested Employee Shares are forfeited upon the giving or receiving of notice of termination of employment or service relationship in accordance with our Articles (prior to IPO, and in accordance with the Vesting Agreements post-IPO) and 2020 Plan. Before IPO, the forfeited shares were converted into deferred shares, with a repurchase right for a nominal amount in favor of us. As of December 31, 2020, we repurchased 1,509,384 deferred shares with the consideration of £0.01 to each holder for all of the deferred shares held by that holder. As part of our reorganization, 109,058 outstanding deferred shares immediately before the IPO were cancelled upon IPO, and a single deferred share with a nominal value of £92,451.851 in the capital of the Company was created. As of December 31, 2021, we had one deferred share which could be repurchased by us at any time for nil consideration.

We measure all share-based awards using the fair value on the date of grant and recognize compensation expense for those awards over the requisite service period, which is generally the vesting period of the respective award. We have granted Employee Shares to employees and non-employees with service-based conditions and record expense for these awards using the straight-line method.

IPO Grants

In connection with our IPO and in the ordinary course thereafter, our board of directors granted awards under the 2021 Plan to certain of our employees, representing an aggregate of 897,243 ordinary shares. These awards are one-time

grants solely related to the IPO offering and the number of ordinary shares subject to the awards described above were priced at a premium to the market at the time of grant. The exercise price of these options was set at $15.28. Each award is subject to the terms and conditions of the 2021 Plan and an option award agreement entered into with the applicable grantee.

C. Board Practices.

Composition of our Board of Directors

Our board of directors presently has six members. As a foreign private issuer, under the listing requirements and rules of Nasdaq, we are not required to have independent directors on our board of directors, except that our audit committee is required to consist fully of independent directors. However, our board of directors has determined that Dr. Moses, Mr. Boess, Mr. Giordano, Ms. O'Neill and Dr. DiRocco, representing five of our six directors, do not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of director and that each of these directors is "independent" as that term is defined under Nasdaq rules.

In accordance with our Articles of Association, our board of directors will consist of one class of directors constituting our entire board. At each annual general meeting, the successors to directors will be elected to serve from the time of election and qualification until the subsequent annual meeting following election. Each director shall serve until his or her successor is duly elected and qualified or until his or her earlier death, resignation or removal.

Committees of our Board of Directors

Our board of directors has three standing committees: an audit committee, a remuneration committee and a nominating committee. The board has adopted a written charter for each of the committees below that is available to shareholders on our website at https://www.achillestx.com.

Audit Committee

The audit committee is composed of Mr. Boess (chairman), Dr.. Moses and Dr.. DiRocco, and assists the board of directors in overseeing our accounting and financial reporting processes. The audit committee consists exclusively of members of our board who are financially literate, and our board of directors has determined that Mr. Boess is an "audit committee financial expert" as defined by applicable SEC rules and has the requisite financial sophistication as defined under the applicable Nasdaq rules and regulations. Our board of directors has determined that each member of the audit committee is an independent director under Nasdaq listing rules and under Rule 10A-3 under the Exchange Act. Our audit committee meets at least four times per year and oversees and reviews our internal controls, accounting policies and financial reporting, and provides a forum through which our independent registered public accounting firm reports. Our audit committee meets regularly with our independent registered public accounting firm without management present.

The primary functions of the audit committee include:

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

- reviewing, approving or ratifying any related party transactions.

Remuneration Committee

The remuneration committee is composed of Dr. Moses (chairman), Mr. Boess and Dr. Giordano. Under SEC and Nasdaq rules, there are heightened independence standards for members of the compensation committee, including a prohibition against the receipt of any compensation from us other than standard board member fees. Although foreign private issuers are not required to meet this heightened standard, all of our compensation committee members meet this heightened standard.

The primary functions of the compensation committee include:

- identifying, reviewing, overseeing and proposing policies relevant to the compensation and benefits of our directors and senior management;
- evaluating the performance of senior management in light of such policies and reporting to the board; and
- overseeing and administering our share option plan, equity incentive plan and other benefit plans in operation from time to time.

Nominating Committee

The nominating committee is composed of Dr.. Moses (chairman), Mr. Boess and Mr. Giordano.

The primary functions of the nominating committee include:

- drawing up selection criteria and appointment procedures for directors; and
- recommending nominees for appointment to our board of directors and its corresponding committees.

D. Employees.

We have made significant investments in our business to support future growth, including a substantial increase in our global employee base. As of December 31, 2021, 2020 and 2019, we had 252, 159 and 75 employees, respectively

	As of December 31,		
	2021	2020	2019
Function:			
General and administrative	42	30	12
Research and development	210	129	63
Total	252	159	75
Geography:			
United Kingdom	243	157	75
United States	9	2	—
Total	252	159	75

We have no collective bargaining agreements with our employees and we have not experienced any labor strikes.

E. Share Ownership.

For information regarding the share ownership of our directors and executive officers, please refer to Item 6.B. “Directors, Senior Management and Employees—Compensation,” Item 7.A. “Major Shareholders and Related Party Transactions—Major Shareholders” and Item 7.B. “Major Shareholders and Related Party Transactions—Related Party Transactions.”

Item 7. Major Shareholders and Related Party Transactions.

A. Major Shareholders.

The following table sets forth information, as of February 1, 2022, regarding the beneficial ownership of our ordinary shares for:

- each beneficial owner of 5% or more of our outstanding ordinary shares;
- each of our directors and members of senior management; and
- all of our directors and senior management as a group.

Beneficial ownership is determined in accordance with the rules of the SEC. These rules generally attribute beneficial ownership of securities to persons who possess sole or shared voting power or investment power with respect to those securities and include ordinary shares that can be acquired within 60 days of February 1, 2022. In computing the number of shares beneficially owned by a person and the percentage ownership of such person, we deemed to be outstanding all shares subject to options held by the person that are currently exercisable or are exercisable within 60 days of February 1, 2022 or issuable upon the conversion of Class A ordinary shares held by the person. However, except as described above, we did not deem such shares outstanding for the purpose of computing the percentage ownership of any other person.

The percentage of shares beneficially owned is computed on the basis of 38,987,122 ordinary shares outstanding (including ordinary shares in the form of ADS calculated as set out above) as of February 1, 2022.

To our knowledge, as of February 24, 2022, 38,987,122 ADSs were held by one record holder in the United States, representing approximately 96.02% of our total outstanding shares. The record holder is The Bank of New York Mellon, the depositary of our ADS program. The number of beneficial owners of our ADSs in the United States is likely to be much larger than the number of record holders of our ADSs in the United States.

Except as otherwise indicated, all of the shares reflected in the table are ordinary shares, which may be in the form of ADSs, and all persons listed below have sole voting and investment power with respect to the shares beneficially owned by them, subject to applicable community property laws. The information is not necessarily indicative of beneficial ownership for any other purpose.

Except as otherwise indicated in the table below, the address of each of the directors, executive officers and named beneficial owners is c/o Achilles Therapeutics plc, 245 Hammersmith Road, London, W6 8PW, United Kingdom.

NAME OF BENEFICIAL OWNER	Number of Ordinary Shares Beneficially Owned (#)	Percentage of Ordinary Shares Beneficially Owned (#)
5% or Greater Shareholders:		
Syncona Portfolio Limited[1]	11,086,909	28.44%
Entities affiliated with RA Capital Management, L.P.[2]	5,014,687	12.86%
Forbion Capital Fund IV Cooperatief U.A.[3]	2,390,050	6.13%
Entities affiliated with Baker Bros. Advisors LP[4]	4,039,480	9.99%
Entities affiliated with Invus Public Equities, L.P.[5]	2,255,375	5.78%
Entities affiliated with Redmile Group, LLC[6]	2,088,089	5.36%
Executive Officers and Directors:		
Iraj Ali	844,631	2.17%
Robert Coutts	132,657	*
Karl Peggs	453,686	1.16%
Sergio Quezada	302,860	*
Edwin Moses	226,250	*
Carsten Boess[7]	35,874	*
Derek DiRocco		*
Michael Giordano[8]	108,553	*
Julie O′Neill		*
All directors and senior management as a group (9 persons)	2,104,511	5.38%

* Represents beneficial ownership of less than one percent.

1. The information shown is based, in part, upon disclosures filed on a Schedule 13G/A on February 11th, 2022 by Syncona Portfolio Limited. Syncona Portfolio Limited is a controlled subsidiary of Syncona Holdings Limited, which in turn is a controlled subsidiary of Syncona Limited. Each of Syncona Holdings Limited and Syncona Limited may be deemed to have voting and dispositive power over the shares held by Syncona Portfolio Limited. Investment and voting decisions with respect to these shares are made by Syncona Portfolio Limited acting upon the recommendation of an investment committee of Syncona Investment Management Limited, also a subsidiary of Syncona Holdings Limited. The members of this investment committee consist of Martin Murphy and Chris Hollowood. For the purposes of Section 13 of the Securities Exchange Act 1934 and the associated SEC Schedule 13G form reporting requirement, each of these entities and individuals disclaims beneficial ownership of these shares except to the extent of any pecuniary interest therein. Martin Murphy, who was formerly a member of our board of directors, is the chief executive officer of Syncona Investment Management Limited. The address for Syncona Investment Management Limited is 2nd Floor, 8 Bloomsbury Street, London WC1B 3SR. The address for Syncona Portfolio Limited is Arnold House, St Julian's Avenue, St Peter Port, Guernsey GY1 3RD.

2. Based on information reported by RA Capital Management, L.P. (the "Adviser"). Consists of (i) 4,050,972 Ordinary Shares held by RA Capital Healthcare Fund, L.P. ("RA Healthcare") and (ii) 963,715 Ordinary Shares held by RA Capital Nexus Fund, L.P. ("RA Nexus"). The Adviser is the investment manager for RA Healthcare and RA Nexus. Derek DiRocco, a Partner at the Adviser, is a member of our board of directors. The general partner of the Adviser is RA Capital Management GP, LLC, (the "Adviser GP"), of which Dr. Peter Kolchinsky and Mr. Rajeev Shah are the managing members. The Adviser, the Adviser GP, Dr. Kolchinsky, and Mr. Shah may be deemed to have voting and investment power over the shares held of record by RA Healthcare and RA Nexus. The Adviser, the Adviser GP, Dr. Kolchinsky, and Mr. Shah disclaim beneficial ownership of such shares, except to the extent of their pecuniary interest therein. The address for the entities listed above is 200 Berkeley Street, 18th Floor, Boston, Massachusetts 02116.

3. The information shown is based, in part, upon disclosures filed on a Form 13G/A on February 11, 2022 by Forbion Capital Fund IV Coöperatief U.A.. or FCF IV. Forbion IV Management B.V., or Forbion Management, the director of FCF IV, may be deemed to have voting and dispositive power over the shares held by FCF IV. Investment decisions with respect to the common shares held by FCF IV can be made by its investment committee which may delegate such powers to the authorized representatives of Forbion Management. Mssrs. Slootweg, van Osch, Mulder, van Houten, van Deventer, Reithinger, Kersten and Rooswinkel and Boorsma are partners of Forbion Management, which acts as the investment advisor to the directors of FCF IV. Rogier Rooswinkel, who was formerly a member of our board of directors, is a partner of Forbion Management and a member of the investment committee of Forbion Management. Forbion Management disclaims beneficial ownership of the shares, except to the extent of their pecuniary interest therein. The address of FCFIV and Forbion Management are Gooimeer 2-35, 1411 DC Naarden, The Netherlands.

4. The information shown is based, in part, upon disclosures filed on a Form 13F on February 14, 2022 by Baker Bros. Advisors LP, and in part upon disclosures filed on a Form 13G/A on February 14, 2022 by Baker Bros. Advisors LP. The number consists of 2,591,366 Ordinary Shares and 1,448,144 Class A non-voting shares. The Class A non-voting ordinary shares are only convertible to the extent that after giving effect to such conversion the holder thereof, their affiliates and any persons who are members of a Section 13(d) group with the holders or their affiliates would beneficially own in the aggregate, for purposes of Rule 13d-3 under the Exchange Act, no more than 9.99% of the outstanding Ordinary Shares ("Beneficial Ownership Limitation"). By written notice to the Company, each holder of Class A non-voting ordinary shares may from time to time increase the Beneficial Ownership Limitation, applicable to that holder to any other percentage not in excess of 19.9%. Any such increase will not be effective until the 61st day after such notice is delivered to the Company. As a result of this restriction, the number of Ordinary Shares that may be issued upon conversion of the Class A non-voting ordinary shares by the above holders may change depending upon changes in the outstanding Ordinary Shares. We refer to 667, L.P. and Baker Brothers Life Sciences, L.P. together as the Baker Entities. Baker Bros. Advisors LP is the investment advisor of the Baker Entities and has sole voting and dispositive power with respect to the ordinary shares held by the Baker Entities. Baker Bros. Advisors (GP) LLC is the sole general partner of Baker Bros. Advisors LP. The managing members of Baker Bros. Advisors (GP) LLC are Julian C. Baker and Felix J. Baker and, as such, they may be deemed to have voting and dispositive power with respect to the ordinary shares held by the Baker Entities. Julian C. Baker and Felix J. Baker disclaim beneficial ownership of the ordinary shares held by the Baker Entities except to the extent of their pecuniary interest. The address for both Baker Brothers Life Sciences, L.P. and 667, L.P. is 860 Washington Street, 3rd Floor, New York, New York 10014.

5. Invus Public Equities Advisors, LLC ("Invus PE Advisors"), as the general partner of Invus Public Equities, L.P., controls Invus Public Equities, L.P. and, accordingly, may be deemed to beneficially own the Shares held by Invus Public Equities, L.P.. The Geneva branch of Artal International S.C.A. ("Artal International"), as the managing member of Invus PE Advisors, controls Invus PE Advisors and, accordingly, may be deemed to beneficially own the Shares that Invus PE Advisors may be deemed to beneficially own. Artal International Management S.A. ("Artal International Management"), as the managing partner of Artal International, controls Artal International and, accordingly, may be deemed to beneficially own the Shares that Artal International may be deemed to beneficially own. Artal Group S.A. ("Artal Group"), as the sole stockholder of Artal International Management, controls Artal International Management and, accordingly, may be deemed to beneficially own the Shares that Artal International Management may be deemed to beneficially own. Westend S.A. ("Westend"), as the parent company of Artal Group, controls Artal Group and, accordingly, may be deemed to beneficially own the Shares that Artal Group may be deemed to beneficially own. Stichting Administratiekantoor Westend ("The Stichting"), as the majority stockholder of Westend, controls Westend and, accordingly, may be deemed to beneficially own the Shares that Westend may be deemed to beneficially own. Mr. Amaury Wittouck, as the sole member of the board of the Stichting, controls the Stichting and, accordingly, may be deemed to beneficially own the Shares that the Stichting may be deemed to beneficially own. The address for both Invus Public Equities, L.P. and Invus Public Equities Advisors, LLC is 750 Lexington Avenue 30th Floor New York, NY 10022 United States.

6. The information shown is based, in part, upon disclosures included on a Schedule 13G filed on February 14th, 2022 by Redmile Group, LLC. Redmile Group, LLC's beneficial ownership of the Company's American Depositary Shares, each representing one Ordinary Share £0.001 par value ("ADSs"), is owned by certain private investment vehicles managed by Redmile Group, LLC, which ADSs may be deemed beneficially owned by Redmile Group, LLC as investment manager of such private investment vehicles. The reported securities may also be deemed beneficially owned by Jeremy C. Green as the principal of Redmile Group, LLC. Redmile Group, LLC and Mr. Green each disclaim beneficial ownership of these shares, except to the extent of its or his pecuniary interest in such shares, if any. The address for this beneficial owner is c/o Redmile Group, LLC, 1 Letterman Drive, Building D Suite D3-300, San Francisco, CA 94129.

7. Consists of 35,874 of our ordinary shares issuable upon exercise of options within 60 days of February 1, 2022.

8. Consists of: (i) 46,663 of our ordinary shares; and (ii) 61,890 of our ordinary shares issuable upon exercise of options within 60 days of February 1, 2022.

B. Related Party Transactions.

Within this section, we have calculated the dollar amounts using the historical exchange rate as of the date of each transaction. Other than compensation arrangements described elsewhere in this document, since January 1, 2018, we have engaged in the transactions set out below with our executive officers, directors or holders of more than 5% of our share capital, including their affiliates, which we refer to as our 'related parties'.

In connection with the subscriptions of our preferred shares, we entered into subscription and shareholder agreements containing information rights, among other things, with certain holders of our preferred shares. These shareholder agreements terminated upon the consummation of our IPO, except for the registration rights granted under our registration rights agreement, as more fully described in our prospectus dated March 30, 2021, filed with the SEC pursuant to Rule 424(b), under the heading "Description of share capital and articles of association—Registration rights."

Pursuant to the Series A shareholder agreement, Syncona companies, or Syncona, including Syncona Portfolio Limited, provided us with the services of up to two directors appointed to our board of directors, from March 2017 to September 2019. Pursuant to the shareholder agreement, if Syncona appointed a director or directors to our board of directors, we were obligated to pay Syncona £20,000 annually per such director appointed to our board or directors. In connection with these appointments, we paid Syncona less than £0.1 million and less than £0.1 million for the years ended December 31, 2018 and 2019, respectively. The Series A shareholder agreement terminated in September 2019, upon the adoption of our Series B shareholder agreement.

Private Placements of Securities

All shares issued by the Company prior to our IPO were converted on IPO into ordinary shares, class A ordinary shares or deferred shares.

Series C Financing

On November 19, 2020, we sold 24,412,603 of our Series C preferred shares at a price per share of £2.1589 and for aggregate gross proceeds of £52,704,368.62.

The following table summarizes the participation in the Series C preferred financing by related persons, or their respective affiliates:

Shareholder	Series C preferred shares	Total purchase price
Entities affiliated with RA Capital Management L.P.[1]	1,830,251	£ 3,951,328.89
Forbion Capital Fund IV Cooperatief U.A.[2]	1,067,646	2,304,940.95
F Entities affiliated with Baker Bros. Advisors LP [3]	10,190,375	22,000,000.59
Total	13,088,272	£28,256,270.43

(1) Represents 1,252,330 Series C preferred shares purchased by RA Capital Healthcare Fund, L.P., 457,563 Series C preferred shares purchased by RA Capital Nexus Fund, L.P. and 120,358 Series C preferred shares purchased by Blackwell Partners LLC – Series A. Derek DiRocco serves as a member of our board of directors and is an affiliate of RA Capital Management, L.P., of which RA Capital Healthcare Fund, L.P. RA Capital Nexus Fund, L.P. and Blackwell Partners LLc – Series A are affiliated entities. Entities affiliated with RA Capital Management, L.P. hold more than 5% of our voting securities.

(2) Rogier Rooswinkel served as a member of our board of directors until June 28, 2021 and is an affiliate of Forbion IV Management B.V., of which Forbion Capital Fund IV Cooperatief U.A. is an affiliated fund. Forbion Capital Fund IV Cooperatief U.A. holds more than 5% of our voting securities.

(3) Represents 9,412,141 Series C preferred shares purchased by Baker Brothers Life Sciences, L.P. and 778,234 Series C preferred shares purchased by 667, L.P. Entities affiliated with Baker Bros. Advisors LP hold more than 5% of our voting securities.

Series B Financing

On September 2, 2019, we agreed to sell 52,192,070 of our Series B preferred shares at a price per share of £1.916 and for aggregate gross proceeds of £100.0 million. This financing was structured in two tranches. The first tranche of this financing closed in September 2019, at which time we sold 34,794,714 Series B preferred shares for aggregate gross proceeds of £66.7 million. The second tranche of this financing closed in November 2020, at which time we sold 17,397,356 Series B preferred shares for aggregate gross proceeds of £33.3 million.

The following table summarizes the participation in the Series B preferred financing by related persons, or their respective affiliates:

Shareholder	Series B preferred shares	Total purchase price
Syncona Portfolio Limited [1]	18,313,675	£35,089,001.30
Entities affiliated with RA Capital Management L.P.[2]	12,526,096	23,999,999.94
Forbion Capital Fund IV Cooperatief U.A.[3]	7,306,890	14,000,001.24
Entities affiliated with Baker Bros. Advisors LP[4]	2,609,604	5,000,001.27
Total	40,756,265	£78,089,003.75

(1) Martin Murphy served as a member of our board of directors until immediately prior to the closing of our initial public offering and is the Chief Executive Officer of Syncona Investment Management Limited, an affiliate of Syncona Portfolio Limited, which holds more than 5% of our voting securities.

(2) Represents 7,979,144 Series B preferred shares purchased by RA Capital Healthcare Fund, L.P., 3,131,524 Series B preferred shares purchased by RA Capital Nexus Fund, L.P. and 1,415,428 Series B preferred shares purchased by Blackwell Partners LLC – Series A. Derek DiRocco serves as a member of our board of directors and is an affiliate of RA Capital Management, L.P., of which RA Capital Healthcare Fund, L.P. RA Capital Nexus Fund, L.P. and Blackwell Partners LLC – Series A are affiliated entities. Entities affiliated with RA Capital Management, L.P. hold more than 5% of our voting securities.

(3) Rogier Rooswinkel served as a member of our board of directors until June 28, 2021 and is an affiliate of Forbion IV Management B.V., of which Forbion Capital Fund IV Cooperatief U.A. is an affiliated fund.

Forbion Capital Fund IV Cooperatief U.A. holds more than 5% of our voting securities.

(4) Represents 2,392,748 Series B preferred shares purchased by Baker Brothers Life Sciences, L.P. and 216,856 Series B preferred shares purchased by 667, L.P. Entities affiliated with Baker Bros. Advisors LP hold more than 5% of our voting securities.

Agreements with Shareholders

In connection with the subscriptions of our preferred shares, we entered into subscription and shareholder agreements containing information rights, among other things, with certain holders of our preferred shares. These shareholder agreements terminated upon the consummation of our initial public offering, except for the registration rights granted under our registration rights agreement, as more fully described in our prospectus dated March 30, 2021, filed with the SEC pursuant to Rule 424(b), under the heading "Description of share capital and articles of association—Registration rights."

Pursuant to the Series A shareholder agreement, Syncona companies, or Syncona, including Syncona Portfolio Limited, provided us with the services of up to two directors appointed to our board of directors, from March 2017 to September 2019. Pursuant to the shareholder agreement, if Syncona appointed a director or directors to our board of directors, we were obligated to pay Syncona £20,000 annually per such director appointed to our board or directors. In connection with these appointments, we paid Syncona less than £0.1 million and less than £0.1 million for the years ended December 31, 2018 and 2019, respectively. The Series A shareholder agreement terminated in September 2019, upon the adoption of our Series B shareholder agreement.

Agreement with Syncona Management

We entered into a services agreement with Syncona Management LLP in May 2016, which was assigned in December 2016 to Syncona Investment Management Limited, or Syncona Management. Syncona Management is a management services entity affiliated with Syncona. Pursuant to the services agreement, Syncona Management provided us with certain services, including the services of Chris Ashton, as our former Chief Executive Officer, from May 2016 to December 2017, and Iraj Ali, as our Chief Executive Officer, from January 2018 to December 2018. In connection with these services, we paid Syncona Management less than £0.2 million for the year ended December 31, 2018 and £0 for each of the years ended December 31, 2019 and 2020. Syncona holds more than 5% of our voting securities.

Agreements with our Senior Management and Directors

We have entered into employment agreements with certain members of our management and service agreements with our non-executive directors and officers. These agreements contain customary provisions and representations, including confidentiality, non-competition, non-solicitation and inventions assignment undertakings by the executive officers and non-executive directors. The enforceability of the non-competition provisions may be limited under applicable law.

Indemnification Agreements

To the extent permitted by the Companies Act 2006 and in accordance with our Articles of Association, we are empowered to indemnify our directors against any liability they incur by reason of their role. Prior to the completion of our IPO, we obtained and maintain directors' and officers' insurance to insure such persons against certain liabilities. We entered into a deed of indemnity with each of our directors, members of our senior management and

other officers. These agreements and our Articles of Association require us to indemnify our directors, members of our senior management and other officers to the fullest extent permitted by law.

Participation in our Initial Public Offering

In March 2020, we sold an aggregate of 9,750,000 ADSs in our initial public offering at a price of $18.00 per ADS. Certain related parties made purchases of our ADSs in our initial public offering as follows:

Shareholder	Number of ADSs	Total purchase price
RA Capital Management, LP	1,388,888	$24,999,984
Forbion Capital Fund IV	275,000	4,950,000
Baker Bros. Advisors LP	975,000	17,550,000
Total	2,638,888	$47,499,984

Related Party Transaction Policy

We have adopted a related party transaction policy. This policy became effective on March 30, 2021, the date on which our registration statement on Form F-1 in connection with our IPO was declared effective by the SEC. Pursuant to this policy, the audit and risk committee has the primary responsibility for reviewing and approving or disapproving "related party transactions," which are transactions between us and related parties in which the related party has a direct or indirect material interest. For purposes of this policy, a related party is defined as a director, executive director, nominee for director, or greater than 5% beneficial owner of any class of our voting securities, and their immediate family members.

C. Interests of Experts and Counsel.

Not applicable.

Item 8. Financial Information.

A. Consolidated Statements and Other Financial Information.

Consolidated Financial Statements

Our consolidated financial statements are included at the end of this Annual Report in "Item 18.Financial Statements."

Legal Proceedings

From time to time, we are subject to various legal proceedings and claims that arise in the ordinary course of our business activities. Although the results of litigation and claims cannot be predicted with certainty, as of the date of this report, we do not believe we are party to any claim or litigation, the outcome of which, if determined adversely to us, would individually or in the aggregate be reasonably expected to have a material adverse effect on our business. Regardless of the outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

Within the past twelve months, we have not been party to any litigation, arbitration proceedings or administrative proceedings that may have a material effect on our financial condition or profitability, and we are not aware of any such proceedings pending or being threatened.

Dividend Distribution Policy

We have not paid any dividends on our ordinary shares since our inception, and we currently intend to retain any future earnings to finance the growth and development of our business. Therefore, we do not anticipate that we will declare or pay any cash dividends in the foreseeable future. Under English law, among other things, we may only pay dividends if we have sufficient distributable reserves (on a non-consolidated basis), which are our accumulated realized profits that have not been previously distributed or capitalized less our accumulated realized losses, so far as such losses have not been previously written off in a reduction or reorganization of capital.

B. Significant Changes.

Not applicable.

Item 9. The Offer and Listing.

A. Offer and Listing Details.

Our ADSs have been listed on Nasdaq Global Select Market under the symbol "ACHL" since March 31, 2021. Prior to that date, there was no public trading market for our ADSs.

B. Plan of Distribution.

Not applicable.

C. Markets.

Our ADSs have been listed on Nasdaq Global Select Market under the symbol "ACHL" since March 31, 2021.

D. Selling Shareholders.

Not applicable.

E. Dilution.

Not applicable.

F. Expenses of the Issue.

Not applicable.

Item 10. Additional Information.

A. Share Capital.

Not applicable.

B. Memorandum and Articles of Association.

The information set forth in our prospectus dated March 30, 2021, filed with the SEC pursuant to Rule 424(b), under the headings "Description of share capital and articles of association—Issued share capital," "Description of share capital and articles of association—Ordinary shares," "Description of share capital and articles of association—Class A ordinary shares," "Description of share capital and articles of association—Deferred shares," "Description of share capital and articles of association—Registration rights," "Description of share capital and articles of association—Key provisions of our post-IPO articles of association," "Description of share capital and articles of association—Other relevant UK laws and regulations," "Description of share capital and articles of association—Differences in corporate law," and "Service of process and enforcement of liabilities" is incorporated herein by reference.

C. Material Contracts.

For additional information on our material contracts, please see the sections of this Annual Report titled "Item 4—Information on the Company," "Item 7.A.—Major Shareholders," and "Item 7.B.—Related Party Transactions."

D. Exchange Controls.

There are no governmental laws, decrees, regulations or other legislation in the United Kingdom that may affect the import or export of capital, including the availability of cash and cash equivalents for use by us, or that may affect the remittance of dividends, interest, or other payments by us to non-resident holders of our ordinary shares or ADSs, other than withholding tax requirements. There is no limitation imposed by the laws of England and Wales or our Articles of Association on the right of non-residents to hold or vote shares.

E. Taxation.

The following summary contains a description of material UK and U.S. federal income tax consequences of the acquisition, ownership and disposition of our ordinary shares or ADSs.

UK Taxation

The following is intended as a general guide to current UK tax law and HM Revenue & Customs, or HMRC, published practice (which is not binding) applying as at the date of this Annual Report (both of which are subject to change at any time, possibly with retrospective effect) relating to the holding of ADSs. It does not constitute legal or tax advice and does not purport to be a complete analysis of all UK tax considerations relating to the holding of ADSs, or all of the circumstances in which holders of ADSs may benefit from an exemption or relief from UK taxation. It is written on the basis that we do not (and will not) directly or indirectly at any time derive 75% or more of our qualifying asset value from UK land, and that we are and will remain solely resident in the UK for tax purposes and will therefore be

subject to the UK tax regime and not the U.S. tax regime save as set out above under "Material U.S. Federal Income Tax Considerations for U.S. Holders."

Except to the extent that the position of non-UK resident persons is expressly referred to, this guide relates only to persons who are resident (and in the case of individuals, domiciled or deemed domiciled) for tax purposes solely in the UK and do not have a permanent establishment, branch or agency (or equivalent) in any other jurisdiction with which the holding of the ADSs is connected, or UK Holders, who are absolute beneficial owners of the ADSs (and do not hold the ADSs through an Individual Savings Account or a Self-Invested Personal Pension) and any dividends paid in respect of the ADSs or underlying ordinary shares (where the dividends are regarded for UK tax purposes as that person's own income) and who hold their ADSs as investments.

This guide may not relate to certain classes of UK Holders, such as (but not limited to):

- persons who are connected with us;
- financial institutions;
- insurance companies;
- charities or tax-exempt organizations;
- collective investment schemes;
- pension schemes;
- market makers, intermediaries, brokers or dealers in securities;
- persons who have (or are deemed to have) acquired their ADSs by virtue of an office or employment or who are or have been our officers or employees or any of our affiliates; and
- individuals who are subject to UK taxation on a remittance basis or to whom split-year treatment applies.

The decision of the First-tier Tribunal (Tax Chamber) in HSBC Holdings PLC and The Bank of New York Mellon Corporation v HMRC (2012) cast some doubt on whether a holder of a depositary receipt is the beneficial owner of the underlying shares. However, based on published HMRC guidance we would expect that HMRC will regard a holder of ADSs as holding the beneficial interest in the underlying shares and therefore these paragraphs assume that a holder of ADSs is the beneficial owner of the underlying ordinary shares and any dividends paid in respect of the underlying ordinary shares (where the dividends are regarded for UK purposes as that person's own income) for UK direct tax purposes.

THESE PARAGRAPHS ARE A SUMMARY OF CERTAIN UK TAX CONSIDERATIONS AND ARE INTENDED AS A GENERAL GUIDE ONLY. IT IS RECOMMENDED THAT ALL HOLDERS OF ADSs OBTAIN ADVICE AS TO THE CONSEQUENCES OF THE ACQUISITION, OWNERSHIP AND DISPOSAL OF THE ADSs IN THEIR OWN PARTICULAR CIRCUMSTANCES FROM THEIR OWN TAX ADVISORS. IN PARTICULAR, NON-UK RESIDENT OR DOMICILED PERSONS OR PERSONS SUBJECT TO TAXATION IN ANY JURISDICTION OTHER THAN THE UK ARE ADVISED TO CONSIDER THE POTENTIAL IMPACT OF ANY RELEVANT DOUBLE TAXATION AGREEMENTS.

Dividends

Dividend Distribution Policy

We have not paid any dividends on our ordinary shares since our inception, and we currently intend to retain any future earnings to finance the growth and development of our business. Therefore, we do not anticipate that we will declare or pay any cash dividends in the foreseeable future. Under English law, among other things, we may only pay dividends if we have sufficient distributable reserves (on a non-consolidated basis), which are our accumulated

realized profits that have not been previously distributed or capitalized less our accumulated realized losses, so far as such losses have not been previously written off in a reduction or reorganization of capital.

Withholding Tax

Dividends that we pay will not be subject to any withholding or deduction for or on account of UK tax.

Income Tax

An individual UK Holder may, depending on his or her particular circumstances, be subject to UK tax on dividends received from us. An individual holder of ADSs who is not resident for tax purposes in the UK should not be chargeable to UK income tax on dividends received from us unless he or she carries on (whether solely or in partnership) a trade, profession or vocation in the UK through a branch or agency to which the ADSs are attributable. There are certain exceptions for trading in the UK through independent agents, such as some brokers and investment managers.

Dividend income is treated as the top slice of the total income chargeable to UK income tax for an individual UK Holder. An individual UK Holder who receives a dividend in the 2021/2022 tax year will be entitled to a dividend tax-free allowance of £2,000. Income within the dividend tax-free allowance counts towards an individual's basic or higher rate limits and may, therefore, affect the level of income tax personal allowance to which they are entitled. Dividend income in excess of the dividend tax-free allowance will (subject to the availability of any income tax personal allowance) be charged at 7.5% to the extent the excess amount falls within the basic rate band, 32.5% to the extent the excess amount falls within the higher rate band, and 38.1% to the extent the excess amount falls within the additional rate band. The government has announced that dividend tax rates will increase by 1.25% from April 2022. The dividend tax-free allowance of £2,000 will remain unaffected. The new rates (expected to be legislated in Finance Bill 2022) will be: basic rate at 8.75%, higher rate at 33.75%, and additional rate at 39.35%.

Corporation Tax

A corporate holder of ADSs who is not resident for tax purposes in the UK should not be chargeable to UK corporation tax on dividends received from us unless it carries on (whether solely or in partnership) a trade in the UK through a permanent establishment to which the ADSs are attributable.

Corporate UK Holders should not be subject to UK corporation tax on any dividend received from us so long as the dividends qualify for exemption, which should be the case, although certain conditions must be met. It should be noted that the exemptions, whilst of wide application, are not comprehensive and are subject to anti-avoidance rules in relation to a dividend. If the conditions for the exemption are not satisfied, such anti-avoidance provisions apply, or such UK Holder elects for an otherwise exempt dividend to be taxable, UK corporation tax will be chargeable on the amount of any dividends (at the current rate of 19% for the tax year 2021/2022 rising to 25% in the tax year 2023/2024 for companies with profits of more than £250,000 whilst the rate of 19% will apply to companies with profits not exceeding £50,000 with a tapered rate applying to profits between £50,000 and £250,000).

Chargeable Gains

A disposal or deemed disposal of ADSs by a UK Holder may, depending on the UK Holder's circumstances and subject to any available exemptions or reliefs (such as the annual exemption), give rise to a chargeable gain or an allowable loss for the purposes of UK capital gains tax and corporation tax on chargeable gains.

If an individual UK Holder who is subject to UK income tax at either the higher or the additional rate is liable to UK capital gains tax on the disposal of ADSs, the current applicable rate will be 20% (for the tax year 2021/2022). For an individual UK Holder who is subject to UK income tax at the basic rate and liable to UK capital gains tax on such disposal, the current applicable rate would be 10% (for the tax year 2021/2022), save to the extent that any capital

gains when aggregated with the UK Holder's other taxable income and gains in the relevant tax year exceed the unused basic rate tax band. In that case, the rate currently applicable to the excess would be 20% (for the tax year 2021/2022).

If a corporate UK Holder becomes liable to UK corporation tax on the disposal (or deemed disposal) of ADSs, the main rate of UK corporation tax would apply (currently at 19% for the tax year 2021/2022 rising to 25% in the tax year 2023/2024 for companies with profits of more than £50,000 whilst the rate of 19% will apply to companies with profits not exceeding £250,000 with a tapered rate applying to profits between £50,000 and £250,000).

Any chargeable gain (or allowable loss) will generally be calculated by reference to the consideration received for the disposal of the ADSs less the allowable cost to the UK Holder of acquiring such ADSs.

A holder of ADSs that is not resident for tax purposes in the UK and, in the case of an individual holder, not temporarily non-resident in the UK, should not normally be liable to UK capital gains tax or corporation tax on chargeable gains on a disposal (or deemed disposal) of ADSs, unless the person is carrying on (whether solely or in partnership) a trade, profession or vocation in the UK through a branch or agency (or, in the case of a corporate holder of ADSs, through a permanent establishment) to which the ADSs are attributable. However, an individual holder of ADSs who has ceased to be resident for tax purposes in the UK or is treated as resident outside the UK for the purposes of a double taxation treaty for a period of five years or less and who disposes of ADSs during that period of temporary non-residence may be liable on his or her return to the UK (or upon ceasing to be regarded as resident outside the UK for the purposes of double taxation treaty) to UK tax on any capital gain realized (subject to any available exemption or relief).

Stamp Duty and Stamp Duty Reserve Tax

The discussion below relates to the holders of our ordinary shares or ADSs wherever resident, however it should be noted that special rules may apply to certain persons such as market makers, brokers, dealers or intermediaries.

Issue of Ordinary Shares

As a general rule (and except in relation to depositary receipt systems and clearance services (as to which see below)), no UK stamp duty or stamp duty reserve tax, or SDRT, is payable on the issue of the ordinary shares underlying the ADSs.

Transfers of Ordinary Shares

An unconditional agreement to transfer ordinary shares will normally give rise to a charge to SDRT at the rate of 0.5% of the amount or value of the consideration payable for the transfer. The purchaser of the shares is liable for the SDRT. Transfers of ordinary shares in certificated form are generally also subject to stamp duty at the rate of 0.5% of the amount or value of the consideration given for the transfer (rounded up to the next £5.00). Stamp duty is normally paid by the purchaser. The charge to SDRT will be cancelled or, if already paid, repaid (generally with interest), where a transfer instrument has been duly stamped within six years of the charge arising, (either by paying the stamp duty or by claiming an appropriate relief) or if the instrument is otherwise exempt from stamp duty.

Clearance Services and Depositary Receipts

Under current UK tax law and published HMRC practice, no SDRT (and, where the transfer is effected by a written instrument, stamp duty) is generally payable where, an issue or transfer of ordinary shares, including an unconditional agreement to transfer ordinary shares to a clearance service or a depositary receipt system (including to a nominee or agent for, a person whose business is or includes the issue of depositary receipts or the provision of clearance services) is an integral part of an issue of share capital unless the clearance service has made and maintained an election under section 97A of the UK Finance Act 1986, or a section 97A election. It is understood that HMRC regards the facilities

of DTC as a clearance service for these purposes and we are not aware of any section 97A election having been made by the DTC.

Any stamp duty or SDRT payable on a transfer of ordinary shares to a depositary receipt system or clearance service or in respect of a transfer within a depositary receipt system or clearance service, will strictly be accountable by the clearance service or depositary receipt system operator or their nominee, as the case may be, but will in practice generally be paid by the transferors or participants in the clearance service or depositary receipt system. Specific professional advice should be sought before incurring or reimbursing the costs of a 1.5% stamp duty or SDRT charge in any circumstances.

Issue or Transfers of ADSs

No UK stamp duty or SDRT is payable on the issue of ADSs in the Company.

No UK SDRT should be required to be paid in respect of a paperless transfer of ADSs through the facilities of DTC, provided that no election under section 97A of the UK Finance Act 1986 has been made by DTC, and such ADSs are held through DTC at the time of any agreement for their transfer.

No UK stamp duty will in practice be payable on a written instrument transferring an ADS provided that the instrument of transfer is executed and remains at all times outside the United Kingdom. Where these conditions are not met, the transfer of, or agreement to transfer, an ADS could, depending on the circumstances, attract a charge to UK stamp duty at the rate of 0.5% of the amount or value of the consideration. If it is necessary to pay stamp duty, it may also be necessary to pay interest and penalties.

No UK stamp duty or SDRT should be required to be paid on the issue or transfer of (including an agreement to transfer) ADSs in the Company.

U.S. Taxation

The following is a description of the material U.S. federal income tax consequences to the U.S. Holders described below of acquiring, owning and disposing of our ordinary shares or ADSs. It is not a comprehensive description of all tax considerations that may be relevant to a particular person's decision to acquire securities. This discussion applies only to a U.S. Holder that is an initial purchaser of the ordinary shares or ADSs pursuant to the offering and that holds our ordinary shares or ADSs as a capital asset for tax purposes (generally, property held for investment). In addition, it does not describe all of the tax consequences that may be relevant in light of a U.S. Holder's particular circumstances, including state and local tax consequences, estate or gift tax consequences, alternative minimum tax consequences, the potential application of the Medicare contribution tax, and tax consequences applicable to U.S. Holders subject to special rules, such as:

- banks, insurance companies, and certain other financial institutions;
- U.S. expatriates and certain former citizens or long-term residents of the United States;
- brokers, dealers or traders in securities, currencies, commodities, or notional principal contracts;
- persons holding ordinary shares or ADSs as part of a hedging transaction, "straddle," wash sale, conversion transaction or integrated transaction or persons entering into a constructive sale with respect to ordinary shares or ADSs;
- persons whose "functional currency" for U.S. federal income tax purposes is not the U.S. dollar;
- tax-exempt entities or government organizations, including an "individual retirement account" or "Roth IRA" as defined in Section 408 or 408A of the Code (as defined below), respectively;

- S corporations, partnerships (including entities or arrangements classified as partnerships for U.S. federal income tax purposes) or other pass-through entities, or persons that will hold our ordinary shares or ADSs through such an entity;
- regulated investment companies, grantor trusts or real estate investment trusts;
- persons that own or are deemed to own 10% or more of the voting power or value of all classes of our ordinary shares or ADSs;
- persons who acquired our ordinary shares or ADSs pursuant to the exercise of any employee stock option or otherwise as compensation;
- persons subject to Section 451(b) of the Code; and
- persons holding our ordinary shares or ADSs in connection with a trade or business, permanent establishment, or fixed base outside the United States.

If an entity that is classified as a partnership for U.S. federal income tax purposes holds ordinary shares or ADSs, the U.S. federal income tax treatment of a partner will generally depend on the status of the partner and the activities of the partnership. Partnerships holding our ordinary shares or ADSs and partners in such partnerships are encouraged to consult their tax advisors as to the particular U.S. federal income tax consequences of acquiring, holding and disposing of ordinary shares or ADSs.

The discussion is based on the Internal Revenue Code of 1986, as amended, or the Code, administrative pronouncements, judicial decisions, final, temporary and proposed Treasury Regulations, and the income tax treaty between the UK and the United States, all as of the date hereof, changes to any of which may affect the tax consequences described herein-possibly with retroactive effect. There can be no assurances that the Internal Revenue Service, or the IRS, will not take a contrary or different position concerning the tax consequences of the acquisition, ownership and disposition of our ordinary shares or ADSs or that such a position would not be sustained by a court. We have not obtained, nor do we intend to obtain, a ruling with respect to the U.S. federal income tax considerations relating to the purchase, ownership or disposition of our ordinary shares or ADSs. Holders should consult their own tax advisors concerning the U.S. federal, state, local and non-U.S. tax consequences of acquiring, owning and disposing of our ordinary shares or ADSs in their particular circumstances.

A "U.S. Holder" is a holder who, for U.S. federal income tax purposes, is a beneficial owner of our ordinary shares or ADSs and is:

(i) An individual who is a citizen or resident of the United States;

(ii) a corporation, or other entity taxable as a corporation for U.S. federal income tax purposes, created or organized in or under the laws of the United States, any state therein or the District of Columbia;

(iii) an estate the income of which is subject to U.S. federal income taxation regardless of its source; or

(iv) a trust if (1) a U.S. court is able to exercise primary supervision over the administration of the trust and one or more U.S. persons have authority to control all substantial decisions of the trust or (2) the trust has a valid election to be treated as a U.S. person under applicable U.S. Treasury Regulations.

The discussion below assumes that the representations contained in the deposit agreement are true and that the obligations in the deposit agreement and any related agreement will be complied with in accordance with their terms. Accordingly, a holder of an ADS should be treated for U.S. federal income tax purposes as holding the ordinary shares represented by the ADS and no gain or loss will generally be recognized upon an exchange of the ADSs for ordinary shares.

As indicated below, this discussion is subject to U.S. federal income tax rules applicable to a "passive foreign investment company," or PFIC.

PERSONS CONSIDERING AN INVESTMENT IN ORDINARY SHARES OR ADSs SHOULD CONSULT THEIR OWN TAX ADVISORS AS TO THE PARTICULAR TAX CONSEQUENCES APPLICABLE TO THEM RELATING TO THE ACQUISITION, OWNERSHIP AND DISPOSITION OF THE ORDINARY SHARES OR ADSs, INCLUDING THE APPLICABILITY OF U.S. FEDERAL, STATE, LOCAL AND NON-U.S. TAX LAWS.

Passive Foreign Investment Company Rules

If we are classified as a passive foreign investment company in any taxable year, in which a U.S. Holder holds the ordinary shares or ADSs, the U.S. Holder will be subject to special rules generally intended to reduce or eliminate any benefits from the deferral of U.S. federal income tax that a U.S. Holder could derive from investing in a non-U.S. company that does not distribute all of its earnings on a current basis.

A non-U.S. corporation will be classified as a PFIC for any taxable year in which, after applying certain look-through rules, either:

- at least 75% of its gross income is passive income (such as interest income), or the income test; or
- at least 50% of the value of its gross assets (determined on the basis of a quarterly average) is attributable to assets that produce passive income or are held for the production of passive income, or the asset test.

We will be treated as owning our proportionate share of the assets and earning our proportionate share of the income of any other entity treated as a corporation for U.S. federal income tax purposes, the equity of which we own, directly or indirectly, 25% or more (by value).

We believe that we were classified as a PFIC for our taxable year ended December 31, 2021. Based on the current and expected composition of our income and assets and the value of our assets, we expect to be a PFIC for the current taxable year ending December 31, 2022. However, no assurances regarding our PFIC status can be provided for any past, current or future taxable years. The determination of whether we are a PFIC is a fact-intensive determination made on an annual basis applying principles and methodologies that in some circumstances are unclear and subject to varying interpretation. As a result, our PFIC status may change from year to year. Subject to certain exceptions, for purposes of the asset test, if we are treated as a non-publicly traded CFC for the year being tested for purposes of the PFIC rules (which is determined, under certain proposed Treasury Regulations that are not yet effective, based on whether such shares and ADSs are publicly traded for the majority of days during the year), the value of our assets for purposes of the asset test will be measured by the adjusted tax basis of our assets, which could increase the likelihood that we are treated as a PFIC. If we are a publicly traded CFC or not a CFC for such year, the value of our assets generally will be determined by reference to the market price of our ordinary shares or ADSs from time to time, which may fluctuate considerably. The income test depends on the nature and composition of our income. The composition of our income and assets is also affected by how fast we spend the cash we raise in any offering.

If we are classified as a PFIC in any year with respect to which a U.S. Holder owns the ordinary shares or ADSs, we will continue to be treated as a PFIC with respect to such U.S. Holder in all succeeding years during which the U.S. Holder owns the ordinary shares or ADSs, regardless of whether we continue to meet the tests described above unless: (i) we cease to be a PFIC and the U.S. Holder has made a "deemed sale" election under the PFIC rules; or (ii) the U.S. Holder makes a Qualified Electing Fund Election, or QEF Election, as discussed below, with respect to all taxable years during such U.S. Holder's holding period in which we are a PFIC. If the "deemed sale" election is made, a U.S. Holder will be deemed to have sold the ordinary shares or ADSs the U.S. Holder holds at their fair market value and any gain from such deemed sale would be subject to the rules described below. After the deemed sale election, so long as we do not become a PFIC in a subsequent taxable year, the U.S. Holder's ordinary shares or ADSs with respect to which such election was made will not be treated as shares in a PFIC and the U.S. Holder will not be subject to the rules described below with respect to any "excess distribution" the U.S. Holder receives from us or any gain from an

actual sale or other disposition of the ordinary shares or ADSs. U.S. Holders should consult their tax advisors as to the possibility and consequences of making a deemed sale election if we cease to be a PFIC and such election becomes available.

For each taxable year we are treated as a PFIC with respect to a U.S. Holder, the U.S. Holder will be subject to special tax rules with respect to any "excess distribution" such U.S. Holder receives and any gain such U.S. Holder recognizes from a sale or other disposition (including, under certain circumstances, a pledge) of ordinary shares or ADSs, unless: (i) such U.S. Holder makes a QEF Election as discussed below; or (ii) our ordinary shares or ADSs constitute "marketable" securities, and such U.S. Holder makes a mark-to-market election as discussed below. Distributions a U.S. Holder receives in a taxable year that are greater than 125% of the average annual distributions the U.S. Holder received during the shorter of the three preceding taxable years or the U.S. Holder's holding period for the ordinary shares or ADSs will be treated as an excess distribution. Under these special tax rules:

- the excess distribution or gain will be allocated ratably over a U.S. Holder's holding period for the ordinary shares or ADSs;
- the amount allocated to the taxable year of the excess distribution or disposition, and any taxable year prior to the first taxable year in which we became a PFIC, will be treated as ordinary income; and
- the amount allocated to each other year will be subject to the highest tax rate in effect for that year for individuals or corporations, as appropriate, and the interest charge generally applicable to underpayments of tax will be imposed on the resulting tax attributable to each such year.

The tax liability for amounts allocated to years prior to the year of disposition or "excess distribution" cannot be offset by any net operating losses for such years, and gains (but not losses) realized on the sale of the ordinary shares or ADSs cannot be treated as capital gains, even if a U.S. Holder holds the ordinary shares or ADSs as capital assets.

If we are a PFIC, a U.S. Holder will generally be subject to similar rules with respect to distributions we receive from, and our dispositions of the stock of, any of our direct or indirect subsidiaries that also are PFICs, as if such distributions were indirectly received by, and/or dispositions were indirectly carried out by, such U.S. Holder. U.S. Holders should consult their tax advisors regarding the application of the PFIC rules to our subsidiaries.

Certain elections exist that may alleviate some of the adverse consequences of PFIC status and would result in an alternative treatment of the ordinary shares or ADSs. A U.S. Holder may avoid the general tax treatment for PFICs described above by electing to treat us as a "qualified electing fund" under Section 1295 of the Code, or QEF, for each of the taxable years during the U.S. Holder's holding period that we are a PFIC. If a QEF election is not in effect for the first taxable year in the U.S. Holder's holding period in which we are a PFIC, a QEF election generally can only be made if the U.S. Holder elects to make an applicable deemed sale or deemed dividend election on the first day of its taxable year in which the PFIC becomes a QEF pursuant to the QEF election. The deemed sale or deemed dividend recognized with respect to such an election would be subject to the general tax treatment of PFICs discussed above. We intend to determine our PFIC status at the end of each taxable year and to satisfy any applicable record keeping and reporting requirements that apply to a QEF, and will endeavor to provide to U.S. Holders, for each taxable year that we determine we are a PFIC, a PFIC Annual Information Statement containing information necessary for a U.S. Holder to make a QEF Election with respect to us. We may elect to provide such information on our website. However, U.S. Holders should be aware that we can provide no assurances that we will provide any such information relating to any of our subsidiaries that are PFICs.

If a U.S. Holder makes a QEF election with respect to a PFIC, it will be taxed currently on its pro rata share of the PFIC's ordinary earnings and net capital gain (at ordinary income and capital gain rates, respectively) for each taxable year that the entity is a PFIC, even if no distributions were received. Any distributions we make out of our earnings and profits that were previously included in such a U.S. Holder's income under the QEF election would not be taxable to such U.S. Holder. Such U.S. Holder's tax basis in its ordinary shares or ADSs would be increased by an amount equal to any income included under the QEF election and decreased by any amount distributed on the ordinary shares

or ADSs that is not included in its income. In addition, a U.S. Holder will recognize capital gain or loss on the disposition of its ordinary shares or ADSs in an amount equal to the difference between the amount realized and its adjusted tax basis in the ordinary shares or ADSs, each as determined in U.S. dollars. Once made, a QEF election remains in effect unless invalidated or terminated by the IRS or revoked by the shareholder. A QEF election can be revoked only with the consent of the IRS. A U.S. Holder will not be currently taxed on the ordinary earnings and net capital gain of a PFIC with respect to which a QEF election was made for any taxable year of the non-U.S. corporation that such corporation is not classified as a PFIC. Each U.S. Holder should consult its tax advisor regarding the availability of, and procedure for making, any deemed sale, deemed dividend or QEF election.

Alternatively, U.S. Holders can avoid the interest charge on excess distributions or gain relating to the ordinary shares or ADSs by making a mark-to-market election with respect to the ordinary shares or ADSs, provided that the ordinary shares or ADSs are "marketable." The ordinary shares or ADSs will be marketable if they are "regularly traded" on certain U.S. stock exchanges or on a foreign stock exchange that meets certain conditions. For these purposes, the ordinary shares or ADSs will be considered regularly traded during any calendar year during which they are traded, other than in de minimis quantities, on at least 15 days during each calendar quarter. Any trades that have as their principal purpose meeting this requirement will be disregarded. The ADSs are listed on Nasdaq, which is a qualified exchange for these purposes. Consequently, if the ADSs remain listed on Nasdaq and are regularly traded, and you are a U.S. Holder of the ADSs, we expect the mark-to-market election would be available to you if we are a PFIC. Each U.S. Holder should consult its tax advisor as to whether a mark-to-market election is available or advisable with respect to the ordinary shares or ADSs.

A U.S. Holder that makes a mark-to-market election must include in ordinary income for each year an amount equal to the excess, if any, of the fair market value of the ordinary shares or ADSs at the close of the taxable year over the U.S. Holder's adjusted tax basis in the ordinary shares or ADSs at that time. An electing U.S. Holder may also claim an ordinary loss deduction for the excess, if any, of the U.S. Holder's adjusted basis in the ordinary shares or ADSs over the fair market value of the ordinary shares or ADSs at the close of the taxable year, but this deduction is allowable only to the extent of any net mark-to-market gains for prior years. Gains from an actual sale or other taxable disposition of the ordinary shares or ADSs will be treated as ordinary income, and any losses incurred on a sale or other taxable disposition of the shares or ADSs will be treated as an ordinary loss to the extent of any net mark-to-market gains for prior years. Once made, the election cannot be revoked without the consent of the IRS, unless the ordinary shares or ADSs cease to be marketable.

However, a mark-to-market election generally cannot be made for equity interests in any lower-tier PFICs that we own, unless shares of such lower-tier PFIC are themselves "marketable." As a result, even if a U.S. Holder validly makes a mark-to-market election with respect to our ordinary shares or ADSs, the U.S. Holder may continue to be subject to the PFIC rules (described above) with respect to its indirect interest in any of the lower-tier PFICs. U.S. Holders should consult their tax advisors to determine whether any of these elections would be available and if so, what the consequences of the alternative treatments would be in their particular circumstances.

Unless otherwise provided by the U.S. Treasury, each U.S. shareholder of a PFIC is required to file an Annual Report containing such information as the U.S. Treasury may require. A U.S. Holder's failure to file the Annual Report will cause the statute of limitations for such U.S. Holder's U.S. federal income tax return to remain open with regard to the items required to be included in such report until three years after the U.S. Holder files the Annual Report, and, unless such failure is due to reasonable cause and not willful neglect, the statute of limitations for the U.S. Holder's entire U.S. federal income tax return will remain open during such period. U.S. Holders should consult their tax advisors regarding the requirements of filing such information returns under these rules.

WE STRONGLY URGE YOU TO CONSULT YOUR TAX ADVISOR REGARDING THE IMPACT OF OUR PFIC STATUS ON YOUR INVESTMENT IN THE ORDINARY SHARES OR ADSs AS WELL AS THE APPLICATION OF THE PFIC RULES TO YOUR INVESTMENT IN THE ORDINARY SHARES OR ADSs.

Taxation of Distributions

Subject to the discussion above under "Passive Foreign Investment Company Rules," distributions paid on our ordinary shares or ADSs, other than certain pro rata distributions of ordinary shares or ADSs, will generally be treated as dividends to the extent paid out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles). Distributions in excess of earnings and profits will be non-taxable to the U.S. Holder to the extent of, and will be applied against and reduce, the U.S. Holder's adjusted tax basis in the ordinary shares or the ADSs. Distributions in excess of earnings and profits and such adjusted tax basis will generally be taxable to the U.S. Holder as either long-term or short-term capital gain depending upon whether the U.S. Holder has held the ordinary shares or the ADSs for more than one year as of the time such distribution is received. However, because we may not calculate our earnings and profits under U.S. federal income tax principles (if we are not or cease to be a PFIC), we expect that distributions generally will be reported to U.S. Holders as dividends, even if that distribution would otherwise be treated as a non-taxable return of capital or as capital gain under the rules described above. Subject to applicable limitations, dividends paid to certain non-corporate U.S. Holders may be taxable at preferential rates applicable to "qualified dividend income" if we are a "qualified foreign corporation" and certain other requirements are met. However, the qualified dividend income treatment will not apply if we are treated as a PFIC with respect to the U.S. Holder for either the taxable year in which the dividend was paid or the preceding taxable year. The amount of the dividend will be treated as foreign-source dividend income to U.S. Holders and will not be eligible for the dividends-received deduction generally available to U.S. corporations under the Code. Dividends will generally be included in a U.S. Holder's income on the date of the U.S. Holder's receipt of the dividend. The amount of any dividend income paid in foreign currency will be the U.S. dollar amount calculated by reference to the exchange rate in effect on the date of actual or constructive receipt, regardless of whether the payment is in fact converted into U.S. dollars. If the dividend is converted into U.S. dollars on the date of receipt, a U.S. Holder should not be required to recognize foreign currency gain or loss in respect of the dividend income. A U.S. Holder may have foreign currency gain or loss if the dividend is converted into U.S. dollars after the date of receipt. Such gain or loss would generally be treated as U.S.-source ordinary income or loss. The amount of any distribution of property other than cash (and other than certain pro rata distributions of ordinary shares or ADSs or rights to acquire ordinary shares or ADSs) will be the fair market value of such property on the date of distribution.

For foreign tax credit limitation purposes, our dividends will generally be treated as passive category income. Because no UK income taxes will be withheld from dividends on ordinary shares or ADSs, there will be no creditable foreign taxes associated with any dividends that a U.S. Holder will receive. The rules governing foreign tax credits are complex and U.S. Holders should therefore consult their tax advisors regarding the effect of the receipt of dividends for foreign tax credit limitation purposes.

Sale or Other Taxable Disposition of Ordinary Shares and ADSs

Subject to the discussion above under "Passive Foreign Investment Company Rules," gain or loss realized on the sale or other taxable disposition of our ordinary shares or ADSs will be capital gain or loss, and will be long-term capital gain or loss if the U.S. Holder held the ordinary shares or ADSs for more than one year at the time of sale or other taxable disposition. The amount of the gain or loss will equal the difference between the U.S. Holder's tax basis in the ordinary shares or ADSs disposed of and the amount realized on the disposition, in each case as determined in U.S. dollars. This gain or loss will generally be U.S.-source gain or loss for foreign tax credit purposes. Subject to the PFIC rules described above, long-term capital gains recognized by certain non-corporate U.S. Holders (including individuals) will generally be subject to reduced rates of U.S. federal income tax. The deductibility of capital losses is subject to limitations.

If the consideration received by a U.S. Holder is not paid in U.S. dollars, the amount realized will be the U.S. dollar value of the payment received determined by reference to the spot rate of exchange on the date of the sale or other disposition. However, if the ordinary shares or ADSs are treated as traded on an "established securities market" and you are either a cash basis U.S. Holder or an accrual basis U.S. Holder that has made a special election (which must be applied consistently from year to year and cannot be changed without the consent of the IRS), you will determine

the U.S. dollar value of the amount realized in a non-U.S. dollar currency by translating the amount received at the spot rate of exchange on the settlement date of the sale. If you are an accrual basis U.S. Holder that is not eligible to or does not elect to determine the amount realized using the spot rate on the settlement date, you will recognize foreign currency gain or loss to the extent of any difference between the U.S. dollar amount realized on the date of sale or disposition and the U.S. dollar value of the currency received at the spot rate on the settlement date , and such gain or loss will generally constitute ordinary income or loss.

Information Reporting and Backup Withholding

Payments of dividends and sales proceeds that are made within the United States or through certain U.S.-related financial intermediaries generally are subject to information reporting, and may be subject to backup withholding, unless: (i) the U.S. Holder is a corporation or other exempt recipient; or (ii) in the case of backup withholding, the U.S. Holder provides a correct taxpayer identification number and certifies that it is not subject to backup withholding on a duly executed IRS Form W-9 or otherwise establishes an exemption.

The amount of any backup withholding from a payment to a U.S. Holder may be allowed as a credit against the U.S. Holder's U.S. federal income tax liability and may entitle the U.S. Holder to a refund, provided that the required information is timely furnished to the IRS.

Information Reporting and Information with Respect to Foreign Financial Assets

Certain U.S. Holders may be required to file IRS Form 926 (Return by a U.S. Transferor of Property to a Foreign Corporation) to report a transfer of property (including cash) to us. Substantial penalties may be imposed on a U.S. Holder that fails to comply with this reporting requirement and the period of limitations on assessment and collection of U.S. federal income taxes will be extended in the event of a failure to comply. In addition, certain U.S. Holders who are individuals (and, under regulations, certain entities) may be required to report information relating to the ordinary shares or ADSs, subject to certain exceptions (including an exception for ordinary shares or ADSs held in accounts maintained by certain U.S. financial institutions), by filing IRS Form 8938 (Statement of Specified Foreign Financial Assets) with their federal income tax return. Such U.S. Holders who fail to timely furnish the required information may be subject to a penalty. Additionally, if a U.S. Holder does not file the required information, the statute of limitations with respect to tax returns of the U.S. Holder to which the information relates may not close until three years after such information is filed. U.S. Holders should consult their tax advisors regarding their reporting obligations with respect to their ownership and disposition of the ordinary shares or ADSs and with respect to their possible obligation to file IRS Form 926.

F. Dividends and Paying Agents.

Not applicable.

G. Statement by Experts.

Not applicable.

H. Documents on Display.

We are subject to certain reporting requirements of the Exchange Act. As a "foreign private issuer," we are exempt from the rules under the Exchange Act prescribing certain disclosure and procedural requirements for proxy solicitations, and our officers, directors and principal shareholders are exempt from the reporting and "short-swing" profit recovery provisions contained in Section 16 of the Exchange Act, with respect to their purchases and sales of shares. In addition, we are not required to file reports and Financial Statements with the SEC as frequently or as promptly as companies that are not foreign private issuers whose securities are registered under the Exchange Act. However, we are required to file with the SEC, within 4 months after the end of each fiscal year, an Annual Report on Form 20-F containing Financial Statements audited by an independent accounting firm and interactive data

comprising Financial Statements in extensible business reporting language. We publish unaudited interim financial information after the end of each quarter. We furnish this quarterly financial information to the SEC under cover of a Form 6-K.

The SEC maintains a website at http://www.sec.gov that contains reports and other information regarding registrants that are required to file electronically with the SEC.

I. Subsidiary Information.

Not applicable.

Item 11. Quantitative and Qualitative Disclosures about Market Risk.

Market risk represents the risk that changes in market prices, such as foreign exchange rates, interest rates or equity prices, will affect Achilles's results of operations or the value of the financial instruments held. Achilles is exposed to both foreign currency exchange risk and interest rate risks.

Foreign Currency Exchange Risk

We maintain our financial statements in our functional currency, which is pound sterling. Monetary assets and liabilities denominated in currencies other than the functional currency are translated into the functional currency at rates of exchange prevailing at the balance sheet dates. Non-monetary assets and liabilities denominated in foreign currencies are translated into the functional currency at the exchange rates prevailing at the date of the transaction. Exchange gains or losses arising from foreign currency transactions are included in the determination of net income (loss) for the respective periods. We recorded foreign currency gains of $2.5 million, foreign currency gains of $0.1 million and foreign currency losses of $0.4 million and for the year ended December 31, 2021, 2020 and 2019, respectively. These exchange gains or losses arising from foreign currency transactions are included in other income (expense), net in the statement of comprehensive loss.

For financial reporting purposes our financial statements have been presented in U.S. dollars, the reporting currency. The financial statements of entities are translated from their functional currency into the reporting currency as follows: assets and liabilities are translated at the exchange rates at the balance sheet dates, revenue and expenses are translated at the average exchange rates and shareholders' equity is translated based on historical exchange rates. Translation adjustments are not included in determining net loss but are included as a foreign exchange adjustment to other comprehensive loss, a component of shareholders' equity.

We do not currently engage in currency hedging activities in order to reduce our currency exposure, but we may begin to do so in the future. Instruments that may be used to hedge future risks may include foreign currency forward and swap contracts. These instruments may be used to selectively manage risks, but there can be no assurance that we will be fully protected against material foreign currency fluctuations.

Interest Rate Risk

As of December 31, 2021, we had cash and cash equivalents of $266.3 million. Our exposure to interest rate sensitivity is impacted by changes in the underlying UK and U.S. bank interest rates. Our surplus cash has been invested in interest-bearing savings accounts and money market funds from time to time. We have not entered into investments for trading or speculative purposes. Due to the conservative nature of our investment portfolio, which is predicated on capital preservation of investments with short-term maturities, we do not believe an immediate one percentage point

change in interest rates would have a material effect on the fair market value of our portfolio, and therefore we do not expect our operating results or cash flows to be significantly affected by changes in market interest rates.

As of December 31, 2021 and 2020, we had no debt outstanding and are therefore not subject to interest rate risk related to debt.

Item 12. Description of Securities Other than Equity Securities.

A. Debt Securities.

Not Applicable.

B. Warrants and Rights.

Not applicable.

C. Other Securities.

Not applicable.

D. American Depositary Shares.

The Bank of New York Mellon, as depositary, registers and delivers ADSs. Each ADS represents one deposited share with The Bank of New York Mellon, as custodian for the depositary in United Kingdom. Each ADS also represents any other securities, cash or other property which may be held by the depositary. The depositary's office at which the ADSs will be administered is located at 240 Greenwich Street, New York, New York 10286. The Bank of New York Mellon's principal executive office is located at 240 Greenwich Street, New York, New York 10286.

A deposit agreement among us, the depositary and the ADS holders sets out the ADS holder rights as well as the rights and obligations of the depositary. New York law governs the deposit agreement and the ADSs. A copy of the deposit agreement is incorporated by reference as an exhibit to this Annual Report.

Fees and Expenses

Persons depositing or withdrawing shares or ADS holders must pay:	***For:***
$5.00 (or less) per 100 ADSs (or portion of 100 ADSs)	Issuance of ADSs, including issuances resulting from a distribution of shares or rights or other property
	Cancelation of ADSs for the purpose of withdrawal, including if the deposit agreement terminates
$0.05 (or less) per ADS	Any cash distribution to ADS holders
A fee equivalent to the fee that would be payable if securities distributed to you had been shares and the shares had been deposited for issuance of ADSs	Distribution of securities distributed to holders of deposited securities (including rights) that are distributed by the depositary to ADS holders
$0.05 (or less) per ADS per calendar year	Depositary services
Registration or transfer fees	Transfer and registration of shares on our share register to or from the name of the depositary or its agent when you deposit or withdraw shares
Expenses of the depositary	Cable and facsimile transmissions (when expressly provided in the deposit agreement) Converting foreign currency to U.S. dollars
Taxes and other governmental charges the depositary or the custodian has to pay on any ADSs or shares	As necessary

underlying ADSs, such as stock transfer taxes, stamp duty or withholding taxes	
Any charges incurred by the depositary or its agents for servicing the deposited securities	As necessary

The depositary collects its fees for delivery and surrender of ADSs directly from investors depositing shares or surrendering ADSs for the purpose of withdrawal or from intermediaries acting for them. The depositary collects fees for making distributions to investors by deducting those fees from the amounts distributed or by selling a portion of distributable property to pay the fees. The depositary may collect its annual fee for depositary services by deduction from cash distributions or by directly billing investors or by charging the book-entry system accounts of participants acting for them. The depositary may collect any of its fees by deduction from any cash distribution payable (or by selling a portion of securities or other property distributable) to ADS holders that are obligated to pay those fees. The depositary may generally refuse to provide fee-attracting services until its fees for those services are paid.

From time to time, the depositary may make payments to us to reimburse us for costs and expenses generally arising out of establishment and maintenance of the ADS program, waive fees and expenses for services provided to us by the depositary or share revenue from the fees collected from ADS holders. In performing its duties under the deposit agreement, the depositary may use brokers, dealers, foreign currency dealers or other service providers that are owned by or affiliated with the depositary and that may earn or share fees, spreads or commissions.

The depositary may convert currency itself or through any of its affiliates and, in those cases, acts as principal for its own account and not as agent, advisor, broker or fiduciary on behalf of any other person and earns revenue, including, without limitation, transaction spreads, that it will retain for its own account. The revenue is based on, among other things, the difference between the exchange rate assigned to the currency conversion made under the deposit agreement and the rate that the depositary or its affiliate receives when buying or selling foreign currency for its own account. The depositary makes no representation that the exchange rate used or obtained in any currency conversion under the deposit agreement will be the most favorable rate that could be obtained at the time or that the method by which that rate will be determined will be the most favorable to ADS holders, subject to the depositary's obligations under the deposit agreement. The methodology used to determine exchange rates used in currency conversions is available upon request.

PART II

Item 13. Defaults, Dividend Arrearages and Delinquencies.

None.

Item 14. Material Modifications to the Rights of Security Holders and Use of Proceeds.

None.

Item 15. Controls and Procedures.

Disclosure Controls and Procedures

We maintain "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, that are designed 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 Officer and Chief Financial Officer, as appropriate to allow timely decisions regarding required disclosure. Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, has evaluated the effectiveness of our disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) as of December 31, 2021.

Based on such evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that, as of December 31, 2021, our disclosure controls and procedures were effective.

Management's Annual Report on Internal Control over Financial Reporting

This Annual Report does not include a report of management's assessment regarding internal control over financial reporting due to a transition period established by the SEC's rules for newly public companies.

Attestation Report of the Registered Public Accounting Firm

This Annual Report does not include an attestation report of our registered public accounting firm due to a transition period established by rules of the SEC for newly public companies. For so long as we qualify as an "emerging growth company" as defined under the JOBS Act, our registered public accounting firm is not required to issue an attestation report on our internal control over financial reporting.

Changes in Internal Control over Financial Reporting

We regularly review our system of internal control over financial reporting and make changes to our processes and systems to further strengthen controls and increase efficiency, while ensuring that we maintain an effective internal control environment. We have continued to expand the capacity and expertise of our internal accounting staff with appropriate expertise to perform specific functions and add additional depth to our technical accounting and financial reporting capabilities.

Other than the aforementioned changes, there were no further changes in our internal control over financial reporting (as defined in Rule 13a-15(f) of the Exchange Act) that occurred during the fiscal year 2021, which have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 16. [Reserved.]

Item 16A. Audit Committee Financial Expert.

Our board of directors has determined that Carsten Boess is an audit committee financial expert as defined by SEC rules and has the requisite financial sophistication under the applicable Nasdaq rules and regulations and that Carsten Boess is independent as such term is defined in Rule 10A-3 under the Exchange Act and under the listing standards of The Nasdaq Stock Market.

Item 16B. Code of Ethics.

We have adopted a written code of business conduct and ethics, or code of conduct, which outlines the principles of legal and ethical business conduct under which we do business. The code of conduct applies to all of our and our subsidiaries' employees, independent contractors, senior management and directors, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. The full text of the code of conduct is available on our website at *www.achillestx.com*. If we make any amendment to our code of conduct or grant any waivers, including any implicit waiver, from a provision of that code, we will disclose the nature of such amendment or waiver on our website to the extent required by the rules and regulations of the SEC.

Item 16C. Principal Accountant Fees and Services.

KPMG LLP, or KPMG, has served as our independent registered public accounting firm for the years ending December 31, 2021 and 2020. The following table sets out the aggregate fees for professional audit services and other services rendered by KPMG and their member firms and/or affiliates in 2021 and 2020 (in thousands):

	Year Ended December 31,	
Description	**2021**	**2020**
Audit fees	$ 798	$ 406
Fees for other assurance services	261	392
Total	$ 1,059	$ 798

Audit fees relate to the audit of the financial statements as set out in this Annual Report, audit of our internal control over financial reporting and services related to our statutory and regulatory filings of our subsidiaries.

Fees for other assurance services in 2021 relate to services in connection with a comfort letter.

The Audit Committee has approved the audit fees and all of the fees for other assurance services and other fees for other services for the years 2021 and 2020. The Audit Committee monitors compliance with the UK and U.S. rules on non-audit services provided by an independent registered public accounting firm. On a yearly basis, the Audit Committee pre-approves non-audit services performed by the independent registered public accounting firm up to a limit in line with UK regulation.

Item 16D. Exemptions from the Listing Standards for Audit Committees.

Not applicable.

Item 16E. Purchases of Equity Securities by the Issuer and Affiliated Purchasers.

Not applicable.

Item 16F. Change in Registrant's Certifying Accountant.

Not applicable.

Item 16G. Corporate Governance.

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

- exemption from filing quarterly reports on Form 10-Q containing unaudited financial and other specified information or current reports on Form 8-K upon the occurrence of specified significant events;
- exemption from Section 16 rules requiring insiders to file public reports of their stock ownership and trading activities and liability for insiders who profit from trades in a short period of time, which will provide less data in this regard than shareholders of U.S. companies that are subject to the Exchange Act;
- exemption from the Nasdaq requirement requiring disclosure of any waivers of the Code of Business Conduct and Ethics, or Code of Ethics, for directors and officers;
- exemption from the requirement to obtain shareholder approval for certain issuances of securities, including shareholder approval of share option plans;
- exemption from the requirement that our audit committee have review and oversight over all "related party transactions," as defined in Item 7.B of Form 20-F;
- exemption from the requirement that our board have a compensation committee that is composed entirely of independent directors with a written charter addressing the committee's purpose and responsibilities; and
- exemption from the requirement to have independent director oversight of director nominations.

We intend to follow UK corporate governance practices in lieu of Nasdaq corporate governance requirements as follows:

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

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

Because we are a foreign private issuer, our directors and senior management are not subject to short-swing profit and insider trading reporting obligations under Section 16 of the Exchange Act. They will, however, be subject to the obligations to report changes in share ownership under Section 13 of the Exchange Act and related SEC rules.

We intend to take all actions necessary for us to maintain compliance as a foreign private issuer under the applicable corporate governance requirements of the Sarbanes-Oxley Act, the rules adopted by the SEC and Nasdaq listing rules.

Accordingly, our shareholders will not have the same protections afforded to shareholders of companies that are subject to all of the corporate governance requirements of Nasdaq.

Item 16H. Mine Safety Disclosure.

Not applicable.

Item 16I. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections.

Not applicable.

PART III

Item 17. Financial Statements.

We have elected to provide financial statements pursuant to Item 18.

Item 18. Financial Statements.

The financial statements required under this Item 18 are filed as part of this Annual Report beginning on page 176. The audit report of KPMG LLP, independent registered public accounting firm, is included herein preceding the financial statements.

Report of Independent Registered Public Accounting Firm

To the Shareholders and Board of Directors
Achilles Therapeutics Plc

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Achilles Therapeutics plc (and subsidiaries) (the Company) as of December 31, 2021 and 2020, the related consolidated statements of operations and comprehensive loss, statements of shareholders' equity, and cash flows for each of the years in the three-year period ended December 31, 2021, and the related notes (collectively, the consolidated financial statements). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the years in the three-year period ended December 31, 2021, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

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

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

/s/ KPMG, LLP

We have served as the Company's auditor since 2020.

Reading, United Kingdom
1 March 2022

ACHILLES THERAPEUTICS PLC

Consolidated Balance Sheets

(in thousands, except share and per share amounts)

(expressed in U.S. Dollars, unless otherwise stated)

	December 31,	
	2021	**2020**
ASSETS		
Current assets:		
Cash and cash equivalents	$ 266,319	$ 177,849
Prepaid expenses and other current assets	18,430	9,948
Total current assets	284,749	187,797
Non-current assets:		
Property and equipment, net	17,743	13,369
Operating lease right of use assets	11,048	14,740
Deferred tax assets	26	4
Restricted cash	33	—
Other assets	3,507	3,008
Total non-current assets	32,357	31,121
TOTAL ASSETS	$ 317,106	$ 218,918
LIABILITIES AND SHAREHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 3,722	$ 6,314
Income taxes payable	—	7
Accrued expenses and other liabilities	10,906	6,590
Operating lease liabilities—current	4,482	3,712
Total current liabilities	19,110	16,623
Non-current liabilities:		
Operating lease liabilities-non-current	7,777	12,271
Other long-term liability	691	652
Total non-current liabilities	8,468	12,923
Total liabilities	27,578	29,546
Commitments and contingencies (Note 13)		
Shareholders' equity:		
Ordinary shares, £0.001 par value; 40,603,489 and 4,389,920 shares authorized, issued and outstanding at December 31,2021 and 2020, respectively	54	6
Deferred shares, £92,451.851 par value, one share authorized, issued and outstanding at December 31, 2021; Deferred shares, £0.001 par value; 30,521 shares issued and outstanding at December 31,2020	128	—
Convertible preferred shares, £0.001 par value; no shares authorized, issued and outstanding as of December 31, 2021; 104,854,673 shares authorized, issued and outstanding at December 31, 2020	—	134
Additional paid in capital	401,821	234,922
Accumulated other comprehensive income	6,636	12,322
Accumulated deficit	(119,111)	(58,012)
Total shareholders' equity	289,528	189,372
TOTAL LIABILITIES AND SHAREHOLDERS' EQUITY	$ 317,106	$ 218,918

The accompanying notes are an integral part of these financial statements.

ACHILLES THERAPEUTICS PLC

Consolidated Statements of Operations and Comprehensive Loss

(in thousands, except share and per share amounts)

	Years ended December 31,		
	2021	**2020**	**2019**
OPERATING EXPENSES:			
Research and development	$ 42,224	$ 22,629	$ 9,072
General and administrative	21,971	11,098	4,703
Total operating expenses	64,195	33,727	13,775
Loss from operations	(64,195)	(33,727)	(13,775)
OTHER INCOME (EXPENSE), NET:			
Other income (expense)	3,133	531	(215)
Total other income (expense), net	3,133	531	(215)
Loss before provision for income taxes	(61,062)	(33,196)	(13,990)
Provision for income taxes	(37)	(3)	—
Net loss	(61,099)	(33,199)	(13,990)
Other comprehensive income:			
Foreign exchange translation adjustment	(5,686)	4,213	8,504
Comprehensive loss	$ (66,785)	$ (28,986)	$ (5,486)
Net loss per share attributable to ordinary shareholders—basic and diluted	$ (2.13)	$ (31.14)	$ (21.79)
Weighted average ordinary shares outstanding—basic and diluted	28,654,760	1,066,208	642,169

The accompanying notes are an integral part of these financial statements.

ACHILLES THERAPEUTICS PLC

Consolidated Statements of Shareholders' Equity

(in thousands, except share amounts)

	Convertible preferred shares												
	Series A $0.001 par value		Series B $0.001 par value		Series C $0.001 par value		Ordinary $0.001 par value		Deferred shares $0.001 par value		Additional paid-in capital	Accumulated other comprehensive income (loss)	Accumulated deficit	Total
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount				
Balance at December 31, 2018	17,850,000	$ 23	$ —	$ —	$ —	$ —	1,407,925	$ 2	71,431	$ —	$ 23,866	$ (395)	$ (10,823)	$ 12,673
Issuance of A series convertible preferred shares, net of issuance costs	10,400,000	13	—	—	—	—	—	—	—	—	13,241	—	—	13,254
Issuance of B series convertible preferred shares, net of issuance costs of $283	—	—	34,794,714	43	—	—	—	—	—	—	80,145	—	—	80,188
Issuance of ordinary shares (Note 7)	—	—	—	—	—	—	1,358,765	2	—	—	(2)	—	—	—
Conversion of ordinary shares into deferred shares	—	—	—	—	—	—	(232,483)	—	920,434	1	(1)	—	—	—
Share-based compensation expense	—	—	—	—	—	—	—	—	—	—	719	—	—	719
Unrealized gain on foreign currency translation	—	—	—	—	—	—	—	—	—	—	—	8,504	—	8,504
Net loss	—	—	—	—	—	—	—	—	—	—	—	—	(13,990)	(13,990)
Balance at December 31, 2019	28,250,000	$ 36	34,794,714	$ 43	—	$ —	2,534,207	$ 4	991,865	$ 1	$ 117,968	$ 8,109	$ (24,813)	$ 101,348
Issuance of B series convertible preferred shares, net of issuance costs of $20	—	—	17,397,356	23	—	—	—	—	—	—	44,101	—	—	44,124
Issuance of C series convertible preferred shares, net of issuance costs of $187	—	—	—	—	24,412,603	32	—	—	—	—	69,862	—	—	69,894
Issuance of ordinary shares (Note 7)	—	—	—	—	—	—	1,993,503	2	—	—	(2)	—	—	—
Conversion of ordinary shares into deferred shares	—	—	—	—	—	—	(137,790)	—	548,040	1	(1)	—	—	—
Repurchase of deferred shares									(1,509,384)	(2)	2	—	—	—
Share-based compensation expense	—	—	—	—	—	—	—	—	—	—	2,992	—	—	2,992
Unrealized gain on foreign currency translation	—	—	—	—	—	—	—	—	—	—	—	4,213	—	4,213
Net loss	—	—	—	—	—	—	—	—	—	—	—	—	(33,199)	(33,199)
Balance at December 31, 2020	28,250,000	$ 36	52,192,070	$ 66	24,412,603	$ 32	4,389,920	6	30,521	—	234,922	12,322	(58,012)	189,372
Conversion of ordinary shares into deferred shares	—	—	—	—	—	—	(18,262)	—	78,537	—	—	—	—	—
Effect of corporate reorganization including conversion of preferred share to ordinary share	(28,250,000)	(36)	(52,192,070)	(66)	(24,412,603)	(32)	26,481,831	34	(109,057)	128	(28)	—	—	—
Issuance of ordinary shares (Note 7)	—	—	—	—	—	—	9,750,000	14	—	—	160,610	—	—	160,624
Share-based compensation expense	—	—	—	—	—	—	—	—	—	—	6,317	—	—	6,317
Unrealized gain on foreign currency translation	—	—	—	—	—	—	—	—	—	—	—	(5,686)	—	(5,686)
Net loss	—	—	—	—	—	—	—	—	—	—	—	—	(61,099)	(61,099)
Balance at December 31, 2021	—	$ —	—	$ —	—	$ —	40,603,489	$ 54	1	$ 128	$ 401,821	$ 6,636	$ (119,111)	$ 289,528

The accompanying notes are an integral part of these financial statements.

ACHILLES THERAPEUTICS PLC
Consolidated statements of cash flows
(in thousands)

	2021	2020	2019
CASH FLOWS FROM OPERATING ACTIVITIES:			
Net loss	$ (61,099)	$ (33,199)	$ (13,990)
Adjustments to reconcile net loss to net cash used in operating activities			
Depreciation and amortization	3,288	772	302
Loss on disposal of property and equipment	156	—	14
Changes in right of use assets and operating lease liabilities, net	(18)	1,179	(9)
Non-cash loss on foreign currency remeasurement	3	—	0
Non-cash share-based compensation	6,317	2,992	719
Changes in operating assets and liabilities			
Prepaid expenses and other current assets	(9,771)	(3,120)	(2,566)
Accounts payable	(2,572)	5,258	548
Income taxes payable	(7)	7	—
Accrued expenses and other liabilities	4,937	3,045	873
Other long-term liability	47	614	—
Deferred tax assets	(22)	(4)	—
Other assets	(543)	(2,796)	(33)
Net cash used in operating activities	(59,284)	(25,252)	(14,142)
CASH FLOWS FROM INVESTING ACTIVITIES:			
Purchases of property and equipment	(7,634)	(11,847)	(942)
Net cash used in investing activities	(7,634)	(11,847)	(942)
CASH FLOWS FROM FINANCING ACTIVITIES:			
Issuance of ADRs in initial public offering, net of issuance costs	160,755	—	—
Proceeds of issuance of convertible preferred shares, net of issuance costs	—	113,825	93,622
Payments of initial public offering costs	—	(121)	—
Net cash provided by financing activities	160,755	113,704	93,622
Effect of exchange rate changes on cash equivalents and restricted cash	(5,334)	3,650	8,373
Net increase in cash	88,503	80,255	86,911
Cash, cash equivalents and restricted cash, beginning of year	177,849	97,594	10,683
Cash, cash equivalents and restricted cash, end of year	$ 266,352	$ 177,849	$ 97,594
SUPPLEMENTAL DISCLOSURE OF CASH FLOW INFORMATION:			
Right of use assets obtained in exchange for new operating lease liabilities	$ 314	$ 15,846	$ 457
Property and equipment purchases in accrued expenses	$ 726	$ 285	$ 343
Issuance costs of convertible preferred shares included in accounts payable	$ —	$ —	$ 192
Deferred offering costs included in accrued expenses	$ —	$ 826	$ —

The following table provides a reconciliation of the cash, cash equivalents and restricted cash balances as of each of the periods, shown above:

	2021	2020	2019
Cash and cash equivalents	$ 266,319	$ 177,849	$ 97,594
Restricted cash	33	$ —	$ —
Total cash, cash equivalents and restricted cash	$ 266,352	$ 177,849	$ 97,594

The accompanying notes are an integral part of these financial statements.

ACHILLES THERAPEUTICS PLC

Notes to Consolidated Financial Statements

1. Nature of the business

Achilles Therapeutics plc (formerly Achilles TX Limited) and subsidiaries, or the Company, is a biopharmaceutical company developing transformative precision T cell therapies to treat multiple types of solid tumors. The Company is focused on advancing immuno-oncology therapeutics by exploiting its pioneering work in the field of tumor evolution and clonal neoantigens.

The Company is a public limited company originally incorporated pursuant to the laws of England and Wales in November 2020 as a private limited company named Achilles TX Limited, with nominal assets and liabilities, for the purposes of becoming the ultimate holding company for Achilles Therapeutics UK Limited (formerly Achilles Therapeutics Limited) and consummating the corporate reorganization described below. Achilles Therapeutics UK Limited was incorporated in May 2016 under the laws of England and Wales and its registered office and principal place of business is currently 245 Hammersmith Road, London W6 8PW. Achilles TX Limited and Achilles Therapeutics Holdings Limited (a wholly owned direct subsidiary of Achilles TX Limited formed in November 2020 for the purpose of becoming the direct holding company of Achilles Therapeutics UK Limited and Achilles Therapeutics US, Inc.) have not conducted any operations prior to the corporate reorganization other than activities incidental to their formation.

The corporate reorganization and initial public offering, or IPO, took place in several steps which were completed on April 6, 2021.

- **Exchange of Achilles Therapeutics UK Limited Shares for Achilles TX Limited Shares**: In December 2020 all shareholders of Achilles Therapeutics UK Limited (except for the holders of deferred shares) exchanged each of the shares held by them for shares of Achilles TX Limited to result in them holding the same number and class of newly issued shares of £1.20 nominal value of Achilles TX Limited and, as a result, Achilles TX Limited became the sole shareholder of Achilles Therapeutics UK Limited.

- **Reduction of the share capital of Achilles TX Limited:** Achilles TX Limited reduced its share capital by way of a reduction of the nominal value of each share in the capital of Achilles TX Limited from £1.20 to £0.001 in order to satisfy the net asset test requirement in section 92 of the Companies Act 2006 for re-registration as a public limited company and to create distributable reserves.

- **Re-registration of Achilles TX Limited as Achilles Therapeutics plc:** In February 2021, Achilles TX Limited was re-registered as a public limited company pursuant to section 92 of the UK Companies Act 2006 and renamed Achilles Therapeutics plc. The Company adopted new Articles of Association appropriate for a public limited company.

As a result of the above Achilles TX Limited is the successor to Achilles Therapeutics UK Limited (the "Predecessor") and the financial information for the period prior to the incorporation of Achilles TX Limited represents that of the Predecessor.

On April 6, 2021, the Company completed the initial public offering, or IPO. In connection with the IPO, the Company sold an aggregate of 9,750,000 ADSs representing the same number of ordinary shares, at a public offering price of $18.00 per ADS. Net proceeds were $160.6 million, after deducting underwriting discounts and commissions and other offering expenses. Upon completion of the IPO, the Company adopted new articles suitable for a listed public limited company.

On April 6, 2021, the Company effected a one-for-0.2526 (rounded to four decimal places) reverse share split of its issued and outstanding ordinary shares except for N ordinary shares and a proportional adjustment to the existing conversion ratios for each class of the Company's convertible preferred shares, and a one-for-0.1792 (rounded to four decimal places) reverse share split of its issued and outstanding N ordinary shares. Accordingly, all share and per

share amounts for all periods presented in the consolidated financial statements and notes thereto have been adjusted retroactively, where applicable, to reflect this reverse share split and adjustment of the preferred share conversion ratios. Two shareholders elected to receive a number of Class A non-voting ordinary shares rather than their full entitlement of ordinary shares following the reverse share split. As part of this reverse share split, a single deferred share with a nominal value of £92,451.851 in the capital of the Company was created.

The Company has devoted its efforts principally to research and development since formation. The Company has not yet completed product development, filed for or obtained regulatory approvals for any products, nor verified the market acceptance and demand for such products. As a result, the Company is subject to risks that are common to emerging companies in the biotech industry, including the uncertainties of the product discovery and development process, dependence on key individuals, development of the same or similar technological innovations by the Company's competitors, protection of proprietary technology, compliance with government regulations and approval requirements, the Company's ability to access capital and uncertainty of market acceptance of products.

Going concern

In accordance with the Financial Accounting Standards Board, or FASB, Accounting Standards Update, or ASU, 2014-15, Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern (Subtopic 205-40), the Company has evaluated whether there are conditions and events, considered in the aggregate, that raise substantial doubt about the Company's ability to continue as a going concern.

The Company has historically been loss making and anticipates that it will continue to incur losses for the foreseeable future and had an accumulated deficit of $119.1 million as of December 31, 2021. The Company has funded these losses principally through the issuance of ordinary and preferred shares. The Company expects to continue to incur operating losses and negative cash outflows until such time as it generates a level of revenue that is sufficient to support its cost structure.

The spread of COVID-19 has impacted the global economy and has impacted the Company's operations, including the interruption of preclinical and clinical trial activities and potential interruption to supply chains. The Company has maintained operations at its GMP manufacturing and research and development sites through 2021 to date. The Company continues to assess the impact COVID-19 may have on its ability to advance the development of drug candidates or to raise financing to support the development of drug candidates, but no assurances can be given that this analysis will enable it to avoid part or all of any impact from the spread of COVID-19 or its consequences, including downturns in business sentiment generally or in its sector in particular.

As of December 31, 2021, the Company had cash and cash equivalents of $266.3 million. The Directors have reviewed the financial projections of the Company for the 12 months subsequent to the date of issuance of these financial statements including consideration of severe but plausible scenarios that may affect the Company in that period. These show that the Company will be able to pay (or otherwise discharge) its debts as they fall due immediately following the date of signing of this Balance Sheet and for the period considered by the forecast.

Accordingly, the financial statements have been prepared on a basis that assumes the Company will continue as a going concern and which contemplates the realization of assets and settlement of liabilities and commitments as they fall due in the ordinary course of business for at least 12 months from the date of issuance of the financial statements.

2. Summary of significant accounting policies

Basis of presentation

The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America or U.S. GAAP and are presented in U.S. dollars. All significant inter–company accounts and transactions between the Company and its subsidiaries have been eliminated upon consolidation.

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Use of estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of income and expenses during the reporting periods. Significant estimates and assumptions reflected in these financial statements include, but are not limited to, the accrual for research and development expenses, the fair value of ordinary shares and incremental borrowing rate for leases. Estimates are periodically reviewed in light of changes in circumstances, facts and experience. Changes in estimates are recorded in the period in which they become known. Actual results could differ materially from those estimates.

Segment information

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision maker in deciding how to allocate resources and assess performance. The Company operates in a single segment, focusing on researching, developing and commercializing potentially novel cancer immunotherapies targeting clonal neoantigens. Consistent with its operational structure, its chief operating decision maker, the Company's chief executive officer, views and manages the Company's operations and manages its business as a single operating segment. All material long-lived assets of the Company reside in the UK.

Foreign currency translation

The functional currency of the Company is pound sterling which is its local currency. Monetary assets and liabilities denominated in currencies other than the functional currency are translated into the functional currency at rates of exchange prevailing at the balance sheet dates. Non-monetary assets and liabilities denominated in foreign currencies are translated into the functional currency at the exchange rates prevailing at the date of the transaction. Exchange gains or losses arising from foreign currency transactions are included in other expense, net in the Consolidated statement of operations and comprehensive loss. The Company recorded foreign exchange gains of $2.5 million, $0.4 million and $0.1 million for the years ended December 31, 2021, 2020 and 2019, respectively.

For financial reporting purposes, the financial statements of the Company have been presented in the U.S. dollar, the reporting currency. The financial statements of entities are translated from their functional currency into the reporting currency as follows: assets and liabilities are translated at the exchange rates at the balance sheet dates, revenue and expenses are translated at the average exchange rates and shareholders' equity is translated based on historical exchange rates. Translation adjustments are not included in determining net loss but are included as a foreign exchange adjustment to accumulated other comprehensive (loss)/income, a component of shareholders' equity.

Cash and cash equivalents

The Company considers all highly liquid investments that have maturities of three months or less when acquired to be cash equivalents. In connection with a lease, the Company maintains a required minimum balance, currently less than $0.1 million in connection with a letter of credit issued for the benefit of the landlord for its commercial facility used as a security deposit for the lease. The total amount is classified as Restricted Cash and has been classified as a non-current asset in the Consolidated Balance Sheets.

Deferred Initial Public Offering Costs

The Company capitalized deferred initial public offering, or IPO, costs, which primarily consist of direct, incremental legal, professional accounting and other third-party fees relating to the Company's IPO, within prepaid expenses and other current assets. The deferred IPO costs were offset against IPO proceeds upon the consummation of the offering.

The Company recorded $1.0 million of deferred IPO costs as of December 31, 2020. The Company did not record any deferred IPO costs as of December 31, 2021 and 2019.

Fair value of financial instruments

The carrying values of the Company's cash and cash equivalents, prepaid expenses and other current assets, accounts payable, and certain accruals approximate their fair value due to their short-term nature. The Company has a money-market fund that is measured under the fair value hierarchy as Level 1 as there are quoted prices in active markets for identical assets. See Note 3, Fair Value of Financial Instruments.

Concentrations of credit risk and off-balance sheet risk

Financial instruments that subject the Company to credit risk consist solely of cash and cash equivalents. The Company maintains cash balances in excess of amounts insured by the UK Government Financial Services Compensation Scheme in the United Kingdom. The Company has no significant off-balance-sheet risk or concentration of credit risk, such as foreign exchange contracts, options contracts, or other foreign hedging arrangements.

Property and equipment

Property and equipment are recorded at cost and depreciated using the straight-line method over the estimated useful lives of the respective assets, which are as follows:

	Estimated useful life
Lab equipment	5 years
Fixture and fittings	5 years
Office equipment and computers	3 years
Leasehold improvements	Shorter of useful life or remaining lease term

Upon retirement or sale, the cost of assets disposed of and the related accumulated depreciation are removed from the accounts and any resulting gain or loss is included in the statement of operations and other comprehensive loss. Expenditures for repairs and maintenance are charged to expense as incurred. Assets under construction are not depreciated until the asset is available and ready for use.

Impairment of long-lived assets

The Company evaluates assets for potential impairment when events or changes in circumstances indicate the carrying value of the assets may not be recoverable. Recoverability is measured by comparing the book values of the assets to the expected future net undiscounted cash flows that the assets are expected to generate. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the book values of the assets exceed their fair value. The Company recognized an impairment loss of $0.1 million in the year ended December 31, 2021. The Company did not recognize any impairment losses in the years ended December 31, 2020 and 2019.

Research and development costs

Research and development costs are expensed as incurred. Research and development expenses consist of costs incurred in performing research and development activities, including salaries, non-cash share-based compensation and benefits, depreciation expense, travel, third-party license fees, and external costs of outside vendors engaged to conduct clinical development activities, clinical trials, cost to manufacture clinical trial materials and net of tax credits associated with research and development activities.

Research contract costs and accruals

The Company has entered into various research and development-related contracts with research institutions and other companies. These agreements are generally cancelable, and related payments are recorded as research and development expenses as incurred. Accruals for research and development expenses typically include fees paid to vendors in conjunction with preclinical development activities, CROs and investigative sites in connection with preclinical and clinical activities and costs to manufacture clinical trial materials in connection with the manufacturing of drug formulations for use in preclinical and clinical activities. When estimating accruals for research and development expenses as of each balance sheet date, the Company analyzes progress of the preclinical activities or clinical trials, including the phase or completion of services performed relative to invoices received and contracted costs. Actual results could differ from the Company's estimates. The Company's historical accrual estimates of research and development expenses have not been materially different from the actual costs.

Asset Retirement and Environmental Obligations

Pursuant to ASC 410, Asset Retirement and Environmental Obligations, an asset retirement obligation ("ARO" or "AROs") is recorded when there is a legal obligation associated with the retirement of a tangible long-lived asset and the fair value of the liability can reasonably be estimated. Upon initial recognition, AROs are recorded as a liability at their estimated present value, with an offsetting increase to the carrying amount of the long-lived asset. Over time, the liabilities are accreted for the change in their present value through charges to operations costs. If the fair value of the estimated ARO changes, an adjustment is recorded to both the ARO and the asset retirement cost. Revisions in estimated liabilities can result from revisions of estimated inflation rates, escalating retirement costs, and changes in the estimated timing of settling ARO liabilities.

Total ARO consists of amounts for decommissioning and restoration of rented facilities to be performed in the future. The Company computes the liability for AROs based on assumptions from third-party estimates of the total restoration costs, adjusted for inflation. These values are discounted to present value using our credit adjusted incremental borrowing rate of the related rental facility and recorded ARO in other long-term liabilities. Periodic accretion of the discount on the ARO is recorded as part of accretion expense.

Share-based compensation

The Company recognizes compensation expense for equity awards based on the grant date fair value of the award, which may include share options and restricted ordinary shares. For equity awards that vest based on a service condition, the share-based compensation expense is recognized on a straight-line basis over the requisite service period. The Company accounts for forfeitures as they occur. For equity awards with performance conditions, the Company recognizes share-based compensation expense using a straight-line basis over the requisite service commitments period when the achievement of a performance-based milestone is probable, based on the relative satisfaction of the performance condition as of the reporting date. The Company uses the fair value of its ordinary shares to determine the fair value of Employee Shares, C ordinary shares and K ordinary shares awarded to employees and directors.

Effective January 1, 2019, the Company adopted ASU No. 2018-07, *Compensation—Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting* ("ASU 2018-7"), which expands the scope of Topic 718 to include share-based payment awards to nonemployees. As a result, stock-based awards granted to nonemployees are accounted for in the same manner as awards granted to employees and directors as described above. The adoption of this new guidance did not have a material impact on the Company's financial statements.

There have been no performance conditions attached to the share options granted by the Company to date. The fair value of each share option grant is estimated on the date of grant using the Black-Scholes option pricing model. See Note 8, "Share-based compensation," for the Company's assumptions used in connection with option grants made

during the periods covered by these consolidated financial statements. Assumptions used in the option pricing model include the following:

Expected volatility. As Achilles became a listed, public company in April 2021, the Company has limited company-specific historical and implied volatility information for its ordinary shares. Therefore, it estimates its expected share volatility based on the historical volatility of publicly traded peer companies and expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded share price.

Expected term. The expected term of the Company's share options has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options as there is a limited trading history of our ordinary shares.

Risk-free interest rate. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods that are approximately equal to the expected term of the award.

Expected dividend. Expected dividend yield of zero is based on the fact that the Company has never paid cash dividends on ordinary shares and does not expect to pay any cash dividends in the foreseeable future.

Effective January 1, 2019, the Company adopted ASU No. 2018-07, *Compensation—Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting* ("ASU 2018-7"), which expands the scope of Topic 718 to include share-based payment awards to nonemployees. As a result, stock-based awards granted to nonemployees are accounted for in the same manner as awards granted to employees and directors as described above. The adoption of this new guidance did not have a material impact on the Company's financial statements.

There have been no performance conditions attached to the share options granted by the Company to date. The fair value of each share option grant is estimated on the date of grant using the Black-Scholes option pricing model. See Note 8, "Share-based compensation," for the Company's assumptions used in connection with option grants made during the periods covered by these consolidated financial statements. Assumptions used in the option pricing model include the following:

Expected volatility. As Achilles became a listed, public company in April 2021, the Company has limited company-specific historical and implied volatility information for its ordinary shares. Therefore, it estimates its expected share volatility based on the historical volatility of publicly traded peer companies and expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded share price.

Expected term. The expected term of the Company's share options has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options as there is a limited trading history of our ordinary shares.

Risk-free interest rate. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods that are approximately equal to the expected term of the award.

Expected dividend. Expected dividend yield of zero is based on the fact that the Company has never paid cash dividends on ordinary shares and does not expect to pay any cash dividends in the foreseeable future.

Given the absence of an active market for the Company's ordinary shares prior to the IPO, the Company estimated the fair value of its ordinary shares with input from an independent third-party valuation specialist firm in accordance with the guidelines in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation* (the "Practice Aid"). The Company's valuations of ordinary shares were prepared using either a market approach based on precedent transactions in the ordinary and preferred shares or a market adjusted equity value method to estimate the Company's total equity value, and using an option-pricing backsolve method ("OPM") to allocate the equity value to each class of the Company's securities. In some cases, the Company determined that there were no significant events occurring between a prior valuation date and a subsequent grant. As such, in these cases the Company used the most recent share

price valuation as an input to the determination of share-based compensation. After IPO, the fair value of ordinary shares is determined by reference to the closing price of ADSs on the Nasdaq Global Select Market on the date of grant.

The OPM backsolve method derives an equity value such that the value indicated for ordinary shares is consistent with the investment price, and it provides an allocation of this equity value to each of the Company's securities. The OPM treats the various classes of ordinary shares and preferred shares as call options on the total equity value of a company, with exercise prices based on the value thresholds at which the allocation among the various holders of a company's securities changes. Under this method, each class of ordinary shares has value only if the funds available for distribution to shareholders exceeded the value of the preferred share liquidation preferences at the time of the liquidity event. Key inputs into the OPM backsolve calculation included the valuation of equity, probability weighted expected time to liquidity and volatility. A reasonable discount for lack of marketability was applied to the total per share value to arrive at an estimate of the total fair value of an ordinary share on a non-marketable basis.

Leases

Effective January 1, 2019, the Company adopted ASU No. 2016-02, Leases (Topic 842), as amended, using the modified retrospective method and utilizing the effective date as its date of initial application, with prior periods presented in accordance with previous guidance under ASC 840, Leases ("ASC 840"). At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease based on the unique facts and circumstances present in the arrangement. Leases with a term greater than one year are recognized on the balance sheet as right-of-use assets and current and non-current lease liabilities, as applicable. Entities may elect not to separate lease and non-lease components. The Company has elected to account for lease and non-lease components together as a single lease component for all underlying assets and to allocate all the contract consideration to the lease component only. All the Company's leases are classified as operating leases.

Lease liabilities and their corresponding right-of-use assets are initially recorded based on the present value of lease payments over the expected remaining lease term. Certain adjustments to the right-of-use asset may be required for items such as incentives received. The interest rate implicit in lease contracts has not been readily determinable. As a result, the Company utilizes its incremental borrowing rate to discount lease payments, which reflects the fixed rate at which the Company could borrow on a collateralized basis the amount of the lease payments in the same currency, for a similar term, in a similar economic environment. As the Company does not have a rating agency-based credit rating, quotes were obtained from lenders to establish an estimated secured rate to borrow based on Company and market-based factors as of the respective lease measurement dates. The Company has elected not to recognize leases with an original term of one year or less on the balance sheet. The Company typically only includes the non-cancelable lease term in its assessment of a lease arrangement unless there is an option to extend the lease that is reasonably certain of exercise. Prospectively, the Company will adjust the right-of-use assets for straight-line rent expense or any incentives received and remeasure the lease liability at the net present value using the same incremental borrowing rate that was in effect as of the lease commencement or transition date.

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 statement of operations. The operating lease cash flows are categorized under net cash used in operating activities in the statement of cash flows.

Income taxes

The Company accounts for income taxes using the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the financial statements or in its tax returns. Deferred tax assets and liabilities are determined on the basis of the differences between the financial statements and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes. The Company assesses the likelihood that deferred tax assets will be recovered in the

future and to the extent management believes, based upon the weight of available evidence, that it is more likely than not that all or a portion of the deferred tax assets will not be realized, a valuation allowance is established through a charge to income tax expense. Potential for recovery of deferred tax assets is evaluated by estimating the future taxable profits expected and considering prudent and feasible tax planning strategies.

The Company uses a two-step approach for recognizing and measuring uncertain tax positions. The first step is to evaluate tax positions taken or expected to be taken in a tax return by assessing whether they are more likely than not sustainable, based solely on their technical merits, upon examination, and including resolution of any related appeals or litigation process. The second step is to measure the associated tax benefit for each position as the largest amount that the Company believes is more likely than not realizable. Differences between the amount of tax benefits taken or expected to be taken in the Company's income tax returns and the amount of tax benefits recognized in the financial statements represent the Company's unrecognized income tax benefits, which is either recorded as a liability or reduction of deferred tax assets.

The Company recognizes interest and penalties related to unrecognized tax benefits on the income tax expense line in the accompanying statement of operations. As of December 31, 2021, 2020 and 2019, no accrued interest or penalties have been incurred.

Research and development tax credit

The Company is subject to corporate taxation in the United Kingdom, or UK. Due to the nature of the business, the Company has generated losses since inception. The benefit from research and development ("R&D") tax credits is recognized in the statements of operations and comprehensive loss as a reduction of research and development costs and represents the sum of the research and development tax credits recoverable in the UK.

The UK research and development tax credit is fully refundable to the Company and is not dependent on current or future taxable income. As a result, the Company has recorded the entire benefit from the UK research and development tax credit as a benefit which is included in net loss before income tax and accordingly, not reflected as part of the income tax provision. If, in the future, any UK research and development tax credits generated are needed to offset a corporate income tax liability in the UK, that portion would be recorded as a benefit within the income tax provision and any refundable portion not dependent on taxable income would continue to be recorded as a reduction of research and development costs.

As a company that carries out extensive research and development activities, the Company benefits from the UK research and development tax credit regime under the scheme for small or medium-sized enterprises ("SME"). Under the SME regime, the Company can surrender some of its trading losses that arise from qualifying research and development activities for a cash rebate of up to 33.35% of such qualifying research and development expenditure. Qualifying expenditures largely comprise employment costs for research staff, consumables, outsourced contract research organization costs and utilities costs incurred as part of research projects. Certain subcontracted qualifying research and development expenditures are eligible for a cash rebate of up to 21.67%. A large portion of costs relating to research and development, clinical trials and manufacturing activities are eligible for inclusion within these tax credit cash rebate claims.

The Company may not be able to continue to claim research and development tax credits under the SME regime in the future because it may no longer qualify as a small or medium-sized company.

Unsurrendered UK losses may be carried forward indefinitely to be offset against future taxable profits, subject to numerous utilization criteria and restrictions. The amount that can be offset each year is limited to £5.0 million plus an incremental 50% of UK taxable profits.

Comprehensive income (loss)

Comprehensive income (loss) includes net loss as well as other changes in shareholders' equity that result from transactions and economic events other than those with shareholders.

Net loss per share

The Company has reported losses since inception and has computed basic net loss per share attributable to ordinary shareholders by dividing net loss attributable to ordinary shareholders by the weighted-average number of ordinary shares outstanding for the period, without consideration for potentially dilutive securities. For purpose of this calculation, unvested Employee Shares and convertible preferred shares are considered potential dilutive ordinary shares. The Company computes diluted net loss per ordinary share after giving consideration to all potentially dilutive ordinary shares, including unvested Employee Shares and convertible preferred shares, outstanding during the period determined using the treasury-stock and if-converted methods, except where the effect of including such securities would be antidilutive. Because the Company has reported net losses since inception, these potential ordinary shares have been anti-dilutive and basic and diluted loss per share were the same for all periods presented.

Government grants

The Group receives certain government grants that support specific research and development activities. Income in respect of grants also includes contributions towards the costs of research and development. Income is recognized when costs under each grant are incurred in accordance with the terms and conditions of the grant and the collectability of the receivable is reasonably assured. Government grants relating to costs are deferred and recognized in the income statement over the period necessary to match them with the costs they are intended to compensate. The Group recognizes income from government grants under 'Other income—net' in the Company's consolidated statement of comprehensive loss.

Recent accounting pronouncements

Recently adopted accounting standards

In December 2019, the FASB issued ASU 2019-12, "*Income Taxes—Simplifying the Accounting for Income Taxes* (Topic 740) ("ASU 2019-12")," which simplifies the accounting for income taxes. The new guidance removes certain exceptions to the general principles in ASC 740 such as recognizing deferred taxes for equity investments, the incremental approach to performing intra-period tax allocation and calculating income taxes in interim periods. The standard also simplifies accounting for income taxes under U.S. GAAP by clarifying and amending existing guidance, including the recognition of deferred taxes for goodwill, the allocation of taxes to members of a consolidated group and requiring that an entity reflect the effect of enacted changes in tax laws or rates in the annual effective tax rate computation in the interim period that includes the enactment date. This guidance is effective for annual periods beginning after December 15, 2020, and interim periods thereafter; however, early adoption is permitted. The new guidance was adopted on January 1, 2021 and it did not have a material impact on the Company's consolidated financial statements and related disclosures.

In November 2021, the FASB issued ASU 2021-10, "*Government Assistance – Topic 832 – Disclosures by Business Entities about Government Assistance*," which increases the transparency of government assistance including the disclosure of (1) the types of assistance, (2) an entity's accounting for the assistance, and (3) the effect of the assistance on an entity's financial statements. The amendments in this Update require the following annual disclosures about transactions with a government that are accounted for by applying a grant or contribution accounting model by analogy: 1. Information about the nature of the transactions and the related accounting policy used to account for the transactions. 2. The line items on the balance sheet and income statement that are affected by the transactions, and the amounts applicable to each financial statement line item. 3. Significant terms and conditions of the transactions, including commitments and contingencies. ASU 2021-10 is effective for annual periods beginning after December

15, 2021; however, early adoption is permitted. The new guidance was adopted on January 1, 2022 and will be effective for the year ended December 21, 2022. This guidance is not expected to have a material impact on the Company's financial statements and related disclosures.

3. Fair Value of Financial Instruments

The following tables show assets measured at fair value on a recurring basis as of December 31, 2021 (in thousands):

	December 31, 2021		
	Level 1	Level 2	Level 3
Cash equivalents:			
Money market funds	$ 40,224	$ —	$ —
	$ 40,224	$ —	$ —

There were no liabilities measured at fair value on a recurring basis as of December 31, 2021. There were no assets or liabilities measured at fair value on a recurring basis as of December 31, 2020.

4. Prepaid expenses and other current assets

Prepaid expenses and other current assets consisted of the following (in thousands):

	December 31,	
	2021	2020
UK R&D tax credit	$ 10,523	$ 6,214
Prepaid research and development	3,608	751
Prepaid insurance	1,525	21
VAT recoverable	650	1,125
Deferred offering costs	—	1,007
Other current assets	2,124	830
	$ 18,430	$ 9,948

5. Property and Equipment, net

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

	December 31,	
	2021	2020
Lab equipment	$ 7,505	$ 4,644
Leasehold improvements	7,021	6,960
Office equipment and computers	1,561	1,168
Fixtures and fittings	757	706
Assets under construction	5,351	1,275
	22,195	14,753
Less: Accumulated depreciation	(4,452)	(1,384)
	$ 17,743	$ 13,369

Depreciation expense was $3.3 million, $0.8 million and $0.3 million for the years ended December 31, 2021, 2020 and 2019, respectively.

6. Accrued expenses and other liabilities

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

	December 31,	
	2021	2020
Compensation and benefits	$ 2,649	$ 1,494
External research and development expenses	2,985	2,201
Facility costs	2,629	868
Property and equipment	712	303
Professional services	663	1,222
Other liabilities	1,268	502
	$ 10,906	$ 6,590

7. Shareholders' equity

Ordinary shares

As of December 31, 2021 and 2020, the Company had the following number of ordinary shares with a par value £0.001 (equivalent to $0.001) issued and outstanding:

	December 31,	
	2021	2020
Ordinary shares	38,987,122	—
Class A non-voting ordinary shares	1,616,367	—
B Ordinary shares	—	505,108
D Ordinary shares	—	155,669
E Ordinary shares	—	80,007
F Ordinary shares	—	327,084
G Ordinary shares	—	194,261
H Ordinary shares	—	88,871
I Ordinary shares	—	48,391
J Ordinary shares	—	262,478
L Ordinary shares	—	1,207,670
M Ordinary shares	—	811,436
N Ordinary shares	—	708,945
Deferred Shares	1	30,521
Total ordinary and deferred shares	40,603,490	4,420,441

As of December 31, 2020 and 2019, the Company issued various classes of ordinary shares as Employee Shares (See Note 8). Each holder of B ordinary shares was entitled to one vote per B ordinary share and, to receive dividends declared with Investor Majority consent and any such dividend as determined by the board of directors of the Company acting with investor director consent, provided that the preferred shares and the B ordinary shares shall, subject to the 2019 Articles and 2020 Articles, rank equally in all respects for the purpose of any dividend that is declared or paid. All other classes of ordinary shares do not have voting rights. All ordinary shares, including B shares, have a liquidation preference that is junior to Preferred Shares.

On April 6, 2021, all the Employee Shares, Convertible Preferred Shares (see below) and B ordinary shares were converted into ordinary shares or Class A non-voting ordinary shares. Please refer to the details in Note 1. Class A non-voting ordinary shares have same rights and privileges as ordinary shares, except for the voting rights.

As of December 31, 2021, the Company has not declared any dividends.

***Deferred* shares**

As of December 31, 2020 and 2019, deferred shares were a unit of equity in the Company. Deferred shares can be repurchased at any time by the Company for £1.00 for all the deferred shares registered in the name of any holder. Deferred shares have effectively no voting or economic rights attached to them.

On April 6, 2021, all the deferred shares were cancelled. In addition, a single deferred share with a nominal value of £92,451.851 in the capital of the Company was created as part of the Company's reorganization (Note 1). As of December 31, 2021, the Company had one deferred share which could be repurchased at any time by the Company for nil consideration.

Convertible preferred shares

The Company issued series A convertible preferred shares ("Series A"), series A-1 convertible preferred shares ("Series A-1"), series B preferred shares ("Series B") and series C preferred shares ("Series C") (collectively, "Convertible Preferred Shares").

As of December 31, 2020, Convertible Preferred Shares consisted of the following (in thousands, except share data):

	Shares		Liquidation	Carrying
	Authorized	Outstanding	preference	value
Series A preferred shares	28,250,000	28,250,000	$ 36,725	$ 36,725
Series B preferred shares (1)	52,192,070	52,192,070	124,615	124,312
Series C preferred shares	24,412,603	24,412,603	70,081	69,894
	104,854,673	104,854,673	$ 231,421	$ 230,931

(1) The liquidation preference amount of Series B preferred shares as of December 31, 2020 illustrated in the above tables represents the liquidation amount under the initial public offering. The liquidation preference amount of Series B preferred shares will be different under other situations.

On April 6, 2021, all the Convertible Preferred Shares were converted into ordinary shares or Class A non-voting ordinary shares. There are no Convertible Preferred Shares outstanding as of December 31, 2021. The rights, preferences, and privileges of Convertible Preferred Shares were as follows as of December 31, 2020:

Conversion

At the option of the holder, Convertible Preferred Shares are convertible into an equivalent number of B ordinary shares at any time at conversion ratio of 1:1 (subject to appropriate adjustment in the event of any share dividend, share split, combination or other similar recapitalization). All Convertible Preferred Shares will automatically convert into an equivalent number of B ordinary shares upon either: (i) the notice of 60% of Convertible Preferred Shareholders that such conversion shall occur; or (ii) immediately upon an initial public offering in which the per share net public offering is at least 1.15 times £2.1589 (subject to appropriate adjustment in the event of any share dividend, share split, combination or other similar recapitalization) and the net aggregate proceeds of the offering are at least £75 million.

In the event the Company issues additional new securities at a price equal to or less than £1.916 per share, the Company shall, unless and to the extent that the holders of 80% of the Series B preferred shares and Series C preferred shares waived, issue to each holder of Series B preferred shares and Series C preferred shares a number of new Series B preferred shares and Series C preferred shares in accordance with the anti-dilution protections within the articles of association.

In the event the Company issues additional new securities at a price equal to or less than £2.1589 per share but higher than £1.916 per share, the Company shall, unless and to the extent that the holders of 80% of the Series C preferred shares waived, issue to each holder of Series C preferred shares a number of new Series C preferred shares in accordance with the anti-dilution protections within the articles of association.

Dividends

Subject to consent of 60% of holders of the Convertible Preferred Shares, dividends may be paid to the holders of Convertible Preferred Shares and B ordinary shares as determined by the board of directors of the Company. Through December 31, 2021, no dividends have been declared or paid.

Voting rights

The holders of the Convertible Preferred Shares were entitled to vote, together with the holders of B ordinary shares, at all general meetings of the Company and to receive and vote on proposed written resolutions of the Company. The Convertible Preferred Shares carried the right to one vote per Convertible Preferred Share held.

Liquidation

In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company, each holder of the then-outstanding Convertible Preferred Shares would be entitled to an amount equal to 100%, 106% and 100% of the subscription price of Series A preferred shares held, Series B preferred shares held and Series C preferred shares held, respectively. After Convertible Preferred Shares, holders of deferred shares would be paid a total of £1.00 for the entire class of deferred shares. Any remaining surplus after liquidation preference to the holders of the Convertible Preferred Shares and deferred shares would then be distributed to the holders of vested ordinary shares (as if they constituted one and the same class) pro rata to the number of vested ordinary shares held.

If the amount each Convertible Preferred Share holder was entitled to by participating in the liquidation event as an ordinary share holder on an as-converted basis (regardless of whether such holder converted its Convertible Preferred Shares to B ordinary shares) was greater than the amount to which the holder was entitled as a Convertible Preferred Share holder, the entitlement of the Convertible Preferred Share holder would be calculated on an as-converted ordinary share basis and is ranked equal to the rights of ordinary shareholders.

If upon any such liquidation, dissolution, or winding-up, the assets available for distribution to shareholders were insufficient to pay the holders of the Convertible Preferred Shares the full amounts to which they were entitled, the holders of Convertible Preferred Shares were to share ratably in any distribution of the assets available for distribution in proportion to the respective amounts which would otherwise be payable in respect of the Convertible Preferred Shares held by them upon such distribution if all amounts payable on or with respect to such shares were paid in full.

8. Share-based compensation

Employee Shares and Options

Under the Company's shareholder and subscription agreements, which were effective until the date of IPO, the Company was authorized to grant equity awards to individuals including a director of and/or a person who is employed by or who directly or indirectly provides consultancy services to the Company, in the form of D, E, F, G, H, I, J, K,

L, M and N ordinary shares, collectively referred to as Employee Shares and share options. All Employee Shares converted into ordinary shares in accordance with the reverse share split implemented on IPO (see Note 1, "Nature of business," to our financial statements appearing at the end of this Annual Report). The share options were granted pursuant to the terms of the 2020 Share Omnibus Plan, or the 2020 Plan.

Upon and following closing of the IPO, no further equity awards were granted under the 2020 Plan. To the extent outstanding options granted under the 2020 Plan are cancelled, forfeited or otherwise terminated without being exercised and would otherwise have been returned to the share reserve under the 2020 Plan, the number of shares underlying such awards will be available for future grant under the Company's 2021 Omnibus Plan (see below). In anticipation of IPO, the holders of Employee Shares and the Company entered into individual vesting agreements, or Vesting Agreements, which apply the same terms to vesting of Employee Shares as applied prior to IPO under the Company's pre-IPO Articles of Association, except that following the IPO Employee Shares that would pre-IPO have converted to deferred shares, will be transferred back to the Company and cancelled within twelve months of an employee leaving the Company.

2021 Share Omnibus Plan

In March 2021, the Company's board of directors adopted, and the Company's shareholders approved, the 2021 Share Omnibus Plan, or the 2021 Plan, which became effective upon the effectiveness of the Company's Registration Statement on Form F-1 in connection with the IPO. The 2021 Plan allows the remuneration committee to make equity-based and cash-based incentive awards to our officers, employees, directors and other key persons (including consultants).

The Company initially reserved 2,572,558 of its ordinary shares for the issuance of awards under the 2021 Plan. The 2021 Plan provides that the number of shares reserved and available for issuance under the plan will automatically increase each January 1, beginning on January 1, 2022, by 4% of the outstanding number of ordinary shares on the immediately preceding December 31, or such lesser number of shares as determined by our remuneration committee. This number is subject to adjustment in the event of a sub-division, consolidation, share dividend or other change in our capitalization. The total number of ordinary shares that may be issued under the 2021 Plan was 2,572,558 shares as of December 31, 2021, of which 1,578,993 shares remained available for future grant.

2021 Employee Share Purchase Plan

The Company's 2021 Employee Share Purchase Plan, or ESPP, was adopted by the Board in March 2021 and approved by shareholders in March 2021 and became effective upon the effectiveness of the Company's Registration Statement on Form F-1 in connection with the IPO. The ESPP initially reserves and authorizes the issuance of up to a total of 467,738 ordinary shares to participating employees. The ESPP provides that the number of shares reserved and available for issuance will automatically increase each January 1, beginning on January 1, 2022 and each January 1 thereafter through January 1, 2022, by the least of (i) 1% of the outstanding number of ordinary shares on the immediately preceding December 31; (ii) 467,738 ordinary shares or (iii) such number of shares as determined by the remuneration committee. The number of shares reserved under the ESPP is subject to change in the event of a share split, share dividend or other change in our capitalization. The total number of ordinary shares that may be issued under the ESPP was 467,738 shares as of December 31, 2021, of which 467,738 shares remained available for future grant. As of December 31, 2021, the initial purchase period under the ESPP has not yet commenced.

Employee Shares

The Company typically grants incentive shares which vest over a four-year service period with 25% of the award vesting on the first anniversary of the vesting commencement date, and the balance vesting periodically over the remaining three years.

Unvested Employee Shares are forfeited upon the giving or receiving of notice of termination of employment or service relationship in accordance with the Articles of the Company (prior to IPO, and in accordance with the Vesting Agreements post-IPO) and 2020 Plan. Before IPO, the forfeited shares were converted into deferred shares, with a repurchase right for a nominal amount in favor of the Company. As of December 31, 2020, the Company repurchased 1,509,384 deferred shares with the consideration of £0.01 to each holder for all of the deferred shares held by that holder. As part of the Company's reorganization, 109,058 outstanding deferred shares immediately before the IPO were cancelled upon IPO, and a single deferred share with a nominal value of £92,451.851 in the capital of the Company was created. As of December 31, 2021, the Company had one deferred share which could be repurchased by the Company at any time for nil consideration.

The Company measures all share-based awards using the fair value on the date of grant and recognizes compensation expense for those awards over the requisite service period, which is generally the vesting period of the respective award. The Company has granted Employee Shares to employees and non-employees with service-based conditions and records expense for these awards using the straight-line method.

A summary of the changes in the Company's unvested ordinary shares from December 31, 2019 through December 31, 2021 are as follows:

	Number of unvested ordinary shares		Weighted average grant date fair value
Unvested ordinary shares as of December 31, 2019	1,727,874	$	2.96
Granted	1,993,503	$	7.58
Vested	(746,095)	$	3.44
Forfeited	(137,790)	$	3.46
Unvested ordinary shares as of December 31, 2020	2,837,492	$	6.38
Granted	—		—
Vested	(916,172)	$	5.61
Forfeited	(18,262)	$	6.80
Unvested ordinary shares as of December 31, 2021	1,903,058	$	6.43

As of December 31, 2021 and 2020, there was $11.3 million and $17.4 million of unrecognized compensation costs related to unvested Employee Shares outstanding, which is expected to be recognized over a weighted-average period of 2.6 years and 3.1 years, respectively.

Share Options

The following table summarizes the Company's share options activity for the year ended December 31, 2021:

	Number of Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2020	240,584	$ 6.75	4.84	$ 313
Granted	1,164,778	$ 13.83		
Exercised	—	—		
Forfeited	(47,515)	$ 12.98		
Outstanding as of December 31, 2021	1,357,847	$ 8.95	8.58	$ 10
Exercisable as of December 31, 2021	102,424	$ 6.99	4.37	$ —
Unvested as of December 31, 2021	1,255,423	$ 9.11	8.92	$ 10

The weighted average grant-date fair value of share options granted during the year ended December 31, 2021 and 2020 was $5.42 and $3.33 per share, respectively.

As of December 31, 2021, there was $5.4 million of unrecognized compensation cost related to share options outstanding, which is expected to be recognized over a weighted-average period of 3.3 years.

Share Option Valuation

The weighted-average assumptions used in the Black-Scholes option pricing model to determine the fair value of the share options granted to employees during the year ended December 31, 2021 and 2020 were as follows:

	Year Ended December 31, 2021	Year Ended December 31, 2020
Expected term (in years)	6.02 Years	3.21 Years
Expected volatility	72.15%	73.81%
Expected dividend yield	0.00%	0.00%
Risk free interest rate	1.07%	0.20%
Fair value of underlying ordinary shares	$ 9.53	$ 6.35

Share-based Compensation Expense

Share-based compensation expense recorded as research and development and general and administrative expenses is as follows (in thousands):

	Years Ended December 31,		
	2021	2020	2019
Research and development	$ 3,362	$ 1,331	$ 332
General and administrative	2,955	1,661	387
	$ 6,317	$ 2,992	$ 719

9. Leases

As of December 31, 2021, the Company had seven operating leases of real property for office and laboratory use, for which the Company recorded right-of-use assets and leases liabilities as of the ASU 2016-02 effective date or lease commencement date, if later. In addition, three of the Company's leases met the short-term exception, having lease terms of 12 months or less, and are therefore not recorded on the Company's balance sheet. The Company's leases do not include purchase options. Where the Company's leases contain options to extend the lease term, the extended lease term is only included in the measurement of the lease when it is reasonably certain to remain in the lease beyond the non-cancelable term. The Company's leases contain variable lease costs, which pertain to common area maintenance and other operating charges, that are expensed as incurred.

Operating leases

On July 8, 2016, the Company entered into a Master Service Agreement with Royal Free London NHS Foundation Trust, which included access rights to the laboratory space at the Royal Free Hospital, Pond Street, London, with a 5-year term. The Master Service Agreement was due to expire on August 31, 2020. On June 1, 2020, the Master Service Agreement was renewed and will expire on August 31, 2023.

On February 1, 2019, the Company entered into six agreements with Stevenage Bioscience Catalyst to lease office and laboratory suites at Gunnels Wood Road, Stevenage, Hertfordshire, which were due to expire on January 31, 2021. In February 2021, the Company renewed six agreements which will expire on July 31, 2022.

On January 10, 2020, the Company entered into a non-cancellable operating lease in relation to office and laboratory premises at Gunnels Wood Road, Stevenage, Hertfordshire for a period of 2 years. The future minimum lease payments committed to in relation to this lease less any landlord incentives to be recognized up to the break total £0.2 million or $0.2 million.

On February 21, 2020, the Company entered into a non-cancellable operating lease in relation to office premises at Hammersmith Road, London for a period of 10 years, with a break clause at 5 years. The future minimum lease payments committed to in relation to this lease less any landlord incentives to be recognized up to the break total £5.4 million or $7.0 million.

On February 28, 2020, the Company entered into a 4-year manufacturing services collaboration agreement for laboratory space access at Gunnels Wood Road, Stevenage, Hertfordshire, with cancellation penalties of up to £2.2 million or $2.7 million should the Company terminate without due cause.

In December 2020, the Company entered into a new lease of a warehouse in west London, United Kingdom for a period of 10 years, with a break clause at 5 years. The Company expects to construct a flexible GMP modular facility to scale up its manufacturing footprint at these premises. The future minimum lease payments to be committed to in relation to this lease up to the break date are £3.8 million or $4.9 million.

In June 2021, the Company entered into a new lease of office premises in London, United Kingdom for a period of 3 years, with a break clause at 2 years. The future minimum lease payments to be committed to in relation to this lease up to the break date are £0.1 million or $0.1 million.

On October 1, 2021, the Company entered into a non-cancellable operating lease in relation to office and laboratory premises in Philadelphia, Pennsylvania in the United States for a period of 38 months. The right-of-use asset and lease liability will be recorded on the lease commencement date, which is in January 2022. In connection with this lease, the Company maintains a required minimum balance, currently less than $0.1 million in connection with a letter of credit issued for the benefit of the landlord for its commercial facility used as a security deposit for the lease. The total amount is classified as Restricted Cash and has been classified as a non-current asset on the Consolidated Balance Sheets. The letter of credit expires on September 30, 2022. However, it automatically extends for additional one-year periods, without written amendment agreement, in each succeeding calendar year, through the lease expiration date.

Summary of lease costs recognized under ASU 2016-02

The following table contains a summary of the lease costs recognized under ASU 2016-02 and other information pertaining to the Company's operating leases for the years ended December 31, 2021, 2020 and 2019 (dollars in thousands):

	Years ended December 31,		
	2021	**2020**	**2019**
Lease cost			
Operating lease cost	$ 4,718	$ 2,927	$ 564
Variable lease cost	5,022	2,891	31
Short-term lease cost	65	49	88
	$ 9,805	$ 5,867	$ 683
Other information:			
Cash paid for amounts included in the measurement of lease liabilities: Operating cash flows used in operating leases	$ 4,736	$ 1,844	$ 574
Right of use assets obtained in exchange for new operating lease liabilities	$ 314	$ 15,846	$ 457
Weighted average remaining lease term (in years)	3.1 years	4.0 years	0.9 years
Weighted average discount rate	4.86%	4.85%	5.01%

Variable lease cost is determined based on usage in accordance with the contractual agreements.

Pursuant to the terms of the Company's non-cancelable lease agreements in effect at December 31, 2021, the following table summarizes the Company's maturities of operating lease liabilities as of December 31, 2021 (in thousands):

	December 31, 2021
Operating lease liabilities payment	
2022	$ 4,974
2023	4,322
2024	3,046
2025	815
Total lease payments	$ 13,157
Less: imputed interest	(898)
Present value of lease liability	$ 12,259

10. License agreements

CRT license

In May 2016, the Company entered into a License Agreement, or the License Agreement, with Cancer Research Technology Limited, or CRT, pursuant to which the Company obtained access rights to intellectual property and know-how from the TRACERx Study. Under the License Agreement, the Company is granted an exclusive, sublicensable license to the TRACERx patents and bioinformatic data for use in: (i) the therapeutic field of neoantigen cell therapies and adoptive cell transfer; and (ii) the neoantigen diagnostic field, for use in research and the potential development of products for commercialization. The Company is further granted, during the vaccine option period, an exclusive license to the TRACERx patents and the bioinformatic data in the private neoantigen therapeutic vaccine field for research and development but not in the development of products for commercial sale, and a non-exclusive license to the same in the public neoantigen therapeutic vaccine field. The Company also obtained a non-exclusive license to the TRACERx bioinformatic pipeline, patient sequencing and medical data, know-how, and materials.

CRT additionally granted the Company certain rights to new patent applications filed by the Founding Institutions in respect of inventions resulting from the TRACERx study through February 2023, including automatic exclusive licenses to patent rights relating to non-severable improvements of technology covered by the original TRACERx patents and non-exclusive rights to severable improvements. CRT granted the Company the right of first negotiation to license certain patents rights generated by the Company's founders outside of the TRACERx study which relate to the licensed technology.

In July 2017, the Company obtained a non-exclusive license to the LOHHLA patent under the License Agreement. In October 2018, the Company obtained an exclusive license to the LOHHLA patent under an addendum to the License Agreement. Under the License Agreement, the Company holds an option to exploit products in the therapeutic vaccine field (the "Vaccine Option"). In March 2021, the Company extended the Vaccine Option from May 2021 to May 2023 with a payment of less than £0.1 million or $0.1 million.

In May 2018, the Company entered into an amendment to the License Agreement that created an additional sample period through July 2020 and specified additional patient tumor and blood materials to be subject to the License Agreement related to the immunology side study. The License Agreement was subsequently amended in July 2020, November 2020 and March 2021.

Upon execution of the License Agreement the Company granted CRT 396,125 B ordinary shares and 67,793 C ordinary shares. The C ordinary shares granted to CRT were forfeited and transferred to the deferred shares during the year ended December 31, 2019, as the applicable performance conditions were not met. The B ordinary shares granted to CRT were converted into ordinary shares upon IPO. The Company recorded $0.3 million of IP research and development expense in 2016. The Company is obligated to pay CRT milestone success payments up to an aggregate of £6.5 million for therapeutic products, and milestone success payments up to an aggregate £0.8 million for non-therapeutic products, as well as sub-single digit to low-single digit percentage royalty on net sales of products that utilize the licensed intellectual property, subject to certain customary reductions. The royalty obligations continue on a product-by-product and country-by-country basis until the later of: (i) the date there ceases to be a valid patent claim covering such product in the country in which it is sold; or (ii) with respect to contribution royalty products, ten years from the first commercial sale of the product, and with respect to a patent royalty product, five years from the first commercial sale of the product. On a product-by-product basis, the Company may also elect to provide other cash consideration at fair market value and forgo the milestone or royalty payment.

Unless terminated earlier, the term of the agreement continues until the later of the expiration of the royalty term in each country and such time as no further milestone payments are due, and upon such termination, the licenses granted shall become fully-paid, royalty-free, irrevocable, and perpetual. The Company has the right to terminate the license agreement for convenience in its entirety upon 90 days' notice. Each party may terminate the agreement if the other party is in material breach subject to a 90 day remedy period. The Company has the right to acquire ownership of the TRACERx patents upon either: (i) the occurrence of a royalty product for use in the therapeutic field; (ii) CRT shareholders cease to hold any ordinary shares in the Company; (iii) the Company undergoes an initial public offering; or (iv) the Company is acquired by a third party for more than £25.0 million. Upon IPO, the Company gave notice to

CRT to exercise the option to acquire the TRACERx patents with no consideration in accordance with the terms of the License Agreement. The acquisition was not finalized as of December 31, 2021.

Less than $0.1 million of expenses were recorded for the year ended December 31, 2021 related to the CRT License Agreement. No expenses were recorded for the years ended December 31, 2020 and 2019 related to the CRT License Agreement.

Secarna license

On October 20, 2021, the Company entered into an agreement, or Secarna Agreement with Secarna Pharmaceuticals GmbH & Co. KG or Secarna, whereby Secarna granted to the Company a non-exclusive worldwide license under certain patent and other intellectual property rights, to use the Secarna technology in the ex vivo manufacture of a T cell pharmaceutical product.

The Company is obligated to pay Secarna development milestone payments up to a maximum aggregate of €6.5 million ($7.4 million using a rate of €1.132 at December 31, 2021) and one-time commercial milestone payments up to €26 million ($29.4 million using a rate of €1.132 at December 31, 2021), as well as tiered low-single digit percentage royalty on net sales of products that utilize the licensed intellectual property, subject to certain customary reductions. The royalty obligations continue until the later of (i) the date there ceases to be a valid patent claim covering such product in the country in which it is sold or (ii) ten years from the first commercial sale of the product. For the year ended December 31, 2021, the Company recorded expenses of €0.7 million ($0.8 million using an average rate of €1.183 for the year ended December 31, 2021) related to the Secarna license agreement.

Unless terminated earlier, the term of the agreement continues until the later of the expiration of the royalty term in each country and such time as no further milestone payments are due, and upon such termination, the licenses granted shall become fully-paid, royalty-free, irrevocable, and perpetual. The Company has the right to terminate the license agreement for convenience in its entirety upon 90 days' notice. Each party may terminate the agreement if the other party is in material breach subject to a 60 day remedy period.

11. Income taxes

The Company is domiciled in the United Kingdom and is primarily subject to taxation in that country. During the years ended December 31, 2021, 2020 and 2019, the Company recorded no income tax benefits for the net operating losses incurred in the UK in each period due to its uncertainty of realizing a benefit from those items. During the year ended December 31, 2021, 2020 and 2019, the Company recorded a tax provision related to income tax obligations of its operating company in the U.S., which generates a profit for tax purposes.

Loss before provision for income taxes consisted of the following (in thousands):

	December 31,		
	2021	**2020**	**2019**
United Kingdom	$ (61,182)	$ (33,204)	$ (13,990)
Foreign	120	8	—
	$ (61,062)	$ (33,196)	$ (13,990)

The income tax provision for the years ended December 31, 2021, 2020 and 2019 is comprised of the following (in thousands):

	December 31,		
	2021	2020	2019
Current expense:			
United Kingdom	$ —	$ —	$ —
Foreign	59	7	—
Total current expense:	59	7	—
Deferred expense (benefit):			
United Kingdom	—	—	—
Foreign	(22)	(4)	—
Total deferred expense (benefit):	(22)	(4)	—
Total income tax expense:	$ 37	$ 3	$ —

The provision for income taxes for the years ended December 31, 2021, 2020 and 2019 was computed at the United Kingdom statutory income tax rate.

A reconciliation of income tax expense computed at the statutory UK income tax rate to income taxes as reflected in the consolidated financial statements is as follows:

	Year Ended December 31,		
	2021	2020	2019
Income taxes at UK statutory rate	19.00%	19.00%	19.00%
R&D expenditure	(6.67)%	(6.69)%	(12.37)%
Change in valuation allowance	(20.12)%	(13.12)%	(6.85)%
Change in UK tax rate	7.64%	—	—
Other	(0.13)%	0.80%	0.22%
	(0.28)%	(0.01)%	—

Significant components of the Company's deferred tax assets and liabilities as of December 31, 2021, 2020 and 2019 consist of the following (in thousands):

	December 31,		
	2021	2020	2019
Deferred tax assets			
Net operating loss carryforwards	$ 17,742	$ 7,065	$ 2,475
Depreciation	(1,311)	(983)	(243)
Non-cash share-based compensation	2,328	769	161
Other	329	241	(2)
Total deferred tax assets	$ 19,088	$ 7,092	$ 2,391
Valuation allowance	(19,062)	(7,088)	(2,391)
Net deferred tax assets	$ 26	$ 4	$ —

As of December 31, 2021, 2020 and 2019, the Company had UK net operating loss carryforwards of approximately $71.0 million, $37.1 million and $13.0 million, respectively, that can be carried forward indefinitely, respectively.

Changes in the valuation allowance for deferred tax assets during the years ended December 31, 2021, 2020 and 2019 related primarily to the increases in net operating loss carryforwards and research and development tax credit carryforwards were as follows (in thousands):

	December 31,		
	2021	2020	2019
Valuation allowance at beginning of year	$ 7,088	$ 2,391	$ 1,342
Increases recorded to income tax provision	7,624	4,628	996
Exchange difference	(313)	69	53
Change in tax rate	4,663	—	—
Valuation allowance at end of year	$ 19,062	$ 7,088	$ 2,391

Future realization of the tax benefits of existing temporary differences and net operating loss carryforwards ultimately depends on the existence of sufficient taxable income within the carryforward period. As of December 31, 2021, 2020 and 2019, the Company performed an evaluation to determine whether a valuation allowance was needed. The Company considered all available evidence, both positive and negative, which included the results of operations for the current and preceding years. The Company determined that it was not possible to reasonably quantify future taxable income and determined that it is more likely than not the net deferred tax assets will not be realized. Accordingly, the Company maintained a full valuation allowance as of December 31, 2021, 2020 and 2019.

The Company applies the authoritative guidance on accounting for and disclosure of uncertainty in tax positions, which requires the Company to determine whether a tax position of the Company is more likely than not to be sustained upon examination, including resolution of any related appeals of litigation processes, based on the technical merits of the position. For tax positions meeting the more likely than not threshold, the tax amount recognized in the financial statements is reduced by the largest benefit that has a greater than fifty percent likelihood of being realized upon the ultimate settlement with the relevant taxing authority. There were no material uncertain tax positions as of December 31, 2021, 2020 and 2019.

The Company will recognize interest and penalties related to uncertain tax positions in income tax expense when in a taxable income position. As of December 31, 2021 and 2020, the Company had no accrued interest or penalties related to uncertain tax positions and no amounts have been recognized in the Company's statement of operations.

The Company files income tax returns in the UK Generally, the tax years through 2020 remain open to examination. To the extent the Company has tax attribute carryforwards, the tax years in which the attribute was generated may still be adjusted upon examination by the UK tax authorities, if such tax attributes are utilized in a future period.

During the second quarter of 2021, the Finance Act 2021 (the Act) was enacted in the United Kingdom. The Act increases the corporate income tax from 19% to 25% effective April 1, 2023 and enhances the first-year capital allowance on qualifying new plant and machinery assets effective April 1, 2021. The effects on the Company's existing deferred tax balances have been recorded and is offset by the valuation allowance maintained against the Company's UK net deferred tax assets.

As of December 31, 2021 and 2020, income taxes on undistributed earnings of the Company's U.S. subsidiary have not been provided for as the Company plans to indefinitely reinvest these amounts in the U.S. The cumulative undistributed foreign earnings were not material as of December 31, 2021 and 2020.

12. Net loss per share

Basic and diluted net loss per share attributable to ordinary shareholders was calculated as follows (in thousands, except share and per share amounts):

	Year ended December 31,		
	2021	2020	2019
Numerator			
Net loss	$ (61,099)	$ (33,199)	$ (13,990)
Net loss attributable to ordinary shareholders—basic and diluted	$ (61,099)	$ (33,199)	$ (13,990)
Denominator			
Weighted-average number of ordinary shares used in net loss per share—basic and diluted	28,654,760	1,066,208	642,169
Net loss per share—basic and diluted	$ (2.13)	$ (31.14)	$ (21.79)

The Company's potentially dilutive securities, which include warrants to purchase ordinary shares, unvested Employee Shares and Convertible Preferred Shares, have been excluded from the computation of diluted net loss per share as the effect would be to reduce the net loss per share. Therefore, the weighted-average number of ordinary shares outstanding used to calculate both basic and diluted net loss per share attributable to ordinary shareholders is the same. The Company excluded the following potential ordinary shares, presented based on amounts outstanding at each period end, from the computation of diluted net loss per share attributable to ordinary shareholders for the year ended December 31, 2021, 2020 and 2019 because including them would have had an anti-dilutive effect:

	Year ended December 31,		
	2021	2020	2019
Series A preferred shares (as converted into ordinary shares)	—	7,134,644	7,134,644
Series B preferred shares (as converted into ordinary shares)	—	13,181,515	8,787,851
Series C preferred shares (as converted into ordinary shares)	—	6,165,672	—
Unvested ordinary shares	1,903,058	2,837,492	1,727,874
Share options	1,357,847	240,584	—
Total	3,260,905	29,559,907	17,650,369

13. Commitments and contingencies

Commitment with suppliers

The Company entered into several agreements with vendors that contain non-cancellable software arrangements and minimum purchase commitments of laboratory materials and consumables for the purpose of research and development activities as well as clinical development. The unused purchase commitment as of December 31, 2021 and 2020 was $7.4 million and $4.3 million, respectively.

In June 2021, the Company entered into an obligation to take on a new lease of lab and office premises in Stevenage, Hertfordshire, United Kingdom for a period of 10 years, with a break clause at 3 and 7 years. The future minimum lease payments to be committed to in relation to this lease up to the break date are £0.6 million or $0.8 million. As of December 31, 2021, the lease was not commenced and no right of use assets and operating lease liabilities were recognized related to that lease agreement.

Asset Retirement Obligations

The following is a reconciliation of our beginning and ending asset retirement obligation balances for 2021 and 2020 (in thousands):

	2021	2020
Balance, beginning of the year	$ 652	$ —
Additions in estimates		652
Accretion of discount	$ 38	—
Balance, end of year	$ 690	$ 652

The Company's asset retirement obligations relate to post-closure reclamation costs for a lease of office and laboratory space.

Legal proceedings

From time to time, the Company may be a party to litigation or subject to claims incident to the ordinary course of business. The Company was not a party to any litigation and did not have contingency reserves established for any liabilities as of December 31, 2021 and 2020.

Indemnification agreements

In the normal course of business, the Company enters into contracts and agreements that contain a variety of representations and warranties and provide for general indemnification. The Company's exposure under these agreements is unknown because it involves claims that may be made against the Company in the future. To date, the Company has not paid any claims or been required to defend any action related to its indemnification obligations. However, the Company may record charges in the future as a result of these indemnification obligations.

In accordance with the indemnification agreements entered into with relevant individuals in accordance with the Company's Articles of Association, the Company has indemnification obligations to its officers and directors, officers and members of senior management for certain events or occurrences, subject to certain limits, while they are serving at the Company's request in such capacity. There have been no claims to date, and the Company has director and officer insurance that may enable it to recover a portion of any amounts paid for future potential claims.

14. Related party transactions

The Company analyzed its transactions with related parties for the years ended December 31, 2021, 2020 and 2019, and determined it had the following material transactions that have not been described elsewhere in the financial statements.

During the year ended December 31, 2019, $0.1 million was charged to the company by Syncona Investment Management Limited for management fees and other costs incurred on behalf of the Company. No such transaction was incurred during the year ended December 31, 2021 and 2020. Syncona Investment Management is a subsidiary of Syncona Limited.

15. Employee benefit plans

In the United Kingdom, the Company makes contributions to private defined contribution pension schemes on behalf of its employees. The contributions to this scheme are expensed to the statement of operations as they fall due. The Company paid $1.8 million, $1.0 million and $0.5 in contributions in the year ended December 31, 2021, 2020 and 2019, respectively.

In the United States, the Company established a defined contribution savings plan under Section 401(k) of the Internal Revenue Code. This plan covers substantially all U.S. employees who meet minimum age and service requirements and allows participants to defer a portion of their annual compensation on a pre-tax basis. The Company paid less than $0.1 million in contributions in the years ended December 31, 2021 and 2020, respectively.

16. Subsequent Events

The Company has completed an evaluation of all subsequent events through March 1, 2022, the date on which the financial statements were issued, to ensure that these financial statements include appropriate disclosure of events both recognized in these financial statements as of December 31, 2021, and events which occurred subsequently but were not recognized in these financial statements.

On February 2, 2022, the Company issued 1,044,410 options with an exercise price of $3.62.

Item 19. Exhibits.

EXHIBIT INDEX

Exhibit Number	Description of Document	Incorporation by Reference			
		Schedule/Form	File Number	Exhibit	File Date
1.1*	Articles of Association of Achilles Therapeutics plc.				
2.1*	Deposit Agreement, dated as of March 30, 2021, by and among the registrant, The Bank of New York Mellon, as the depositary bank, and the holders and beneficial holders from time to time of American Depositary Shares issued thereunder.				
2.2*	Form of American Depositary Receipt (included in Exhibit 2.1).				
2.3*	Description of Securities				
4.1#	2020 Omnibus Plan, as amended, and forms of award agreements thereunder.	Form F-1	333-253735	10.1	3/1/2021
4.2#	2021 Equity Stock Purchase Plan	Form F-1	333-253735	10.2	3/1/2021
4.3#	2021 Omnibus Plan	Form F-1	333-253735	10.3	3/1/2021
4.4	Form of Amended and Restated Registration Rights Agreement, by and between the registrant, Cancer Research Technology Limited and the shareholders listed therein.	Form F-1	333-253735	10.4	3/1/2021
4.5	Lease Agreement, by and between Achilles Therapeutics Limited, 245 Hammersmith Road Nominee 1 Limited, 245 Hammersmith Road Nominee 2 Limited and 245 Hammersmith Road Limited Partnership, dated as of February 21, 2020.	Form F-1	333-253735	10.5	3/1/2021
4.6	Collaboration Agreement, by and between Achilles Therapeutics Limited and Cell Therapy Catapult, dated as of February 28, 2020.	Form F-1	333-253735	10.6	3/1/2021
4.7†	License Agreement, by and between Achilles Therapeutics Limited and Cancer Research Technology Limited, dated as of May 24, 2016, as amended.	Form F-1/A	333-253735	10.7	3/10/2021

Exhibit Number	Description of Document	Incorporation by Reference			
		Schedule/Form	File Number	Exhibit	File Date
4.8	Lease Agreement, by and between Achilles Therapeutics Limited and RLUKREF Nominees (UK) One Limited and RLUKREF Nominees (UK) Two Limited, dated as of December 16, 2020.	Form F-1	333-253735	10.8	3/1/2021
4.9#	Form of Employment Agreement with Iraj Ali.	Form F-1	333-253735	10.9	3/1/2021
4.10#	Form of Deed of Indemnity between Achilles Therapeutics plc and each of its Directors and Officers.	Form F-1	333-253735	10.10	3/1/2021
8.1*	List of Subsidiaries.				
12.1*	Certification of Chief Executive Officer Pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934.				
12.2*	Certification of Chief Financial Officer Pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934.				
13.1+	Certification of Chief Executive Officer Pursuant to Rule 13a-14(b) of the Securities Exchange Act of 1934.				
13.2+	Certification of CFO Chief Financial Officer to Rule 13a-14(b) of the Securities Exchange Act of 1934.				
15.1*	Consent of Independent Registered Public Accounting Firm.				
101.INS*	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document.				
101.SCH*	Inline XBRL Taxonomy Extension Schema Document.				
101.CAL*	Inline XBRL Taxonomy Extension Calculation Linkbase Document.				
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document.				

Exhibit Number	Description of Document	Incorporation by Reference			
		Schedule/Form	File Number	Exhibit	File Date
101.LAB*	Inline XBRL Taxonomy Extension Label Linkbase Document.				
101.PRE*	Inline XBRL Taxonomy Extension Presentation Linkbase Document.				

* Filed herewith.
+ Furnished herewith.
† Certain portions of this exhibit have been omitted pursuant to Item 601(b)(10) of Regulation S-K.
# Indicates a management contract or any compensatory plan, contract or arrangement.

SIGNATURES

The registrant hereby certifies that it meets all of the requirements for filing on Form 20-F and that it has duly caused and authorized the undersigned to sign this annual report on its behalf.

ACHILLES THERAPEUTICS PLC

Date: March 1, 2022

By: /s/ Iraj Ali
Name: Iraj Ali, Ph.D.
Title: Chief Executive Officer